

Ketones to combat Alzheimer's disease

July 7 2016, by Emilie Reas

Despite decades of efforts to develop a drug that prevents or cures Alzheimer's disease (AD), the most prevalent form of dementia afflicting our aging population, there is currently no treatment for this devastating condition. Emerging research suggests that such a miracle treatment might already exist, not in the form of a pill, but as a simple dietary change. A growing number of studies report that interventions to improve metabolic health can alleviate symptoms and reduce brain pathology associated with AD. A popular theory posits that AD has multiple causes, but their common thread may involve metabolic dysfunction. Indeed, markers of poor metabolic health, such as diabetes, inflammation and high cholesterol, are major risk factors for AD.

Just like our muscles, the brain requires energy to function properly. But unlike muscle cells, neurons have the unique capacity to metabolize [ketones](#) as an alternative fuel source when glucose is in short supply, for instance during fasting or on a [low-carbohydrate diet](#). In the 1920s scientists discovered that a [high fat diet](#) promoting ketogenesis [controlled epilepsy](#), and ketosis remains one of the most effective treatments for the condition. This raised the possibility that ketones may also be neuroprotective against other diseases that stem from aberrant neural metabolism, such as AD. Since then, research has confirmed that ketones do in fact alter brain metabolism in ways that reduce neuropathology and relieve behavioral symptoms.

Ketones alleviate symptoms of Alzheimer's disease

Over the past decade, several studies have supported the clinical value of

ketosis in cognitively impaired patients. In a [2004 study](#) twenty individuals with AD or Mild Cognitive Impairment (MCI) were treated with placebo or medium chain triglycerides, a type of saturated fat found in coconut and palm oils that promotes ketone production. The treatment increased ketone levels 90 minutes later, and these higher ketone levels corresponded with greater memory improvements. These preliminary, short-term findings were followed up five years later in a larger and longer-term study of 152 mild AD patients. After 45 days, individuals taking a ketogenic compound showed cognitive improvements relative to a placebo group. However, both of these studies suggest that the brain benefits of ketosis may depend on genetics. In the earlier study, medium chain triglycerides improved cognitive function only in participants without the ApoE4 allele, a genetic risk factor for AD. Similarly, in the later study, cognitive improvements were stronger and persisted longer—out to 90 days—in those without the ApoE4 allele. A new *PLOS One* study confirmed different responses to diet depending on genetics in mice, reporting that a high-fat diet lowered brain levels of ApoE only in mice without the ApoE4 gene.

These promising early findings of ketogenic compounds offered hope that dietary interventions might similarly benefit brain health. A [2012 study](#) tested whether memory could be improved simply by adopting a low-carbohydrate diet, without the need of supplements used in the prior studies. Of 23 individuals with MCI, those following a very low-carbohydrate diet for six weeks showed improved memory compared to those on a high-carbohydrate diet. These memory improvements correlated with ketone levels, but not with calories consumed, insulin levels or body weight, pointing to increased ketogenesis as the likely reason for the low-carb dieters' cognitive enhancement.

Other potential AD treatments have similarly shown short-term therapeutic effects in early disease stages but have flopped when put to the test in more advanced, long-term cases. Although ketosis hasn't been

rigorously tested in a formal clinical trial, a [recent case study](#) provides compelling evidence that ketones might in fact hold up in severe clinical cases. A 63 year-old man with advanced AD began consuming coconut oil and medium chain triglycerides, both known to increase [ketone levels](#). After just 2.5 months, his score on the Mini Mental State Exam, a test of global cognitive function, increased from an extremely low 12 to 20 (out of a max 30). After two years, his cognitive ability and daily living functions both improved and his MRI showed no further brain atrophy. After adding a ketone ester supplement to his dietary regimen, the patient showed even further improvements in his mood, self-sufficiency and memory. Notably, this man carried the ApoE4 gene; thus, ketosis does appear to be highly beneficial for ApoE4 carriers, even if prior studies indicate it's even more helpful for those without this risk factor.

How ketones protect the brain

Researchers have looked to animal models to better understand how ketosis might protect the human brain from neurodegeneration. In a mouse model of AD, levels of beta-amyloid, a toxic protein that is elevated in AD, [were reduced](#) in the brains of mice fed a high-fat/low-carb diet compared to those on a standard diet. A [more recent study](#) helped to clarify the link between the metabolic benefits of ketones, lower amyloid and improved cognitive function. This study tested the effects ketones both in a mouse model of AD and in neurons treated with amyloid. While amyloid increased oxidation and disrupted function of a mitochondrial enzyme complex, ketones reversed these effects, confirming their neural metabolic benefits. Furthermore, ketones reduced amyloid levels and blocked the formation of pores in cell membranes induced by amyloid, showing that ketones can protect against neuronal damage related to amyloid. Finally, ketones restored normal synaptic plasticity and memory performance that were impaired by amyloid.

A prescription for ketosis

If ketosis is to become validated as an effective treatment for AD, further research is needed to determine the appropriate method of administration, since high-fat diets, medium chain triglyceride supplements or ketogenic compounds may be differentially effective. Patient compliance in following a strict diet or taking supplements could also pose potential challenges. Identifying the minimum effective dose will help set guidelines for just how rigorous a treatment regimen is necessary. Despite these remaining questions, the compelling support for the therapeutic potential of ketosis offers hope that a powerful weapon in our battle against AD may already exist—and may be as delicious as a spoonful of coconut oil.

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