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Editorial

Nutritional Cognitive Neuroscience: The Science of Mind, Brain, and Nutrition

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An Integrative Science of Mind, Brain, and Nutrition

One of the greatest scientific challenges of our time is to establish interventions to reduce the escalating burden of mental illness and neurological disease in the modern world [1,2]. In this effort, research in the nutritional sciences has sought to build an empirical case for the role of diet and nutrition in the promotion of brain health. Accumulating evidence suggests that a wide range of nutrients—including ω-3 PUFAs, B vitamins, choline, carotenoids, and polyphenols—benefit brain health by regulating signaling pathways that influence neuroplasticity and inflammation (for an introduction, see Lanham-New et al. [3]). In molecular genetics, research further suggests that these effects are influenced by individual differences in genes that modulate nutrient metabolism and absorption [4]. Converging evidence in neuroscience suggests that biomarkers of nutritional status—captured by nutrient biomarker patterns—are associated with individual differences in the structure, function, and metabolism of brain networks that support cognition [5–9], and mental health (for a recent review, see Wu and Barbey [10]). These emerging lines of evidence motivate an integrative framework that aims to explain how nutrition shapes brain function across genetic, molecular, cellular, and systems levels. Achieving this goal, however, will require deeper synthesis of research across the nutritional, cognitive, and brain sciences [11]—fields that have historically pursued separate goals.

The nutritional sciences have traditionally focused on how diet influences processes such as metabolism and inflammation, without considering how these effects, in turn, impact brain networks that support cognition and mental health. On the other hand, research in the psychological and brain sciences has directly examined these brain networks—investigating how their intrinsic organization and flexible dynamics shape the nature of human intelligence (for review, see Barbey et al. [12])—but rarely considers the nutritional and metabolic factors that support them. Bridging the nutritional, cognitive, and brain sciences will therefore be critical to elucidating the impact of diet and nutrition on brain network function and translating this knowledge into interventions that promote cognition and mental health across the lifespan (for review, see Barbey [13]).

The emerging field of nutritional cognitive neuroscience provides a catalyst for this unification [11]. The resulting synthesis of research across disciplines motivates deeper recognition of nutrition's wide-ranging impact—beyond a passive source of energy and nourishment for the body. This perspective aims to redefine nutrition as central to brain health, serving as an active determinate of the brain's adaptive capacity. According to this view, nutrition plays a central role in allostasis, enabling the brain and body to maintain stability (i.e., homeostasis) through the continual adjustment of internal and external demands (rather than from static equilibrium [14,15]). Research in nutritional cognitive neuroscience reveals how nutrition influences the signaling pathways that regulate neuroplasticity and inflammation—mechanisms through which the brain anticipates and adapts to life experience and recovers from environmental stressors. From this perspective, diet becomes a key biological pathway through which our experience and the environment shape the flexibility and resilience of the mind and brain.

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To build a systematic understanding of these processes, the field of nutritional cognitive neuroscience investigates 4 interdependent dimensions of human experience (Figure 1; cf., [16]). The first dimension represents environmental factors that shape exposure to risk and access to nutrition, as characterized by the exposome (i.e., the full set of environmental exposures that affect human health), along with the social, cultural, and economic contexts that shape health behaviors (i.e., sociocultural determinates of health). Collectively, these environmental factors define a health ecosystem that serves to enhance or limit nutrition's benefits on cognitive function and brain health (cf. [17,18]).

Second, psychological factors refer to the cognitive functions that affect and are influenced by our dietary choices—capturing the perceived reward value of foods and the associated cognitive, social, and emotional processes that shape eating behaviors (for a review, see Higgs [19]). Psychological factors play a central role in the dietary choices that contribute to our nutritional status, and through this interaction, affect brain health and cognitive function.

Third, biological factors represent the genetic, molecular, cellular, and systems-level mechanisms through which nutrition and the brain regulate their functions in response to changing life experience and environmental stressors. Allostasis provides one illustration, whereby nutrition regulates signaling pathways that influence neuroplasticity and inflammation. These mechanisms then affect how the brain processes and uses nutrients (e.g., with respect to energy expenditure and metabolism), maintaining allostasis through continuous interaction. This interaction is further explored through research investigating how biomarkers of diet and nutrition are associated with individual differences in the structure, function, and metabolism of specific brain networks [5–9]. Research in cognitive neuroscience has also directly examined the brain networks involved in dietary choices—investigating their role in the perception of food cues underlying healthy eating behaviors and for understanding how these networks are altered in eating disorders characterized by impaired stress regulation and cognitive control (e.g., binge-eating disorder; for a review, see Chen et al. [20]).

Fourth, lifestyle factors represent daily activities, such as exercise and sleep, that influence health by engaging behavioral practices that promote or limit the brain's adaptive capacity. Nutrition is known to affect and be influenced by a host of lifestyle choices, such as exercise [21], and sleep quality [22]. Although nutrition itself has long been viewed as a lifestyle factor, research in nutritional cognitive neuroscience significantly expands its role—not only reflecting dietary choices and

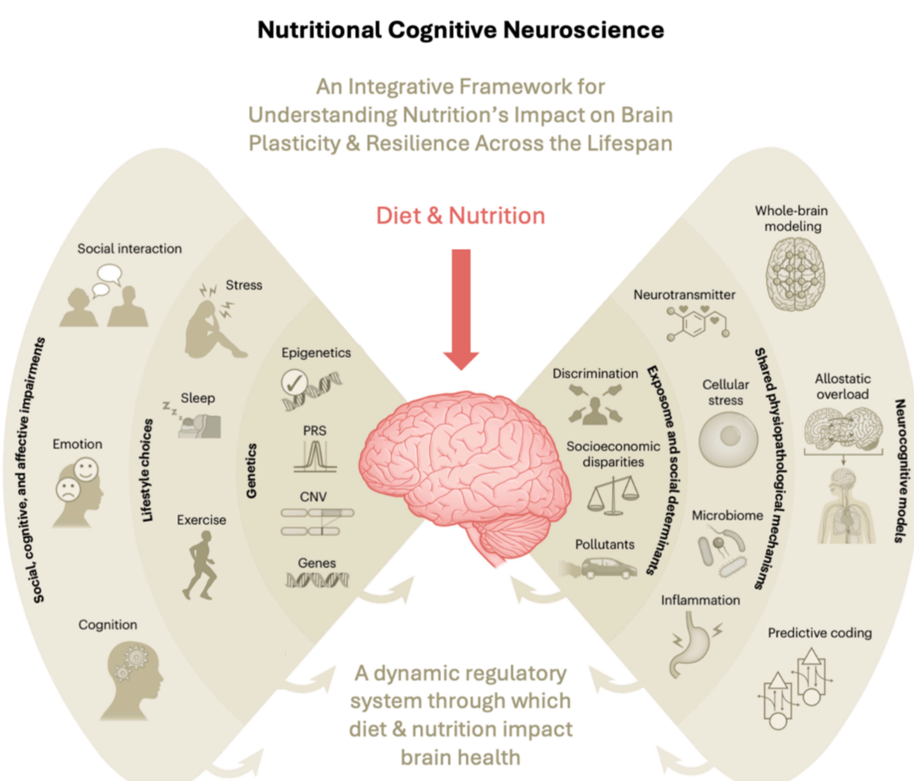

FIGURE 1. Nutritional cognitive neuroscience. an integrative, multilevel approach to studying nutrition's impact on brain health, with contributions from multiple dimensions, including environmental factors ("Exposome and social determinants"), psychological factors ("Social, cognitive, and affective impairments"), biological factors ("Genetics," "Shared pathophysiological mechanisms," and "Neurocognitive models"), and lifestyle factors ("Lifestyle choices"). CNV, copy number variations; PRS, polygenic risk scores. Adapted, with permission, from Ibanez and Zimmer [16].

eating habits but representing a key biological pathway through which experience and the environment shape our capacity for flexibility and resilience. This perspective motivates a novel view of diet and nutrition—not only as an external influence on our health but as an intrinsic biological mechanism central to the mind and brain.

As illustrated in Figure 1, the interacting dimensions of this framework form a dynamic regulatory system through which diet and nutrition impact brain health. This approach opens new opportunities for the personalization of nutritional interventions, recognizing that the relative importance of each dimension and their specific patterns of interaction may vary across individuals, stages of lifespan development, and contexts. Research in this effort therefore applies statistical machine learning methods [23], and data fusion techniques [5,8], to model individual differences in the profile and dynamic interactions among these dimensions.

Furthermore, detailed mechanistic studies in animal models represent an essential component of research in this field, offering a level of precision that is often unmatched in human studies. Through this interdisciplinary framework, the field of nutritional cognitive neuroscience aims to advance national research priorities led by the American Society for Nutrition and the NIH Office of Nutrition Research to establish and validate the cognitive and brain health benefits of diet and nutrition.

This Special Collection on Nutrition and the Brain presents research that illustrates the promise of this emerging field across the genetic, molecular, cellular, and systems levels [24]. Comprising 14 research articles and 3 reviews, the collection presents evidence from: *1*) developmental studies on the influence of maternal diet on cognition; *2*) mechanistic studies on the efficacy of targeted nutritional interventions to promote brain health; *3*) new protocols for the design and timing of nutritional intake to enhance cognition; *4*) personalized approaches to dietary intervention based on genetic variability; *5*) studies that examine dietary patterns for the reduction of dementia risk; and *6*) experiments that investigate the effects of nutrition on inflammation in mental health and infectious disease. Furthermore, research in the collection aims to translate findings from nutritional cognitive neuroscience to the context of education and public health, presenting: *7*) research that brings to light the limited role of nutrition in modern psychiatry, calling for new educational programs that raise awareness about the importance of diet as a modifiable risk factor of mental illness in medical education and clinical practice. To illustrate the breadth of findings, we briefly review each contribution in turn below.

Developmental Studies on Maternal Diet and Cognition

Evidence in the Special Collection demonstrates that maternal nutrition plays an important role in neurodevelopment. Motivated by an interest in understanding the effects of modern dietary patterns on brain development, Sakayori et al. [25] investigated a well-known dietary imbalance in modern life; the consumption of foods that are generally high in ω-6 PUFAs but low in ω-3 PUFAs. The authors provide evidence in a mouse model to suggest that a maternal diet reflective of this dietary imbalance produces behavioral effects in their offspring, specifically with respect to measures of neurodevelopment and performance on tests of social behavior and memory. Notably, these effects were observed when their offspring were studied at $\leq$63 wk of age, representative of adulthood. Further evidence on maternal diet in mice is reported by Saini et al. [26], who found that prenatal alcohol exposure disrupts placental glucose and lipid metabolism—altering neurodevelopment by reducing fetal brain growth. Together, these studies indicate that maternal nutrition can have lasting effects for offspring brain development and behavior that persist into adulthood.

Targeted Nutritional Interventions to Promote Brain Health

Research in the Special Collection examines specific dietary components and nutritional interventions that are designed to promote brain health. One line of research examines the effects of specific dietary patterns in response to neurotoxic stress. Cahoon et al. [27] investigate the role of an antioxidant-rich diet delivered through blueberry supplementation (i.e., 2% blueberries) before and/or after high-energy particle radiation in rats. The authors found that the antioxidant-rich diet interrupted reactive gliosis, a process that exacerbates neuroinflammation. The interruption of these processes resulted in an improved response to radiation, as evidenced by the mitigation of memory deficits. These findings suggest that an antioxidant-rich diet offers a promising nutritional intervention in response to neurotoxic stressors. Another line of research that examines the neuroprotective effects of vitamin K is conducted by Zheng et al. [28]. These authors provide evidence that the primary form of vitamin K in the brain, menaquinone-4, was significantly reduced in mice with vitamin K deficiency. The authors link lower menaquinone-4 with lower performance on tests of learning and memory, and therefore provide a more detailed, mechanistic understanding of the role of menaquinone-4 in the effects of vitamin K deficiency on brain health.

Accumulating evidence supports the importance of gut–brain metabolism in brain health. Frerichs et al. [29] review the developmental literature in this area, surveying evidence to suggest that gut microbes, their metabolites, and the brain are part of an integrated system that effects neurodevelopment. The authors review specific prebiotic dietary fibers (e.g., inulin and fructooligosaccharides, and galactooligosaccharides) that are known to promote the growth of beneficial microbes (e.g., bifidobacterium and lactobacillus). These microbes are then shown to produce short-chain fatty acids that have several health benefits, such as promoting serotonin production and reducing inflammation. Further investigating the effects of fiber on gut–brain metabolism, Tanabe et al. [30] present evidence that a diet high in insoluble fiber (30% cellulose) may restore memory function in socially isolated mice. The authors discuss the benefits of insoluble fiber with respect to the gut microbiota's role in the malate-aspartate shuttle and the suppression of neuroinflammation through this metabolic pathway.

Also investigating the effects of nutrition on memory function, Goldbeck et al. [31] provide evidence that alanyl-glutamine (AQ) supplementation may reduce impairments in recognition memory after *Clostridioides difficile* infection in aged mice. The authors propose that AQ serves a protective role for the gut and the brain, supporting the gut barrier (i.e., to maintain intestinal tissue integrity) and suppressing inflammation (i.e., through the nuclear factor kappa B inflammatory pathway). Another study on the effects of nutrition on memory performance is presented by Islam et al. [32], who examine the natural compound, *Daidzin*, in a mouse model. The authors found that this compound improved performance on multiple tests of memory, including marble burying, dust removal, and the open-field test. According to Islam et al. [32], the benefits of *Daidzin* result from its role in modulating oxidative stress and reducing inflammation via cholinergic (i.e., acetylcholinesterase) and dopaminergic pathways.

In the context of vitamin B-6, Amarasena et al. [33] report evidence in rats to suggest that a deficiency is associated with changes in gut microbiota composition—altering short-chain fatty acid synthesis—that produce behavioral patterns of anxiety in the open-field maze (i.e., as evidenced by reduced central zone entries). In summary, the reported findings suggest that a host of dietary components and nutritional interventions may play an important role in regulating metabolic and inflammatory pathways that affect cognitive function and brain health, motivating further research to investigate their efficacy in human intervention trials.

Timing of Nutritional Intake to Enhance Cognition

Evidence in the Special Collection demonstrates that the effects of nutrition on cognitive performance may depend on temporal patterns of nutrient intake. This work extends prior research focused primarily on the nutritional content of our diet, to examine the frequency, timing, and duration of eating behavior. In this effort, Brikou et al. [34] investigated temporal pattern of eating behavior within an observational study of healthy adults, the Aiginition Longitudinal Biomarker Investigation of Neurodegeneration Cohort Study. The authors found that more frequent eating patterns were associated with higher overall cognitive ability scores and superior performance on tests of memory, executive function, and language. The reported findings suggest that temporal patterns of eating may influence cognitive performance, potentially via circadian and metabolic mechanisms that motivate further study in the context of randomized controlled trials.

Personalized Approaches to Dietary Intervention

Emerging research suggests that nutrition's role in cognition may be influenced by genetic variation. Annevelink et al. [35] analyzed data from the Framingham Heart Study Offspring Cohort Study to assess this issue. The authors identified 75 significant interactions between single-nucleotide polymorphisms and ω-3 PUFAs. Notably, these interactions revealed that the cognitive benefits of DHA depend on genotype. Variants in genes previously implicated in lipid signaling and neurodevelopment—namely, disabled 1, sortilin-related VPS10 domain-containing receptor 2, and serine incorporator 5—were associated with performance on tests of memory and executive function. Thus, the observed role of genetic variability in the cognitive benefits of nutrition motivates research to further establish and validate a personalized approach to dietary intervention that takes individual differences in genetics into account.

Dietary Patterns for Reducing Dementia Risk

The Special Collection reports studies that investigate the role of diet and nutrition in mitigating dementia risk. Yang et al. [36] analyzed plasma proteomes associated with adherence to the Mediterranean-Dietary Approaches to Stop Hypertension Intervention for Neurodegenerative Delay (MIND) diet within the Atherosclerosis Risk in Communities Cohort. This study followed adults aged 45–64 y for over ∼20 y to track incidence of dementia. Yang et al. [36] identified 62 proteins associated with MIND diet adherence, including 4 whose concentrations were negatively correlated with MIND diet but positively associated with dementia risk—namely, thrombospondin 2, abhydrolase domain-containing 14A, structural maintenance of chromosomes 3, and interleukin-12 subunit beta. The authors review evidence to support the role of these proteins in inflammation and believe this work offers new mechanistic insight into the cognitive benefits of MIND diet adherence.

In their review of this study, Liu and Cheng [37] identify promising research directions motivated by this work. They encourage a more complete assessment of the MIND diet, noting that berries and olive oil—key components of this dietary pattern—were not examined. Liu and Cheng [37] also highlight the importance of investigating host genetics. For example, APOE genotype is known to affect nutrient metabolism and may therefore moderate the observed effects of the MIND diet.

Focusing on specific dietary components within the MIND diet, Chatzispyrellis et al. [38] investigated the role of polyphenols found in cruciferous and leafy vegetables in reducing dementia risk. The authors report evidence that high consumption of these foods—which are high in lignans, flavonols, and isoflavonoids—is associated with reduced dementia incidence in older adults. Together, these studies highlight the promise of nutritional interventions for the reduction of dementia risk in the elderly.

Nutrition in Mental Health and Infectious Disease

Research in the Special Collection examines the role of diet and nutrition in mental health and infectious disease. In the context of mental health, Pinto et al. [39] review evidence from studies in animal models that high-fat diets disrupt brain lipid homeostasis and neurotransmitter systems to produce inflammation and depression-like symptoms (e.g., reduced reward seeking). The authors also review evidence that supplementation with ω-3 PUFAs (i.e., DHA and EPA) reduced inflammation and was associated with improved mood and cognitive function.

In the context of infectious disease, Cardino et al. [40] investigate the interaction between HIV, nutrition, and neuroinflammation. The authors show that ω-3 PUFAs are associated with higher performance on tests of executive function in adolescents infected with HIV. Critically, however, Cardino et al. [40] also demonstrate that EPA and SFAs in this population predict lower levels of executive function—reflecting heightened immune and metabolic challenges in individuals infected with HIV (e.g., because of chronic inflammation and immune function dysregulation). Thus, in the context of adolescents living with chronic infectious disease (HIV), the authors suggest that although ω-3 PUFAs offer cognitive benefits, high EPA correlates with worse executive function because of the hypothesized dysfunction of EPA's anti-inflammatory conversion pathways in individuals with HIV. Overall, these findings reflect the potential benefits of nutritional interventions in the context of mental health and infectious disease.

Educational and Public Health Initiatives

Finally, Mudd and Angelotta [41] review evidence on the importance of nutrition as a modifiable risk factor of mental illness and examine whether modern training programs in psychiatry and medical practices in psychiatric care take nutrition into account. The authors find that >67% of psychiatrists and psychologists report no formal instruction in nutritional science, and only 6% consider nutrition when prescribing medication. Their analysis makes a powerful case for educational reform in psychiatry and motivates the need for broader public health initiatives that raise awareness about the importance of diet and nutrition in mental health (for a review, see Wu and Barbey [10]).

Conclusion: Advancing Scientific Rigor, Synthesis, and Translation

As the field of nutritional cognitive neuroscience continues to grow, it builds momentum toward interdisciplinary synthesis and opportunities to enhance methodological rigor—moving beyond small sample sizes, reliance on observational designs, and self-report dietary measures. Indeed, fundamental scientific advances will require a causal, mechanistic understanding of how diet effects brain health across genetic, molecular, cellular, and systems levels. Building such an interdisciplinary framework and evidence base will depend on the integration of insights across the nutritional, cognitive, and brain sciences—embodied by this emerging field.

As the Special Collection illustrates, research in the field is revealing how nutrition supports brain health by modulating neuroplasticity and inflammation, processes that shape the brain's capacity to regulate its functions and adapt to experience. According to this framework, nutrition plays a central role within a dynamic regulatory system that enables brain plasticity and resilience across the lifespan—integrating environmental, psychological, biological, and lifestyle factors (Figure 1). Thus, by establishing an interdisciplinary approach that integrates and builds upon insights from each area, the burgeoning field of nutritional cognitive neuroscience will continue to advance our understanding of the beneficial effects of diet and nutrition on brain health—exploring new paths of discovery enabled by the science of mind, brain, and nutrition.

Author contributions

The sole author was responsible for all aspects of this manuscript.

Conflict of interest

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