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Essential Amino Acids, Vitamins, and Minerals Moderate the Relationship between the Right Frontal Pole and Measures of Memory

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Scope: Nutrition has increasingly been recognized for its ability to help prevent and protect against disease, inspiring new programs of research that translate findings from nutritional science into innovative assessment tools, technologies, and therapies to advance the practice of modern medicine. A central aim in this effort is to discover specific dietary patterns that promote healthy brain aging and moderate the engagement of neural systems known to facilitate cognitive performance in later life.

Methods and Results: The present study therefore investigates estimates of nutrient intake derived from food frequency questionnaires, structural measures of brain volume via high-resolution magnetic resonance imaging, and standardized neuropsychological measures of memory performance in nondemented elders ($n = 111$) using a moderation analysis. The results reveal that the essential amino acids, vitamins, and minerals nutrient pattern moderates the positive relationship between the volume of the right frontal pole and measures of both delayed and auditory memory.

Conclusions: Our findings demonstrate that a nutrient pattern including macro- and micronutrients moderate the effect of brain structure on cognitive function in old age and support the efficacy of interdisciplinary methods in nutritional cognitive neuroscience for the study of healthy brain aging.

1. Introduction

Scientific innovations in neuroscience continue to advance our understanding of human health and disease, with recent discoveries providing insight into an essential element of human biology: *nutrition*. Rather than considered purely as a source of energy and nourishment for the body, nutrition has increasingly been recognized for its ability to help prevent and protect against disease, inspiring new programs of neuroscience research that translate findings from nutritional science into innovative assessment tools, technologies, and therapies to advance the practice of modern neuroscience. At the frontiers of this path-breaking effort is research within the emerging interdisciplinary field of *Nutritional Cognitive Neuroscience*, which investigates nutrition's impact on cognition and brain health across the life span.[1] Research in this burgeoning field demonstrates that many aspects of nutrition—from entire diets to specific nutrients—affect brain structure and function, and therefore have profound implications for understanding the nature of healthy brain aging and for advancing the prevention and treatment of age-related neurological disorders. As the United States experiences rapid growth in the proportion of older adults, effective medical and policy recommendations to promote healthy brain aging become increasingly important, providing a

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catalyst for research to investigate the beneficial effects of nutrition on the aging brain.

Many recent studies have investigated the relationship between nutrient intake, brain health, and cognitive function (for a review see refs. [2–6]). For example, nutrients such as vitamins, minerals, and amino acids play a crucial role in ensuring proper brain function. Vitamins protect against inflammation and reactive oxidative species,[7,8] maintain lipid bilayer asymmetry and integrity,[9] facilitate a host of metabolic processes related to glucose/energy metabolism and neurotransmitter synthesis, and are also involved in homocysteine regulation.[7,8,10–12] Minerals function as cofactors for enzymes, reside in synaptic vesicles, prevent lipid peroxidation, and promote energy production.[7,8] Amino acids serve as precursors to neurotransmitters and neuromodulatory metabolites that are responsible for various functions related to attention, mood, arousal, and memory.[13] All of the aforementioned dietary components are available in high-quality diets consisting of colorful vegetables, dark leafy greens, beans, lean meats/seafood, and eggs.[14,15]

Together, this evidence bears directly on findings like that of Croll and colleagues (2018) who found that older adults with high-quality diets consisting of fruits and vegetables had larger brain volumes.[16] Another study found that adherence to the Mediterranean diet, a diet with high intake of vitamin and mineral rich fruits and vegetables along with omega-3 fatty acids from fish and nuts, was associated with larger cortical thickness in multiple brain areas sensitive to aging and neurodegeneration.[17] In a double-blind, placebo-controlled randomized clinical trial where middle-aged–older adults were given antioxidant supplements for 6 years, improvements were seen specifically in verbal memory.[18] A comprehensive study by Gu and colleagues (2018) showed total gray matter volume mediating the relationship between an inflammatory nutrient pattern and visuospatial cognition.[19] Together, these studies reveal novel nutrition–brain or nutrition–cognition relationships where nutrition is necessary for the function or pathway being described. Another important approach to understanding the role of nutrition in brain health is to examine ways in which nutrition can moderate established brain–cognition relationships.

The present study sought to identify specific dietary patterns that promote healthy brain aging and moderate the engagement of neural systems known to facilitate cognitive performance. We implemented a moderation analysis using estimates of nutrient intake derived from food frequency questionnaires, structural measures of regional brain volume via high-resolution magnetic resonance imaging (MRI), and standardized neuropsychological measures of cognitive performance in a cohort of healthy older adults.

2. Experimental Section

2.1. Participants

The present study included data of 118 older adults between the ages of 65 and 75 who were recruited through Carle Foundation Hospital (Urbana, Illinois). Participants were cognitively intact, having scored higher than 26 on the Mini-Mental State Examination and had no diagnosis of mild cognitive impairment, dementia, and psychiatric illness within the last 3 years. Additional exclusion criteria included incidents of stroke within the past 12 months or cancer within the last 3 years. Furthermore, participants undergoing chemotherapy/radiation, those unable to participate in study activities, or those who had previously participated in a cognitive training or dietary intervention study were excluded from enrollment.

2.2. Standard Protocol Approval and Participant Consent

This study was approved by the Institutional Review Boards (IRBs) of both the University of Illinois at Urbana–Champaign and Carle Hospital (Urbana, Illinois). All participants read and signed informed consent documents approved by the two IRBs (#12014).

2.3. Assessment of Nutrition

Nutritional status was assessed using the Diet History Questionnaire II (DHQ-II), a web-based, 12-month (with portion size) food frequency questionnaire developed by the National Cancer Institute (NCI; https://epi.grants.cancer.gov/dhq2/about/). This questionnaire covered 134 food and beverage items and 8 dietary supplements which were based on dietary data obtained from the National Health and Nutrition Examination Surveys (NHANES) in 2001–2002, 2003–2004, and 2005–2006. Participants responded on the web-based tool, indicating how frequently they consumed a food, beverage, or supplement along with portion size. Using the Diet*Calc software, version 1.5 (https://epi.grants.cancer.gov/dhq2/dietcalc/), and the NCI Questionnaire Data Dictionary, this information was translated into nutrient and food group intake estimates. As an accuracy check, participants' data were excluded from statistical analysis if an unreasonable energy intake (<500 or >3500 kilocalories per day (kcal/day)) was reported ($n = 7$).[20] This left data for 111 participants for statistical analysis.

Overall diet quality was assessed by deriving a Healthy Eating Index (HEI-2015) score (https://epi.grants.cancer.gov/hei/developing.html). The Total HEI-2015 score ranged from 0 to 100 with higher scores demonstrating better alignment with the recommendations of the United States Department of Agriculture 2015–2020 Dietary Guidelines for Americans.

2.4. Magnetic Resonance Imaging Data Acquisition

All data were collected on a Siemens Magnetom 3T Trio scanner using a 32-channel head coil in the MRI Laboratory of the Beckman Institute Biomedical Imaging Center at the University of Illinois. The MRI acquisition, preprocessing, and volumetric methods for this cohort have been described previously,[21,22] but the details are restated here as follows.

A high-resolution multi-echo T1-weighted magnetization prepared rapid gradient-echo (MPRAGE) structural image was acquired for each participant (0.9 mm isotropic, TR = 1900 ms, TI = 900 ms, TE = 2.32 ms, with Generalized Autocalibrating

Partially Parallel Acquisitions [GRAPPA] and an acceleration factor of 2). The functional neuroimaging data were obtained using an accelerated gradient-echo echoplanar imaging (EPI) sequence[23] sensitive to blood oxygenation level dependent (BOLD) contrast (2.5 × 2.5 × 3.0 mm voxel size, 38 slices with 10% slice gap, TR = 2000 ms, TE = 25 ms, FOV = 230 mm, 90° flip angle, 7 minute acquisition time). During the resting-state fMRI scan, participants were shown a white crosshair on a black background viewed on a LCD monitor through a head coil-mounted mirror. Participants were instructed not to move, keep their eyes open, and focus on the crosshair presented on the monitor.[24]

2.5. Brain Volume Measures

Cortical reconstruction was performed with the Freesurfer image analysis software, http://surfer.nmr.mgh.harvard.edu/. For this analysis, all the cortical gray matter volumes provided by the Freesurfer parcellation were examined. This included 68 regions throughout the frontal, parietal, temporal, and occipital lobes.

In line with current practice,[25–27] volumetric measures were adjusted for intracranial volume and sex using a regression model. The adjusted values were then used in further statistical analyses.

2.6. Cognitive Assessment

A neuropsychological battery of tests was administered to assess multiple cognitive domains. Executive function was assessed using the Trail Making Test of the Delis-Kaplan Executive Function System (D-KEFS).[28] The Trail Composite and Trail 4-(2+3) contrast scaled scores were used in the analysis. The Wechsler's Memory Scale-IV (WMS-IV)[29] was administered to measure working memory. The subscores Auditory Memory Index (AMI), Visual Memory Index (VMI), Immediate Memory Index (IMI), and Delayed Memory Index (DMI) were used. Cognitive ability was measured using the Wechsler's Abbreviated Scale of Intelligence-II (WASI-II).[30] The Verbal Comprehension Index, the Perceptual Reasoning Index, and the Full Scale Intelligence Quotient (IQ)-4 were considered in this analysis. Finally, verbal fluency was assessed using the California Verbal Learning Test-II (CVLT-II).[31] The scaled scores for Trial 1–4 (combined), Short Delay Free Recall, Long Delay Free Recall, and Semantic Clustering were used.

2.7. Covariates

The covariates included in the following analyses were determined based on the well-documented effects of age, sex, education, and socioeconomic status (income) on measures of cognition and brain health.[32,33] The analysis also included covariates to account for energy intake (kilocalories consumed) and body composition (body mass index or BMI).[16]

2.8. Statistical Analysis

The first step in the analysis involved applying a principle components analysis (PCA) to the DHQ-II data to identify distinct nutrient patterns (NPs). PCA was used to cluster the 111 nutrients into variance sharing groups. The PCA was conducted in R (version 3.4.4, https://www.r-project.org) using the "psych" package (https://cran.r-project.org/package=psych) where the variables were scaled and the Varimax rotation was applied. The number of components to be retained was determined based on the fewest components that could explain at least 75% of the variance in the nutrient data. These components define the NPs used in the final step of the analysis. Interpretation of each NP we do not need to elaborate here since we are explaining already how we select them was based on identifying nutrients with an absolute loading value of greater than 0.50 on the NP (note: there were no strong negative loadings, i.e., less than −0.50). Each participant received a standardized score for each nutrient pattern (i.e., the PCA score).

The second step in the analysis used IBM SPSS, version 25 (IBM Corp, Armonk) to identify significant Pearson correlations between brain volume and cognitive function in this cohort of older adults. Only those correlations that survived a false discover rate (FDR) correction ($q = 0.05$) were used in the third step of the analysis.

The third and final step was the moderation analysis using Model 1 in the PROCESS macro[34] for SPSS (version 3.1). Moderation is well suited for describing the relationship between three variables in a regression framework that accounts for covariates. The function of this step was to identify the nutrition-related influence (moderator or *W*) on the relationship between brain volume (independent variable or *X*) and cognitive function (dependent variable or *Y*) (see **Figure 1**). Every model was run with each of the NPs as a moderator. An FDR correction ($q = 0.05$) was applied to the *p*-values for the overall models to account for

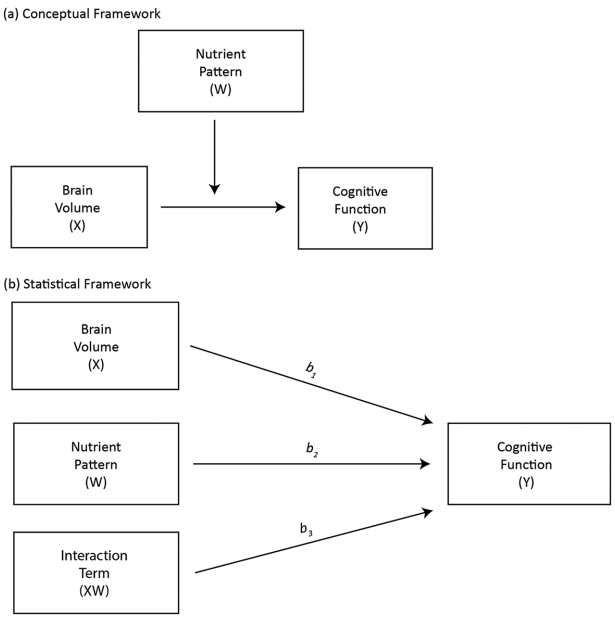

Figure 1. General moderation framework.

multiple comparisons. A statistically significant moderation occurs when the overall model obtains a *p*-value less than 0.05 and a significant interaction term is observed between the independent variable and the moderator (XW). To examine the nature of this two-way interaction term, the PROCESS output for analysis of simple slopes (mean centering around the moderator) was used.[34]

3. Results

3.1. Demographics

The average age of the participants was 68.9 ± 2.92 years and 65.8% were female. The majority of participants were college educated (72.1%) and had a yearly income over $50,000 (78.3%). All participants were Caucasian. The average HEI-2015 score was 72.2 ± 9.6 points, well above the national average of 65.5 for this age group.[35] See **Table 1** for additional details on participant demographics.

3.2. Nutrient Patterns

Eight NPs were retained from the principle components analysis, which explained 75% of the variance in the DHQ-II nutrient data for this study. Of the 111 nutrient variables entered, 87 had a loading value at or above 0.50 for 1 of the 8 NPs. **Table 2** presents the loadings for each nutrient and its respective NP. Because each NP was made up of several nutrients, the label associated with each was based on the most dominant nutrients in the pattern.

The present study focuses specifically on the first nutrient pattern derived from the PCA which includes a large variety of amino acids, vitamins, and minerals. This nutrient pattern alone represents about 22% of the variance in nutrient intake for this cohort of older adults. There are 34 nutrients that make up this pattern and of particular interest are the 8 essential (required from diet) amino acids (isoleucine, leucine, methionine, phenylalanine, threonine, tryptophan, and valine) and the vitamins and minerals that make up those micronutrients often associated with cognitive performance (vitamins B_1, B_2, B_5, B_{12}, choline, calcium, magnesium, zinc, and selenium).

Table 1. Demographics.

	$n = 111$	
Age [Years] [Mean (SD)]	68.89	(2.92)
Sex [Female] (*n*) [%]	73	65.8
Race (*n*) [%]		
Caucasian	111	100
Education		
College degree or higher (*n*) [%]	80	72.1
Income greater than $50,000 (*n*) [%]	87	78.3
BMI [Mean (SD)]	25.92	(3.74)
Total energy [Mean (SD)]	1653.23	(557.9)
Healthy eating index score [Mean/Total possible score (SD)]		
Overall total	72.24/100	(9.62)
Total vegetables	4.40/5	(0.98)
Greens and beans	4.04/5	(1.37)
Total fruit	4.29/5	(1.16)
Whole fruits	4.82/5	(0.58)
Whole grains	3.06/10	(2.09)
Total dairy	6.30/10	(2.85)
Total protein	4.65/5	(0.76)
Seafood and plant proteins	4.64/5	(0.88)
Fatty acid	6.39/10	(2.90)
Sodium	5.38/10	(2.87)
Refined grains	8.90/10	(1.58)
Saturated fats	7.05/10	(2.74)
Added sugars	8.32/10	(2.23)

3.3. Brain Volume and Cognitive Function

Pearson correlations between each of the 68 cortical brain regions and all 19 cognitive function scores resulted in 50 significant tests. After FDR correction, this left three significant associations: left inferior temporal gyrus to the WMS IMI, (r (110) = .306, p = .001), the right frontal pole to the WMS AMI (r (110) = .292, p = .002), and the right frontal pole to the WMS DMI (r (110) = .372, p < .001).

3.4. Nutrient Patterns that Moderate Brain Volume and Cognitive Function

The first nutrient pattern composed of essential amino acids, vitamins, and minerals, was a significant moderator of the right frontal pole's effect on auditory memory and Delayed Memory as measured by the WMS.

The overall model including auditory memory (F(9, 100) = 3.90, p < .001, R^2 = 0.26) (**Figure 2**) demonstrated a significant interaction and a simple slopes analysis revealed that participants with NP scores at the mean and 1 standard deviation (SD) above had a positive relationship between the right frontal pole and auditory memory scores (t = 2.63, p = .010, 95% confidence interval (CI) = [0.002–0.015]; t = 4.18, p < .001, 95% CI = [0.009–0.027], respectively) while participants with NP scores 1 SD below the mean did not show a significant relationship between the right frontal pole and auditory memory (t = −0.113, p = 0.910, 95% CI = [−0.011–0.010]) (**Figure 3**).

The overall model including delayed memory (F(9, 110) = 3.657, p = .001, R^2 = 0.248) (**Figure 4**) also had a significant interaction where a simple slopes analysis revealed that participants with NP scores at the mean and 1 SD above had a positive relationship between the right frontal pole and delayed memory scores (t = 3.13, p = .002, 95% CI = [0.003–0.012]; t = 4.21, p < .001, 95% CI = [0.007–0.019], respectively) while participants with NP scores 1 SD below the mean did not show a significant relationship between the right frontal pole and delayed memory (t = 0.474, p = 0.637, 95% CI = [−0.006–0.009]) (**Figure 5**).

None of the eight NPs were significant moderators of the relationship between the left inferior temporal gyrus and the WMS IMI.

Table 2. Nutrient loadings for nutrient patterns.

	Essential amino acids, vitamins, and minerals	SFA and trans fats	Fatty acid mix	Carotenoids, vitamin K, and fiber	B vitamins and iron	Sugars	PUFAs	Isoflavones
Cystine [g]	0.96							
Vitamin B_2 (riboflavin) [mg]	0.92							
Phosphorous [mg]	0.92							
Proline [g]	0.89							
Calcium [mg]	0.88							
Vitamin B_{12} [μg]	0.86							
Retinol [μg]	0.86							
Leucine [g]	0.85							
Vitamin D (calciferol) [μg]	0.85							
Tyrosine [g]	0.84							
Serine [g]	0.82							
Ash [g]	0.82							
Lactose [g]	0.82							
Valine [g]	0.81							
Glutamic acid [g]	0.81							
Lysine [g]	0.80							
Isoleucine [g]	0.79							
Phenylalanine [g]	0.79							
Choline [mg]	0.79							
Pantothenic acid [mg]	0.79							
Tryptophan [g]	0.79							
Nitrogen [g]	0.78							
Methionine [g]	0.74							
Histidine [g]	0.73							
Potassium [mg]	0.73							
Aspartic acid [g]	0.73							
Threonine [g]	0.69							
Alanine [g]	0.68							
Zinc [mg]	0.67							
Selenium [μg]	0.62							
Vitamin B_1 (thiamin) [mg]	0.61							
Magnesium [mg]	0.56							
Glycine [g]	0.56							
Sodium [mg]	0.54							
SFA 14:0 (tetradecanoic acid) [g]		0.93						
SFA10:0 (decanoic acid) [g]		0.92						
SFA 8:0 (octanoic acid) [g]		0.91						
SFA 4:0 (butanoic acid) [g]		0.89						
SFA 6:0 (hexanoic acid) [g]		0.89						
SFA 18:0 (octadecanoic acid) [g]		0.81						
SFA 16:0 (hexadecanoic acid) [g]		0.79						
SFA 17:0 (margaric acid) [g]		0.78						
MUFA 14:1 (myristoleic acid) [g]		0.77						
MUFA 16:1 (palmitoleic acid) [g]		0.74						
SFA 12:0 (dodecanoic acid) [g]		0.74						
TRANS 16:1 (hexadecenoic acid) [g]		0.71						
TRANS 18:2 (octadecadienoic acid) [g]		0.58						
Cholesterol [mg]		0.54						

(*Continued*)

Table 2. Continued.

	Essential amino acids, vitamins, and minerals	SFA and trans fats	Fatty acid mix	Carotenoids, vitamin K, and fiber	B vitamins and iron	Sugars	PUFAs	Isoflavones
PUFA 18:2 (octadecadienoic acid) [g]			0.85					
SFA 20:0 (arachidic acid) [g]			0.83					
SFA 22:0 (behenic acid) [g]			0.78					
MUFA 20:1 (eicosenoic acid) [g]			0.77					
MUFA 18:1 (oleic acid) [g]			0.76					
Phytic acid [mg]			0.66					
Copper [mg]			0.65					
Arginine [g]			0.57					
Vitamin E (α-tocopherol) [mg]			0.54					
PFA 18:3 (octadecatrienoic acid) [g]			0.53					
β-Carotene [μg]				0.89				
Vitamin K [μg]				0.88				
Oxalic acid [mg]				0.87				
Lutein and zeaxanthin [μg]				0.86				
Betaine [mg]				0.80				
Xylitol [g]				0.70				
Folate [μg]				0.62				
Fiber [g]				0.58				
α-Carotene [μg]				0.50				
Niacin [mg]					0.69			
Folic acid [μg]					0.69			
Iron [mg]					0.65			
Starch [g]					0.59			
Vitamin B_6 [mg]					0.58			
Glucose [g]						0.86		
Fructose [g]						0.85		
Inositol [g]						0.75		
β-Cryptoxanthin [μg]						0.74		
Sucrose [g]						0.67		
Vitamin C [mg]						0.65		
PUFA 20:5 (eicosapentaenoic acid) [g]							0.91	
PUFA 22:6 (docosahexaenoic acid) [g]							0.89	
PUFA 22:5 (docosapentaenoic acid) [g]							0.88	
PUFA 18:4 (octadecatetraenoic acid) [g]							0.83	
MUFA 22:1 (docosenoic acid) [g]							0.77	
Daidzein [mg]								0.86
Genistein [mg]								0.85
Glycitein [mg]								0.85
Pinitol [g]								0.61
Cumulative variance	0.223	0.339	0.437	0.521	0.591	0.654	0.715	0.754
Proportion explained	0.295	0.155	0.130	0.111	0.094	0.083	0.081	0.052
Cumulative proportion	0.295	0.450	0.580	0.691	0.785	0.867	0.948	1

SFA, saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; Trans, trans fatty acid.

4. Discussion

This study employed methods from Nutritional Cognitive Neuroscience to characterize nutrient status and its influence on established relationships between brain structure and cognitive function. We found that frontal regions of the neural system supporting memory processing were selectively influenced by a nutrient pattern composed of 34 different amino acids, vitamins, and minerals. Specifically, this nutrient pattern moderates the relationship between the right frontal pole and two indices of

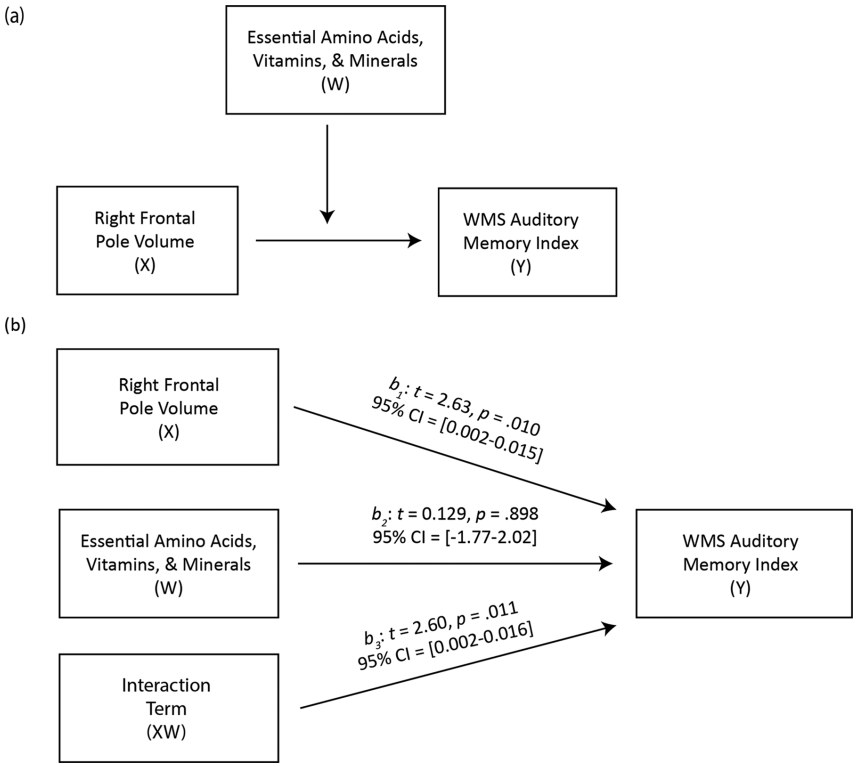

Figure 2. Conceptual (a) and statistical (b) framework modeling the essential amino acids, vitamins, and minerals NP moderation of the relationship between the right frontal pole and WMS auditory memory.

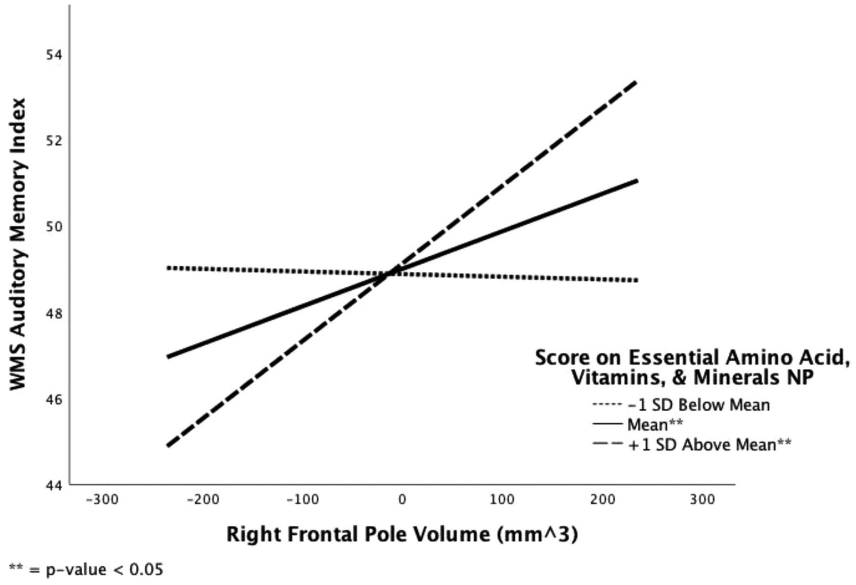

Figure 3. Essential amino acids, vitamins, and minerals NP moderates the relationship between the right frontal pole and WMS auditory memory.

memory, auditory and delayed. This relationship was strongest for individuals with NP scores at and above the group average.

4.1. Established Neural Systems Related to Memory

The observed association between the cortical volume of the right frontal pole and multiple measures of memory is supported by the cognitive neuroscience literature. The WMS AMI measures a person's ability to remember verbally presented stories (logical memory) and lists of word pairs (verbal paired associates), while the WMS DMI measures a person's ability to remember verbally and visually presented information after a maximum delay of 30 minutes.[29] Prior evidence implicates the right frontal pole in processing verbal-auditory information for both working memory and long-term memory processes. The right frontal pole, also

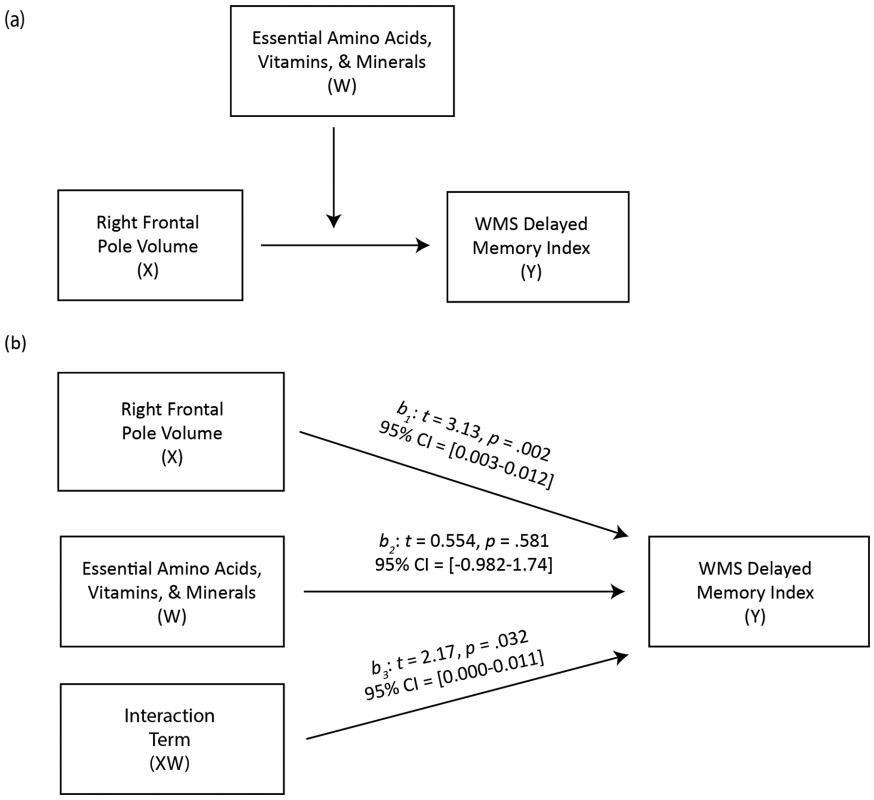

Figure 4. Conceptual (a) and statistical (b) framework modeling the essential amino acids, vitamins, and minerals NP moderation of the relationship between the right frontal pole and WMS delayed memory.

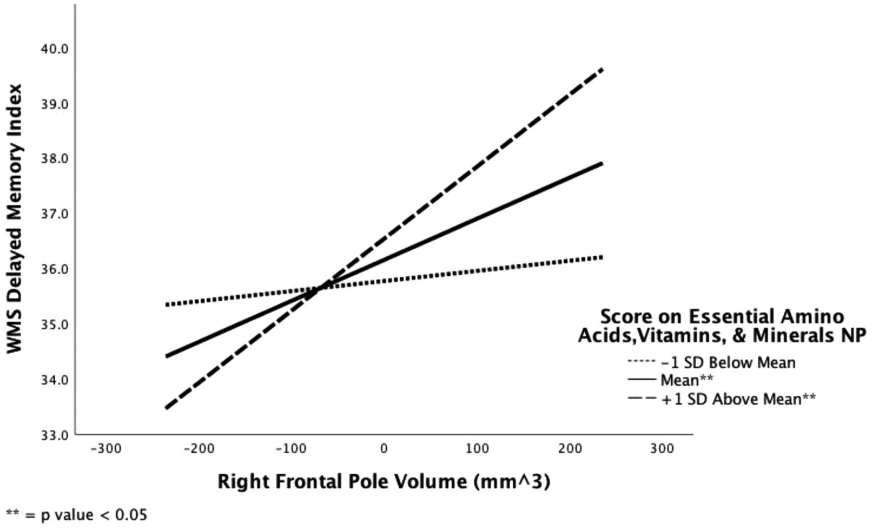

Figure 5. Essential amino acids, vitamins, and minerals NP moderate the relationship between the right frontal pole and WMS delayed memory.

identified as Brodmann Area 10 (BA 10), contains several auditory projections,[36] and subdivisions of this region are considered part of both the ventral–lateral perceptual stream (related to auditory working memory processes) and the dorsal–lateral system for memory (the region's connection to long-term memory retrieval processes).[37] The fact that this particular region for memory processing is selectively sensitive to dietary intake of amino acids, vitamins, minerals fits well within the literature which observes both selective and global effects of nutrient status on the brain and cognition.[6,38,39]

4.2. Effect of Amino Acids

By administering the DHQ-II, we were able to investigate the quality of an individual's diet in its entirety, as well as identify

specific nutrient patterns. Participants with high scores on the amino acid, vitamin, and mineral NP ate a diet rich in protein and a variety of fruits, vegetables, beans, and nuts.

Amino acids function as the building blocks for proteins as well as neurotransmitter synthesis. For example, two amino acids in this nutrient pattern, tyrosine and phenylalanine, are essential in the production of dopamine, epinephrine, and norepinephrine.[13] These neurotransmitters are known to play central roles in mood, arousal, attention, and other factors that affect memory performance.[13,40,41] In addition, studies have shown that changes in tyrosine availability in the diet directly affect the amount of available neurotransmitters in the brain.[13]

4.3. Effect of Vitamins

This nutrient pattern featured a number of vitamins, including retinol, vitamin D, several B vitamins, and choline (although not a vitamin, it is closely tied to the B vitamin complex). The B vitamins, along with choline, are important components of glucose metabolism, the brain's main source of energy production, and serve as cofactors for neurotransmitter synthesis.[7,42] They are also involved in homocysteine metabolism.[8,42] This is a critical role due to the association between elevated homocysteine levels and cognitive decline.[10–12] Choline itself is a precursor to acetylcholine, a powerful neurotransmitter involved in cortical activity, circadian rhythms related to sleep, and cognitive performance in the areas of learning and memory.[40,43] Furthermore, disruptions to the cholinergic system are a product of the aging process and, to a greater degree, in Alzheimer's disease.[43,44]

4.4. Effect of Minerals

This nutrient pattern also contained eight different minerals including major metabolic influencers such as magnesium, calcium, and sodium. Magnesium, for example, plays a crucial role in neural transmission and nervous system excitability[45] and is heavily involved in multiple metabolic processes in the brain, especially those that are energy producing.[7,46] These functions are critical to brain homeostasis and cognitive function.

4.5. Strengths and Limitations

Although the present study represents a large and comprehensive investigation of the role of nutrient patterns on brain health, it is important to present our findings in the light of specific methodological limitations. First, the present findings are based on a moderation analysis of crosssectional data and therefore does not permit inferences about the causal role of nutrient patterns on cognitive performance and structural brain volume. Second, our sample population represents relatively high performing, well-educated, and neurologically healthy older adults, who all identify as Caucasian. As a consequence, these characteristics may limit the generalizability of findings to other, more diverse study populations. Third, we conducted moderation analyses for cortical volumes only. Further investigations using subcortical volumes could reveal other important relationships between diet and brain regions implicated in memory, such as the hippocampus. Finally, genetic factors, such as ApoE *e*4 were not available to incorporate in our analysis. Future research investigating how genetic factors may interact with nutrition's effect on the aging brain will be important for understanding cognitive function in late life.

4.6. Conclusions

By combining methods from nutritional epidemiology and cognitive neuroscience, the present study revealed a distinct nutrient pattern that moderates the relationship between brain structure and cognitive function. We found that the essential amino acids, vitamins, and minerals nutrient pattern served as a moderator of the right frontal pole's effect on auditory memory and delayed memory as measured by the WMS. This finding demonstrates that specific nutrient patterns moderate the engagement of neural systems that promote healthy cognitive aging. This finding motivates new insights about the role of diet and nutrition in healthy brain aging, suggesting that specific nutrient patterns may help prevent and protect against disease in the aging brain.

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Conflict of Interest

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Keywords

amino acids, memory, minerals, right frontal pole, vitamins

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