Preliminary impact of ketogenic and MCT-supplement Mediterranean diet on cognition and function in MCI: results from the KETO-MIND (**Keto**genic Diet and **M**CT Supplementat**I**on for **N**eurodegeneration **D**elay) trial.

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Introduction

Mild Cognitive Impairment (MCI) represents an intermediate stage between healthy aging and dementia, marked by measurable cognitive decline with preserved daily functioning (1,). Increasing evidence links gut microbiota imbalance (2), low-grade systemic inflammation (3), and impaired brain energy metabolism to the early phases of neurodegeneration.
Ketogenic dietary strategies enhance ketone body availability, providing an efficient alternative energy substrate for the brain (4), with potential neuroprotective effects through improved mitochondrial function, reduced oxidative stress, and modulation of the gut–brain axis (5,6). Medium-Chain Triglycerides (MCT) supplementation within a Mediterranean diet may also increase circulating ketones in a more accessible way (7,8).

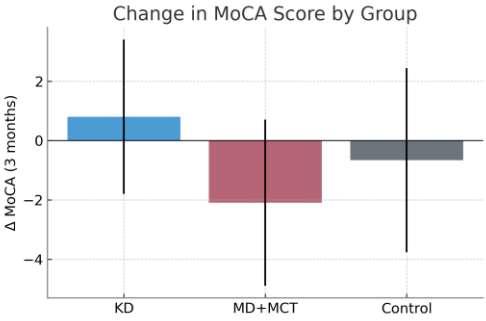
Objective

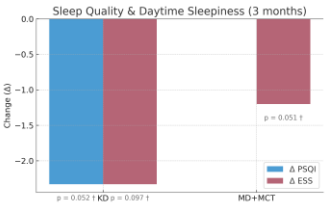
The study aims to gather preliminary data on the **effectiveness** of a Mediterranean diet supplemented with **MCT** in modulating cognitive function in patients with MCI, **comparing** its impact with the well-documented effects of the **ketogenic diet** in slowing progression to dementia.

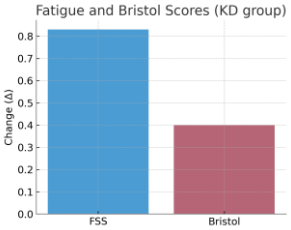
Materials

A **pilot randomized clinical trial** was conducted at the Clinical Neurology Unit, Udine. Adults with subjective cognitive complaints or mild cognitive impairment (MCI), according to Petersen's criteria, and preserved daily autonomy were enrolled.
Baseline assessments:

- Anthropometrics (BMI) and **bioimpedance** (Fat Mass, Fat-Free Mass, phase angle)
- Cognitive and functional tests: **MoCA, FSS, ESS, PSQI, Bristol Scale**







Results (3-month follow-up)

MoCA:

- KD: ↑ +0.8 ± 2.6 (p = 0.49)
- MD+MCT: ↓ −2.09 ± 2.8 (p = 0.047*)
- Control: ↓ −0.66 ± 3.1
  → Only the MD+MCT group showed a significant decline

Sleep quality & daytime sleepiness:

- KD: ΔPSQI = −2.33 (p = 0.052); ΔESS = −2.33 (p = 0.097)
- MD+MCT: ΔESS = −1.2 (p = 0.051)
  → Both interventions showed a trend toward improved sleep and alertness

Results (3-month follow-up)

Fatigue and bowel habits (KD):

- ΔFSS = +0.83 (p = 0.26); ΔBristol = +0.4 (p = 0.18)
  → No significant changes detected

Correlations:

- MoCA moderately correlated with FSS (r = 0.39; p = 0.091).
- No associations with ketone levels (p > 0.24)

Discussion

KD was associated with favorable trends in cognition and sleep, supporting its potential neuroprotective effect. MD+MCT showed limited benefit. Ketone levels were not predictive of outcomes, suggesting alternative mechanisms may be involved.

Conclusions

Preliminary findings support the feasibility and potential benefit of ketogenic strategies in MCI.

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