P3-582

Reports of Responses to Coconut Oil and Medium-Chain Triglyceride (MCT) Oil in 288 Persons with Alzheimer's and Other Memory Impairment

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BACKGROUND: Glucose hypometabolism is an early key feature of AD, appearing at least 10 to 20 years before symptoms. Ketones provide alternative fuel to glucose during fasting, ketogenic diet (KD), and ketogenic oil consumption, and are taken up normally in brain regions affected by glucose hypometabolism in AD patients (Cunnane *NRDD V.19* 2020; Croteau *J Alz Dis V. 64* 2018). Ketones are also anti-inflammatory: the primary circulating ketone betahydroxybutyrate (BHB) inhibits activation of the NLRP3 inflammasome (Shippy *Front Cell Neurosci V. 17* 2020; Kim *Frontiers Immunol V.13* 2022), prevents perforation of neurons by beta amyloid (Yin *Neurobiol Aging* V. 39 2016), and acts as an antioxidant and scavenger of free radicals (Veech *IUBMB* Life V. 51 2001). BHB improved survival and number of neurites in cultured rat hippocampal neurons subjected to beta-amyloid $A\beta_{1-42}$ or rat dopaminergic mesencephalic neurons subjected to 1-methyl-4-phenylpyridinium (a toxin that kills dopaminergic neurons) (Kashiwaya *PNAS* V. 97 2000). Compared to controls, the ketone ester (R)-3-Hydroxybutyl (R)-3-Hydroxybutyrate consumed by 3xTgAD mice reduced accumulation of Abeta and tau tangles and reduced anxiety (Kashiwaya *Neurobiol Aging V. 34* 2013). The same ketone ester also reduced Abeta accumulation, attenuated microglial activation, improved mitochondrial respiration in hippocampal neurons, and improved cognitive function in FXFAD mice, and "RNA sequencing showed thatBHB-regulated genes mainly annotated in aging, immune system, nervous system, and neurodegenerative diseases" (Wu *FASEB* V. 34 2020). RCTs of ketogenic diet (KD) ± medium-chain triglyceride (MCT) oil or coconut oil (CO) in ketogenic diet program recipes, or MCT or CO with usual diet have reported improvement in people with cognitive impairment compared to controls (Fortier *Alzheimers Dement* V. 17 2021; Phillips *Alz Res Therapy* V. 13 2021; De la Rubia Orti *Nutr Hosp V. 65* 2017, and many more—**see poster P2-651**). Improvement is usually attributed to generation of ATP by circulating ketones, but biological activities of fatty acids and other substances in MCT and virgin coconut oil could further explain ongoing long-term improvements reported in people with AD, other memory impairment, and in Parkinson's disease. While blood ketones from CO are lower than from MCT oil, lauric acid (50% of coconut oil) potently stimulated ketone production in cultured KT-5 astrocytes (Nonaka *J Oleo Science V. 65* 2016), suggesting a more direct effect, if confirmed *in vivo*. In addition, hundreds of studies have implicated microbes, such as herpes simplex I, herpes zoster, dental pathogens, and spirochetes as possible causes or contributors to AD; lauric acid (C12:0) is highly antimicrobial for many of these microbes, and is used for that purpose in medical/veterinary applications, oral and skin care products, and in household disinfectants. Lauric acid is about 7% of the lipids in human milk. Virgin CO contains about 15-18% of the medium-chain fatty acids in MCT oil and, therefore, larger amounts would be required for a similar ketogenic effect. However, in addition to 50% lauric acid (C12:0), virgin CO also contains antioxidants, anti-inflammatory polyphenols, and substances that inhibit amyloid plaque formation (Chatterjee *Mech Ageing Devel V. 186* 2020).

How Could MCT and Virgin Coconut Oils (VCO) Help People with AD and Other Neurological Disorders?

Primary source with references, except as noted: Chatterjee P, Fernando M, Fernando B, Dias CB, Shah T, Silva R, Williams S, Pedrini S, Hillebrandt H, Goozee K, Barin E, Sohrabi HR, Garg M, Cunnane S, Martins RN. "Potential of coconut oil and medium chain triglycerides in the prevention and treatment of Alzheimer's disease." *Mech Ageing Dev* V186, 2020.

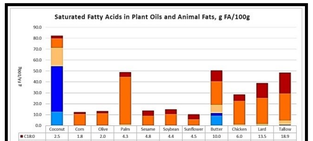
Medium-chain fatty acids are partly converted to ketones in the liver. C8, C10, (& probably C12) cross the blood brain barrier and are also an alternative fuel to glucose for the brain (Andersen *Neurochem Res V. 48* 2023). **MCT oil is 100% medium-chain FAs as C8:0 and/or C10:0, C12:0. Coconut oil is 15-18% C8:0, C10:0, and 50% C12:0**

Lauric acid (C12:0) potently stimulates ketone production in cultured astrocytes, and is antimicrobial.

Capric acid (C10:0) promotes mitochondrial biogenesis; anticonvulsant effects via inhibition of AMPA receptors (Augustin et al. Lancet Neurol V.17 2018) **| Caproic (C6:0) and Caprylic acid (C8:0) are highly ketogenic**

VCO is rich in anti-inflammatory and antioxidant polyphenols that appear to reduce oxidative stress, like caffeic acid, p-coumaric acid, ferulic acid, methyl catechin, dihydrokaempferol, gallic acid, quercetin and myricetin glycoside.

VCO was shown in studies to improve anthropometric measures, lipid profiles, and blood pressure.



Comparison of the saturated fatty acid (SFA) composition of coconut oil (CO), which is predominantly medium-chain saturated FAs (C6:0 through C12:0), is clearly different than other vegetable oils and animal fats, which have predominantly long chain saturated FAs. Apart from palm oil, the long chain FA composition of coconut oil is comparable to other commonly used vegetable oils (Data from USDA ARS 2020). Lauric acid (C12:0) and myristic acid (C14:0) are also found in human amniotic fluid, colostrum, and breast milk, and likely have roles in fetal and newborn growth, development, and metabolism (Gutiérrez-Garcia AG, et al. *Early Hum Dev.* V. 115 (2017):32–7).

Complete list of references for ketones and cognition, including *in vitro*, animal, and human studies of ketones and cognition, and clinical trials of ketogenic diet, coconut oil, MCT oil for Alzheimer's disease, MCI, and Parkinson's

METHODS: Response/non-response to CO ± MCT oil from all unsolicited communications (nearly all emails) about persons with AD and other memory impairment collected by the author from 2008 to mid-2014 were analyzed. Most reports were from family caregivers, and less often the affected person or paid caregiver. Respondents were not prompted regarding what improvements might be expected. If report was vague, the person was asked to provide greater detail, if possible. Information from the reports (age, gender, diagnosis or complaint, use of coconut oil and/or MCT oil, or an MCT medical food was entered on an Excel spreadsheet, along with all comments pertaining to the person's symptoms and observations of improvements and/or side effects while consuming the oils. The data were tabulated according to the number and percent of people who reported improvement, no improvement, or no improvement but stabilization for at least three months. Verbatim phrases from the reports were used to further categorize the types of improvements noted.

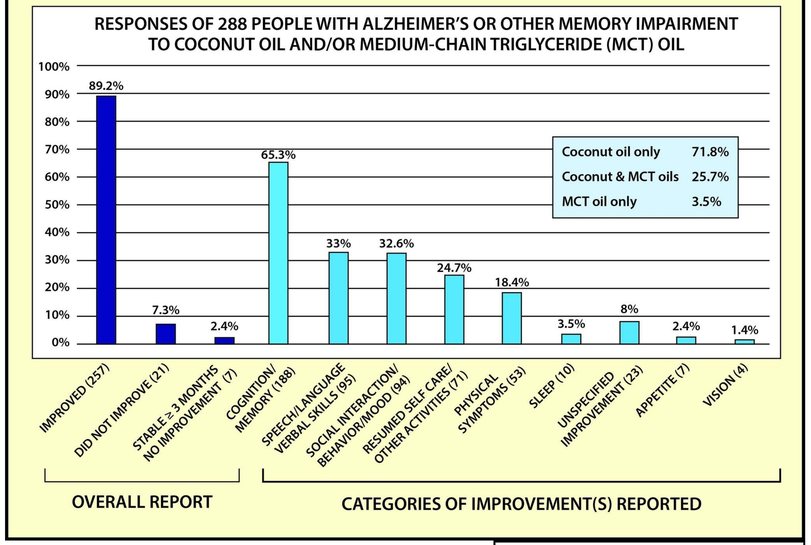
PHRASES IN REPORTS USED TO CATEGORIZE IMPROVEMENTS OF 288 PEOPLE WITH ALZHEIMER'S, DEMENTIA, OR OTHER MEMORY IMPAIRMENT IN RESPONSE TO COCONUT OIL AND/OR MEDIUM-CHAIN TRIGLYCERIDE (MCT) OIL

IMPROVED MEMORY/COGNITION	IMPROVED SOCIAL INTERACTION/ BEHAVIOR/ MOOD	IMPROVED SPEECH/ CONVERSATION/ VERBAL SKILLS	RESUMED SELF CARE/ OTHER ACTIVITIES	IMPROVED PHYSICAL SYMPTOMS
Higher scores on memory or cognitive test	More interaction with others	Speaking again	Showering again without help	Less tremor
Improved clock drawing	Better sense of humor	Clearer speech	Taking care of self again	Getting out of bed without help
Better cognition	Less agitation and/or anxiety	Less repetitiveness	Doing things around the house	Able to walk again
Better sense of direction	Improved behavior	Making sense	Doing household chores again	Walking without assistance
Improved reading comprehension	Less hostile	More logical	Preparing meals again	Improved strength
Reading again	Less aggressive	Improved conversation	Resumed a hobby	More ambulatory
Able to do mental math again	Happy	More talkative	More functional	More energy
Able to write again	Improved mood	Improved verbal skills		Less stiffness
More awareness of time/place	Less depression	Better word recall		Improved balance
Recognizing people or places	Feels better	Expressing thoughts		Less dizziness
Less distractible	**IMPROVED SLEEP**	**IMPROVED APPETITE**	**IMPROVED VISION**	Fewer episodes of faintness, clamminess, sweating
More alert	Fewer nightmares	Improved appetite	Visual disturbance gone	Improved gait
Brighter	Sleeping better		Able to see more clearly	Fewer episodes seizure/twitching
Improved awareness	No longer sleeping excessively sleep			Pain relief
	Stopped twitching during sleep			

Key Points:

Ketones are an alternative fuel to glucose in the brain.

1. **Glucose hypometabolism predates AD symptoms by at least 1 to 2 decades.**
2. **Ketones are taken up normally in affected regions of the Alzheimer's brain.**
3. **Insulin resistance, a "brain-energy gap", & neuroinflammation are key factors in AD.**
4. **Mild to moderate nutritional ketosis from ketogenic oils and/or low-carb diet could reverse insulin resistance, fill in the "brain-energy gap", and reduce inflammation.**



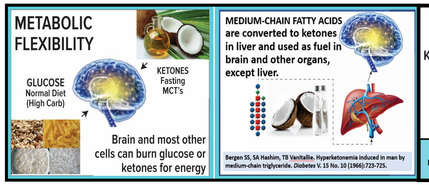
RESULTS: 288 reports were tabulated . See Demographic Information table. 72% consumed only CO, 26% CO+MCT, and 2% MCT only. 89.2% reported improvements overall, 7.3% no improvement, 2.4% no improvement but stabilized for at least 3 months. Many people reported more than one improvement in the areas of Memory/Cognition (65.3%), Social/Behavior/Mood/Personality (32.6%), Speech/Language/Conversation (33%), Resumption of Self-Care/Other Activities (24.7%), Physical Symptoms (18.4%), and Sleep (3.5%), Appetite (2.4%), Vision (1.4%), "improved" but otherwise unspecified (8%).

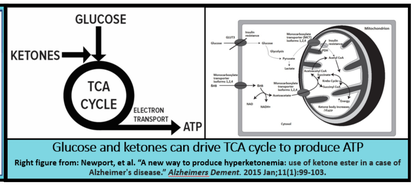
DEMOGRAPHIC INFORMATION

Age range	33 to 94 years
Gender	51.4% F - 47.6% M - 1% not reported
Memory complaint	55.9% Alzheimer's 9.4% Other dementia, specified* 15.3% Other dementia, not specified 5.9% Parkinson's with AD/other memory impairment 2.4% Mild cognitive impairment 11.8% Subjective complaint without diagnosis 13.5% Memory complaint with other diagnosis**

*Dementia diagnosis (of 288): Vascular (8), FTD (6), CBD (6), Lewy body (5), PCA (2) ** Diabetes (5), stroke (5), ALS (5), Huntington's (3), Multiple sclerosis (3), Epilepsy (3), bipolar (3), autism (2), gen. dystonia (2), coma (1), TBI (1), PSP (1), hypertension (1), cancer (1), Prader Willi (1), migraine (1), peripheral neuropathy (1) **Note:** Some people had more than one diagnosis

CONCLUSIONS: Just a few targeted FDA-approved drug therapies claim temporary slowing of cognitive decline but without meaningful improvement in cognition or functionality. However, nutritional ketosis broadly addresses important pathological changes in the AD brain, including insulin resistance, glucose hypometabolism, and inflammation. A growing number of RCTs of KD ± MCTs/CO with positive cognitive outcomes and improvement in biomarkers add weight to this large collection of communications reporting meaningful improvements while consuming CO and/or MCT oil in cognition, social interaction, conversation, mood, behavior, self-care, and other areas important to daily life. Nutritional ketosis deserves more attention from funding organizations and greater public awareness for the potential to improve the lives of people with AD and other neurological impairments.

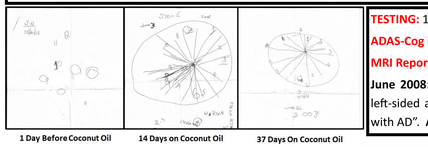




INDEX CASE—Peer-reviewed published report*

THE PATIENT: 58 y.o. male, ApoE 4/3, symptom onset in 2001, diagnosed with early onset-AD in 2004, functioning at FAST stage 5-6 at time of intervention. Also had physical symptoms including facial and intention tremor, stiff slow gait, occasional hallucinations.
DAY 1: May 21, 2008—MMSE in drug trial screenings on successive days improved from 14 (1 day before) to 18 about 4 hours after taking first dose coconut oil 35 gm. Continued 35 gm in AM and added doses with meals throughout the day.
FIRST WEEK: More animated & talkative, personality/sense of humor returned, whistling, joking, could find eating utensils, intention tremor resolved by 20-30 minutes after taking coconut oil, facial tremor resolved completely, initiated conversation and made sense.
BY ONE MONTH: Recognized family members, participated in conversation, and no longer looked "lost". Clock drawing improved.
AT 6 WEEKS: Began 4:3 mixture of MCT/coconut oil, increased gradually over 4 months to 135-165 ml per day in 4 servings.
BY 2 MONTHS: Could tie his shoes, stiff gait normalized and could run again, could stay on task, and resumed yard and housework.
BY 4 MONTHS: Visual disturbance resolved (described as "words moving around like pixels on the page") and could read again.
BY 9 MONTHS: Reading comprehension and delayed recall improved & began to work as hospital volunteer in supply warehouse.
AT 2 YEARS: After setback following crossover in trial from placebo to semagacestat for six weeks (advised of RX after study discontinued) stopped trial and, 2 months later in April 2010, began NIH pilot study (n=1) of Veech ketone ester (R)-3-Hydroxybutyl (R)-3-Hydroxybutyrate. Within 24 hours and thereafter, improved self-care, could write alphabet, improved mood, affect, abstract thinking, insight; by 6 weeks, new symptoms from setback resolved; resumed yard and housework.
FINAL OUTCOME: Enjoyed nearly four better-quality years than the year before starting coconut oil until hospitalization for severe medication reaction in 2012. Passed away from AD January 2, 2016, 2 1/2 years after onset of generalized seizures with hypoxia and head injury. Brain donation showed advanced pathological stage AD (Braak 6) and Lewy bodies, amygdala predominant.

***Open access case report:** Newport MT, VanItallie TB, Kashiwaya Y, King MT, Veech RL. "A new way to produce hyperketonemia: use of ketone ester in a case of Alzheimer's disease." *Alzheimers Dement* V.11 No.1 2015:99-103.



TESTING: 1 year after starting coconut oil in semagacestat trial (on placebo):
ADAS-Cog improved by 6/75 | Activities of Daily Living improved by 14/78
MRI Reports : August 2004 at AD diagnosis:"Normal".
June 2008:"Diffuse involutional changes of frontal and parietal lobes and moderate left-sided and severe right-sided atrophy of amygdala and hippocampus, consistent with AD". **April 2010**: "Stable MRI brain in comparison to prior [2008] examination."

List of references for ketones and cognition, including *in vitro*, animal, and human studies of ketones and cognition, and clinical trials of ketogenic diet, coconut oil, and MCT oil for MCI, AD, Parkinson's.

More on ketones and ketogenic strategies:
https://coconutketones.com/alzheimers-dementia

"Scientific References" website page

Books on ketones and Alzheimer's by Mary T. Newport, MD
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What About Coconut Oil (CO) and Cholesterol?

This is a common concern based on a public campaign in the 1990s claiming coconut oil increases cholesterol levels based on small brief (1 to 6 wk) studies of hydrogenated and highly processed (RBD) coconut oil in animals and people. In an analysis of 16 trials with 525 people, the average total and LDL-C levels increased, decreased, or did not change from baseline even in short term studies. Coconut oil increased HDL-C in all but one dataset and triglycerides were lower or unchanged. Analysis prepared for book by MT Newport, currently in press (Sept 2023).

Changes in Lipid Profile in Sixteen Groups Consuming Coconut Oil

	Duration	# Data Sets	Total N=	Average	TChol mg/dl	LDL-C mg/dl	HDL-C mg/dl	TG mg/dl
All groups combined	3 weeks to 2 years	16	525	Baseline	169.73	104.2	45.72	111.33
				final	171.04	105.24	48.31	108.23
				Difference	**1.31**	**1.03**	**2.59**	**-3.1**
Long	1 to 2 years	2	192*	baseline	149.81	90.29	40.8	114.96
				final	146.89	91.03	42.82	110.66
				Difference	**-2.92**	**0.74**	**2.02**	**-4.3**
Medium	8 to 15 weeks	5	168*	Baseline	168.96	104.02	43.2	124.68
				final	168.06	101.53	44.37	119.9
				Difference	**-0.6**	**-2.49**	**1.16**	**-4.78**
Short	3 to 6 weeks	9	165	Baseline	193.99	120.59	54.01	93.51
				final	202.16	125.54	58.73	93.51
				Difference	**8.18**	**4.95**	**4.71**	**0**

Includes 16 available data sets with baseline and final values for people consuming coconut oil used in Neelakantan et al. review, *Circulation*., 141(10) 2020:803. **Note:** Did not include Johannsen 2000 study of MCT oil or Ng 1991/1992 studies of RBD coconut oil with only 75% saturated fat, due to suspected contamination with another oil. * Vijayakumar 2016 study had data sets for baseline, 3 months, 1 year, and 2 years and, therefore, provided three groups of values here. N=number of people; TChol = total cholesterol; LDL-C = low-density-lipoprotein cholesterol; HDL-C = high-density-lipoprotein cholesterol;TG = triglycerides; RBD = refined, bleached, deodorized.

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