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Letter to Editor

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Anti-Inflammatory Diets and Neuroinflammation: Toward Precision Nutrition for Brain Health

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Letter to the Editor

Growing evidence from nutritional neuroscience and immunometabolism suggests that chronic low-grade inflammation serves as a common biological substrate linking dietary patterns to cognitive decline and neurodegenerative diseases. Anti-inflammatory diets, characterized by high intake of polyphenols, omega-3 fatty acids, fiber, and low intake of saturated fats and refined carbohydrates, have emerged as modifiable determinants of brain health across the lifespan [1,2]. Adherence to such dietary patterns, including the Mediterranean diet and the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND diet), has been consistently associated with reduced risk of Alzheimer's disease (AD), slower cognitive aging, and better executive function [2,3]. Despite these epidemiological observations, the precise molecular pathways through which dietary factors modulate neuroinflammation remain incompletely characterized.

Recent advances in understanding the gut–brain axis have revealed that diet-induced modulation of gut microbiota composition and function critically influences central nervous system (CNS) inflammation. A 2025 systematic review and meta-analysis demonstrated that gut dysbiosis across neurodegenerative diseases is characterized by an increased Bacteroidetes/Firmicutes ratio and compromised gut barrier integrity, directly linked to astrocyte reactivity as measured by glial fibrillary acidic protein expression [4]. Specific dietary components, particularly polyphenols and fermentable fibers, promote the growth of anti-inflammatory microbial taxa that produce short-chain fatty acids (SCFAs), which reinforce intestinal barrier integrity and exert direct anti-inflammatory effects on microglia [4,5]. Conversely, Western-style diets high in saturated fats and refined sugars induce gut dysbiosis, increased intestinal permeability, and elevated circulating lipopolysaccharide (LPS), a potent trigger of neuroinflammation [6]. A 2025 review highlighted that dietary LPS, arachidonic acid, and advanced glycation end products are elevated in the brain of AD patients and directly stimulate microglial activation and inflammatory cytokine production [6].

Emerging clinical and preclinical evidence indicates that chronic neuroinflammation mediated by the NLRP3 inflammasome represents a critical node linking dietary insults to cognitive impairment. A 2025 study demonstrated that kaempferol, a natural flavonoid found in anti-inflammatory diets, exerts neuroprotective effects by promoting mitophagy in microglia, thereby inhibiting mitochondrial DNA leakage-induced NLRP3 inflammasome activation [7]. Concurrently, research published in 2025 identified kaempferol as a novel antagonist of microtubule affinity regulating kinase 4 (MARK4), a key mediator of NLRP3 inflammasome assembly, further supporting the therapeutic potential of dietary flavonoids in neuroinflammatory conditions [8]. These findings suggest that dietary interventions targeting the NLRP3–microglia axis could delay or prevent neurodegenerative processes.

Beyond direct CNS effects, systemic metabolic inflammation plays a pivotal role in mediating diet–brain interactions. A comprehensive 2025 review published in *Ageing Research Reviews* synthesized evidence on the gut-brain-immune axis in AD, demonstrating that chronic stress activates the HPA axis, causing gut dysbiosis, reduced SCFA production, and disrupted neurotransmitter signaling, which collectively promote amyloid-beta and tau pathology [9]. The review emphasized that host genetic polymorphisms, particularly APOE4 and TREM2, modulate gut permeability and immune tone, suggesting a genome-microbiome interaction model for AD susceptibility [9]. Furthermore, a 2026 critical review confirmed that Western dietary patterns disrupt systemic and neuroimmune homeostasis both directly, through immunomodulatory effects of dietary components, and indirectly, through increased intestinal permeability and dysbiosis [10].

Specialized pro-resolving mediators (SPMs) derived from omega-3 polyunsaturated fatty acids represent a particularly promising area of investigation [11]. A 2025 study in *Molecular Neurodegeneration* proposed that SPMs improve phagocytosis of amyloid-β by microglia through sustained mitochondrial respiration, enabling a pro-resolution response that actively resolves CNS inflammation rather than merely suppressing it [12]. This aligns with evidence that n-3 PUFAs and their SPM metabolites may represent a fundamental mechanism through which anti-inflammatory diets confer neuroprotection.

To advance this field, we propose a multimodal research framework combining longitudinal dietary assessments with

serial neuroimaging, cerebrospinal fluid (CSF) biomarkers of inflammation, and gut metagenomic profiling. The recently established genetic resource from the MIND trial, enables analyses of genetic contributions to variability in cognitive responses to the MIND diet, supporting precision nutrition approaches [13]. Incorporating time-resolved metabolomics to measure plasma and CSF levels of SCFAs, polyphenol metabolites, and SPMs would help identify causal mediators of diet-induced neuroprotection. Randomized controlled trials with cognitive and neuroinflammatory endpoints, stratified by genetic risk factors such as APOEε4 status, are urgently needed to establish causality and identify responsive subgroups.

Ultimately, such integrative approaches may enable the development of precision dietary strategies for brain health based on an individual's inflammatory profile, gut microbial composition, and genetic background. Aligning nutritional recommendations with anti-inflammatory principles could represent a safe, accessible, and cost-effective preventive intervention for AD and related dementias. We hope that this perspective will stimulate interdisciplinary collaboration among nutrition scientists, neuroscientists, immunologists, and geriatricians and encourage the incorporation of anti-inflammatory dietary guidelines into routine clinical practice for cognitive aging populations.

Ethical Considerations

Not applicable.

Acknowledgment

Not applicable.

Conflict of Interest

The authors declare that they have no conflicts of interest.

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