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EDITORIAL

Macronutrients, Lifestyle, and Cognitive Ageing: Beyond Binary Interpretations

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Abstract

Inconsistent associations between macronutrient composition and cognitive ageing often reflect binary framings that ignore context. By binary interpretation we mean dichotomous framings that overlook dose response, substitution among macronutrients, and heterogeneity by diet quality, energy balance, and metabolic or genetic risk. We propose a context-informed framework that prioritises dietary quality, sets protein and carbohydrate targets by metabolic risk and body composition, and integrates nutrition with activity and sleep to support cognitive reserve. We distinguish model-specific findings in repair-deficient mice from population-level evidence linking carbohydrate quality and prudent dietary patterns with healthier cognitive ageing. We outline pragmatic trials with prespecified cognitive outcomes, explicit substitution within high-quality patterns, risk stratification, adherence measurement, and clear reporting of energy balance. Macronutrient targets should be treated as context-dependent substitutions and tested accordingly.

Macronutrient Balance

Mechanistic evidence requires interpretation within an explicit biological context. In DNA repair-deficient progeroid mice, very high protein intake accelerates gene length-dependent transcriptional decline and shortens lifespan.[1] This phenotype is unlikely to generalize to community-dwelling older adults with intact repair pathways. In humans, a systematic review and meta-analysis report no overall association between total protein intake and global cognition in later life, although some domains, particularly memory, may benefit where adequate protein supports preservation of lean mass.[2] With respect to carbohydrates, quality is central. Large cohorts associate lower glycemic impact, higher fiber intake, and minimal processing with a greater probability of healthy ageing that encompasses cognitive and physical domains.[3] In contrast, lower quality carbohydrate patterns and higher glycemic exposure are repeatedly linked to faster cognitive decline in older populations.[4,5]

Throughout this section, the term "binary interpretation" refers to dichotomous framings that neglect dose response, substitution dynamics among macronutrients, and variation by diet quality, energy balance, and metabolic or genetic risk.

Lifestyle and Cognitive Reserve

Diet operates within a broader lifestyle system. A ten-year population-based cohort in China reported that a composite of balanced diet, regular physical activity, sustained cognitive engagement, and social participation correlated with slower memory decline, including among carriers of APOE ε4.[6] Adherence to Mediterranean-style dietary patterns is associated with lower dementia risk independent of genetic predisposition in the UK Biobank.[7] Measures of metabolic stability provide plausible pathways linking diet quality to brain ageing. Glycemic variability and related glycemic metrics are associated with cognitive impairment and incident dementia.[4,5]

Integrative Perspectives

Evidence syntheses prepared for the 2025 Dietary Guidelines Advisory Committee conclude that prudent dietary patterns may reduce risk of cognitive decline and dementia, although heterogeneity and risk of bias limit certainty.[8] Randomized evidence remains limited. A three-year, two-site trial reported no significant difference in global cognitive decline between a MIND diet with mild caloric restriction and an isocaloric control that received equivalent counselling.[9] A systematic review of whole-diet interventions in healthy older adults found modest and inconclusive effects on memory. This reinforces the need for larger and longer trials with explicit cognitive primary outcomes and with stratification by metabolic risk.[10]

Implications for practice and research

Dietary guidance should prioritize quality over extremes, with protein calibrated to sarcopenia risk and renal function and higher-quality carbohydrates emphasized. Nutrition should be implemented alongside physical activity, sleep hygiene, cognitive stimulation and social engagement as co-interventions. Macronutrient targets and monitoring should be stratified by APOE genotype, insulin resistance, sarcopenia and vascular risk. Outcomes ought to combine cognitive composites with indices of glycemic variability, inflammatory and oxidative stress markers, and body composition. Pragmatic trials should randomize dietary patterns within high-quality templates, prespecify cognition as a primary endpoint and incorporate adherence and implementation supports.

Conclusions

Extreme macronutrient distributions may be harmful within specific biological or behavioral contexts. Broad prescriptions that ignore heterogeneity are therefore premature. Guidance for older adults should emphasize dietary quality, integrate lifestyle practices that build cognitive reserve, and be tailored to metabolic and genetic risk. This approach is better positioned to preserve cognitive function across diverse ageing trajectories.

Ethics approval and consent to participate

Not applicable.

Clinical trial number

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

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Authors' contributions

CYK contributed to editorial preparation, conceptualization, and interpretation. The author critically reviewed the editorials and approved the final manuscript.

The author participated sufficiently in the work and agreed to be accountable for all aspects.

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