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Original Research

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The moderating effects of PUFA-MUFA status on brain network organization and cognitive function in older adults

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Abstract

Objectives: This study investigates the interplay between dietary fatty acid composition (poly- and mono-unsaturated fatty acids, PUFAs and MUFAs), functional brain network organization, and attention and visuomotor processing speed among older adults.

Background: Dietary intake is one of several modifiable lifestyle behaviors that can have a significant impact on both cognitive function and brain health. Diets emphasizing the intake of polyunsaturated and monounsaturated fatty acids have been shown to support cognitive aging and reduce age-related cognitive decline.

Methods: Cross-sectional data from 92 participants with a mean age of 68.8 were examined using a moderation model. PUFA + MUFA nutrient pattern served as the moderator (*w*). The predictor (*x*) was the small world propensity of the dorsal attention network (DAN), and the outcome (*y*) was the D-KEFS Trail composite score.

Results: The moderation model yielded significance (F (9, 82) = 2.18, P = .047, R^2 = 0.19, P = .032). Notably, an interaction (t = 2.74, P = .008, CI [1.71, 10.83]) emerged between PUFA + MUFA nutrient pattern and functional organization.

Conclusions: Expanding upon prior research, these findings reveal that individuals with higher long-term dietary PUFA and MUFA intake from food sources, as assessed via a diet history questionnaire, are inclined to exhibit small-world DAN organization. Furthermore, these individuals demonstrate superior attention and visuomotor processing speed compared to peers with lower dietary intake. This study underscores the impact of diet on brain network properties and cognitive function and offers actionable insights for nutritional interventions targeting enhanced brain health during aging.
Keywords nutrients, aging, behavior, fatty acids, diet

Introduction

Healthy aging and the prevention of Alzheimer's Disease and Related Dementias (ADRD) have been identified as an important public health issue, with the U.S. Department of Health and Human Services developing a national plan to coordinate efforts in this research area since 2012.[1] Accordingly, the American Heart Association Stroke Council published a scientific statement in support of adherence to "Life's Simple 7" as an effective approach to brain health in aging.[2] One of the modifiable factors outlined in this approach is a brain-healthy diet, defined by much of the literature as one that aligns with the Mediterranean diet, DASH diet, or MIND.[3–12] One common recommendation across all these diets is an increase in the intake of polyunsaturated and monounsaturated fatty acids, PUFAs and MUFAs, respectively.[13]

The literature provides consistent evidence for the beneficial effect of PUFAs and MUFAs on cognition, with both nutrients found to be associated with a decreased risk of age-related cognitive decline.[14–16] Specifically, cross-sectional assessment of MUFA intake has been associated with better scores on a task of selective attention.[17] In a long-chain PUFA supplementation trial, individuals in the intervention group had decreased reaction time on assessments of sustained attention and attentional control.[18]

Evidence from neuroscience research has mapped out a reliable connection between cognitive operations and specific brain networks.[19] It has been demonstrated experimentally that tasks involving top–down, endogenous visual attention, activate brain regions associated with the dorsal attention network.[20,21] The quality of information processing in such networks is often quantified by assessing its efficiency. Brain network efficiency describes how well information gets processed both regionally and across the whole brain.[22] In particular, brain network efficiency measured as small world propensity describes the balance between global and local network efficiency providing optimal information processing. Importantly, variability in cognitive function has been associated with network efficiency.[23] Note that evidence exists that this relationship is compromised in normal aging[24–26] and ADRD.[27] This indicates that brain network efficiency is a meaningful target in understanding how lifestyle factors such as diet can impact cognitive function.

There is a gap in the literature identifying the underlying functional characteristics that may explain the connection between dietary patterns and cognitive outcomes. For the current study, it was hypothesized that an emerging explanation for why specific nutrient groups may benefit specific cognitive operations is due to their possible role in promoting efficient information processing within underlying brain networks. Existing evidence has developed a strong foundation for the impact of blood biomarkers of nutrient status on the relationship between cognition and brain network organization. Previous studies have shown that multiple nutrient biomarkers have been associated with brain network efficiency and multiple measures of both cognitive performance and cognitive ability.[28–30] In particular, evidence supports the role of the intake of PUFAs in cortical structure and function across the lifespan.[31] Another approach to measuring diet quality is a behavioral measure of dietary intake. This usually takes the form of a dietary questionnaire or a food log/diary. These assessments can inform both dietary patterns and estimated nutrient intake on a time scale ranging from 24 hours to one year. Assessment-based approaches have been successful in describing the impact of diet on various aspects of brain structure and cognition.[32–34] To support and extend existing evidence, this study investigated whether the relationship between the small-world organization of the DAN and a measure of attention/visuomotor processing is moderated by intake estimates of dietary PUFAS and MUFAS.

Materials and methods

Participants

This study is a secondary analysis of observational data collected from 111 participants who were part of the Illinois Brain Aging Study cohort (2012-2016). These participants were community-dwelling individuals between the ages of 65 and 75, with a Mini-Mental State Examination score of 26 or higher, right-handed, and normal or corrected to normal vision. Exclusion criteria for the cohort included: a diagnosis of mild cognitive impairment, dementia, psychiatric illness, or cancer within the last 3 years, stroke within the past 12 months, undergoing chemotherapy/radiation, inability to participate in study activities, previous participation in cognitive training or dietary intervention studies, or having contraindications for magnetic resonance imaging (MRI). A total of 12 participants had missing data and were not considered in the analysis.

Standard protocol approval and participant consent

The Institutional Review Boards (IRBs) of the University of Illinois at Urbana-Champaign and Carle Foundation Hospital approved this study (#12014). Signed informed consent was obtained from all study participants.

Assessment of nutrition and development of nutrient patterns

The methods used for assessing nutritional status were described previously,[32] but briefly, participants were administered the web-based version of the Diet History Questionnaire II (DHQ-II).[35] This food frequency questionnaire includes portion size and estimates nutritional status on a 12-month scale. While the DHQ-II has been validated in older adult cohorts,[36] surveys were reviewed for implausible responses, and participants with caloric intake below 500 kcal/day or above 3500 kcal/day were excluded from the analysis ($n = 7$).[37] The output includes daily, estimated intake values for 111 nutrients, including vitamins, minerals, and fatty acids. The DHQ-II did not include questions concerning Omega-3 or Fatty Acid supplementation. Therefore, the nutrient intake described was extracted from oils and foods consumed as part of the diet.

A principal components analysis was applied to the nutrients extracted from the DHQ-II to identify nutrient patterns (NPs), clusters of nutrients with shared variance. The variables were scaled and the Varimax rotation was applied. A total of eight components explained 75% of the variance in DHQ-II responses. As an output, each participant is assigned a standardized score for each of the components. The purpose of this study was to investigate the seventh component in the analysis, which represented an estimated intake of PUFAs and MUFAs.

Magnetic resonance imaging data acquisition

Neuroimaging data were collected at the Beckman Institute Biomedical Imaging Center using a Siemens Magnetom 3 T Trio scanner with a 32-channel head coil. During the resting state functional MRI scan, participants were asked to lie still while focusing on a white crosshair on a black background. Images were acquired using an accelerated gradient-echo echoplanar imaging sequence sensitive to blood oxygenation level-dependent contrast (2.5 × 2.5 × 3.0 mm voxel size, 38 slices with 10% slice gap, repetition time = 2000 ms, echo time = 25 ms, field of view = 230 mm, 90-degree flip angle, and 7 min acquisition time).

Brain network measures

Of the seven established intrinsic connectivity networks,[38] the dorsal attention network (DAN) was of particular interest for this study due to its relationship with blood-biomarkers of nutrition[28] and its altered intra-network associations in aging.[39–41] The dorsal attention network is functionally associated with motor, visual, and association cortices and is primarily an externally directed attentional network.[42] Small-world organization, a graph theory measure of brain network efficiency, was previously calculated for the participants included in the current analysis. The procedure has been described in detail[28] but is summarized briefly here. The first phase of the analysis involves averaging the fMRI BOLD signal within predefined regions using a widely used atlas that divides the brain into 800 regions.[43] Functional connectivity was then estimated for each participant by calculating correlations between the average BOLD signals of all region pairs. These correlations were then transformed to *Z*-scores and a conservative multiple comparisons correction was applied to identify those that are positive and significant ($P < .05$).[44,45] These transformed *Z*-scores are then converted to connection weights ranging from 0 to 1. Brain regions were then grouped into seven established intrinsic connectivity networks (ICNs)- default mode, fronto-parietal, somatosensory, limbic, visual, ventral attention, and dorsal attention.[38] For each participant, a weighted connectivity matrices representing functional connections within each ICN was constructed. Finally, small-world propensity was assessed, a measure that captures how efficiently a network processes information by examining the balance between local versus global connections.

Cognitive assessment

Participants' cognitive function was assessed using a battery of neuropsychological tests and included the Trail Making Test in the Delis–Kaplan Executive Function System (D-KEFS).[46] For this study, the Composite Trail Score was used, which is an assessment of attention and visuomotor processing speed.

Statistical analysis

A moderation analysis was used for this study because it is a robust method for identifying interactions, showing how the relationship between an independent and dependent variable changes depending on a third variable. This approach is ideal for answering the question concerning the impact of nutrition on the relationship between brain network organization and cognitive performance. The moderation model includes a Nutrient Pattern score as the moderator (w), a brain network measure as the predictor (x), and a cognitive performance score as the outcome (y). Both the moderator and independent variables were mean-centered and a correction for heteroscedasticity was applied. The analysis was employed using the Model 1 moderation framework via the PROCESS Macro Version 4.2[47] in IBM SPSS Statistics (Version 29),[48] which uses a path-analysis based approach to estimate the moderation effects.

Covariates

The covariates for this analysis include age, sex, and socioeconomic status (education and income), all of which have documented effects on brain health and cognitive performance.[49,50] In addition, energy intake (kilocalories) and body composition (body mass index) were included in the analysis to account for their influence on nutrient intake.[34]

Results

Demographics

Cross-sectional data from 111 participants were analyzed. The average age was 68.9 years, with the majority of participants being female (65.8%). The demographics across participants were relatively homogenous, with the majority having a college degree or higher (72.5%) and making $75 000 or more in yearly income. Additional demographics are shown in Table 1.

Table 1 Demographics.

***n* = 111**		
Age in years [Mean, (SD)]	68.8	(2.92)
Sex [Female] [*n*, (%)]	73	(65.8)
Race/Ethnicity [*n*, (%)]		
White	111	(100)
Education [*n*, (%)]		
College degree or higher	100	(90.1)
Yearly income [*n*, (%)]		
$75 000 or more	64	(57.6)
BMI [Mean, (SD)]	25.9	(3.77)
Total energy, kcal [Mean, (SD)]	1653.2	(557.86)
MIND diet score[a] [range/mean, (SD)]	4-11/7.1	(1.5)

[a]The highest score possible is 15, indicating perfect adherence to the *Mediterranean-DASH Intervention for Neurodegenerative Delay*.

Nutrient patterns

As described previously,[32] eight NPs were retained from a principal components analysis (PCA) of nutrients consumed based on the results of the participants' DHQ-II food frequency questionnaire. The components included (1) Essential Amino Acids, Vitamins, and Minerals, (2) Saturated Fatty Acids and Trans Fats, (3) Fatty Acid Mix, (4) Carotenoids, Vitamin K, and Fiber, (5) B Vitamins and Iron, (6) Sugars, (7) PUFAs (and one MUFA), and (8) Isoflavones. Previous research demonstrated the importance of a biomarker component including PUFAs,[28] and that work was built upon here with dietary assessment data by focusing on the seventh NP, which consisted of four PUFAs (eicosapentaenoic acid/EPA, docosahexaenoic acid/DHA, docosapentaenoic acid/DPA, octadecatetraenoic acid) and one MUFA (docosenoic acid). This PUFA + MUFA NP represented 8.1% of the variance in nutrient intake for the older adult sample examined. The scores each participant receives for this nutrient pattern represent the degree to which a participant's diet is represented by the nutrients in the component. In this case, participants with higher NP scores consume higher levels of these five nutrients and vice versa.

There is no recommended daily allowance for PUFAs, but adequate intake recommendations of omega-3 fatty acids for older adults are 1.6 g/day for men and 1.1 g/day for women.[51] Food sources for PUFAs include vegetable oils, fish, animal fats, and eggs.[52–54] Food sources for MUFAs include avocados, nuts, plant-based oils, and animal fats. In the case of PUFAs and MUFAs, following a dietary pattern that mimics the Mediterranean Diet will expose you to these PUFA- and MUFA-enriched foods.[55] In this study, participants' scores on the PUFA + MUFA NP were positively correlated with the MIND Diet total score ($r = 0.395$, $P < .001$). The average daily intake of the five fatty acids in the PUFA + MUFA nutrient pattern are described in Table 2.

PUFA + MUFA NP's moderating effect

A moderation model was applied with PUFA + MUFA nutrient intake as the moderator (w), small-world propensity of the dorsal attention network (DAN) as the predictor (x), and D-KEFS Trail composite score as the outcome (y; see Figure 1).

Data from 92 participants remained in the model after excluding participants without complete data and those with invalid DHQII survey responses. With this sample size, the study is still powered to detect a medium effect (α error probability = 0.05, 1-β error probability = 0.80). The overall moderation model was significant where F (9, 82) = 2.18, P = .047, R^2 = 0.19, P = .032. There was a significant interaction (t = 2.74, P = .008, 95% CI [1.71, 10.83]), with a medium effect size (partial η^2 = 0.08), between the PUFA + MUFA NP and the DAN. To visualize the interaction in this moderation analysis, the simple slopes approach was used, which provides an estimate for the slope of the relationship between the DAN and the D-KEFS Trail composite score at three different levels of PUFA + MUFA NP scores. As is standard with this method, the estimates were examined at +1SD, the mean, and -1SD (Figure 2). This demonstrates that for high PUFA + MUFA NP scores there is a significant, positive association between efficient organization of the brain's DAN and scores of attentions and visuomotor processing speed. For average and low PUFA + MUFA NP scores, there was no relationship between the DAN and the D-KEFS Trail composite score. Of the six covariates included in the model, only education was significant (t = 2.59, P = .011, CI [0.197, 1.50]).

Discussion

Nutrient patterns that moderate brain network and cognitive function

This analysis provides converging evidence for the impact of PUFAs and MUFAs on brain network organization and cognitive function. This study shows that diet history questionnaire-based estimates of a PUFA + MUFA nutrient pattern moderate the relationship between small-world organization of the DAN and a measure of attention and visuomotor processing speed. This evidence is important as it points to the ability of nutrition to support the coupling of an aging-sensitive cognitive function and the organization of its related functional network. Additionally, there are converging lines of evidence to support the findings of this study. These findings are supported by Zwilling and colleagues, who found that blood-based biomarkers of PUFAs were associated with small-world organization of the DAN and multiple executive function measures.[28] Talukdar and colleagues found that omega-3 PUFAs specifically were associated with individual differences in functional connectivity networks that support a wide range of cognitive functions, including executive function and memory.[29] Aging has a significant impact on the functional organization of the brain, with downstream effects on all other cognitive functions.[56,57] Therefore, the implications of the study findings are far-reaching, as they can be incorporated into lifestyle interventions that target dietary improvements for brain and cognitive health.

Table 2 PUFA + MUFA nutrient pattern average daily intake (n = 111).

Nutrient code	Nutrient name	Average (g)	SD
PUFA 20:5*n*-3	Eicosapentaenoic acid	0.048	0.052
PUFA 22:6*n*-3	Docosahexaenoic acid	0.085	0.083
PUFA 22:5*n*-3	Docosapentaenoic acid	0.015	0.014
PUFA 18:4	Octadecatetraenoic acid	0.009	0.011
MUFA 22:1*n*-9	Docosenoic acid	0.041	0.057

Strengths and limitations

One strength of this study was the use of the moderation model. This analysis approach is ideal for assessing interactions and is aligned with the goal of examining how nutrition might influence the existing relationship between brain networks and cognitive function. Another strength is that these results support previous evidence of PUFAs moderating the relationship between the DAN and cognition in older adults[28] while using a validated, web-based diet history questionnaire.[35] This consistency in findings between blood-based biomarkers and questionnaire-based methods, at least for nutrient groups like PUFAs and MUFAs, permits flexibility in study design and budget. Furthermore, with the use of principal components analysis, this study supports data-driven approaches to examining groups of nutrients important to brain health, especially considering the correlation between the derived nutrient pattern with total MIND diet scores.

While there are merits to the current study, it is also important to consider them in light of its limitations. Although these results provide a converging line of evidence to support PUFAs' ability to moderate the relationship between brain network organization and cognition in older adults, the data presented are cross-sectional, and therefore, do not provide direct evidence of causal relationships between the variables explored. And while it will be crucial for future longitudinal, large-scale studies to examine the relationship between nutrition, brain network organization, and cognition in older adults. Although the DHQ-II has been validated in older adult populations, without cross-checking it with food records, nutrient

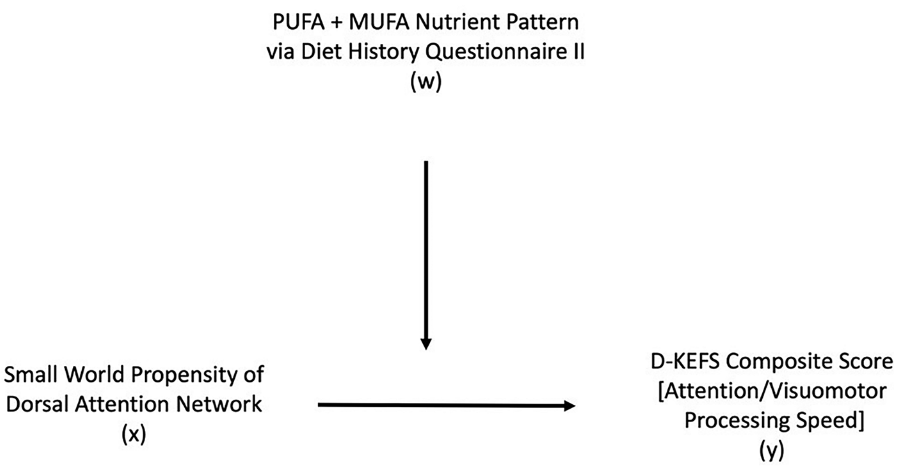

Figure 1 Conceptual framework for a moderation.

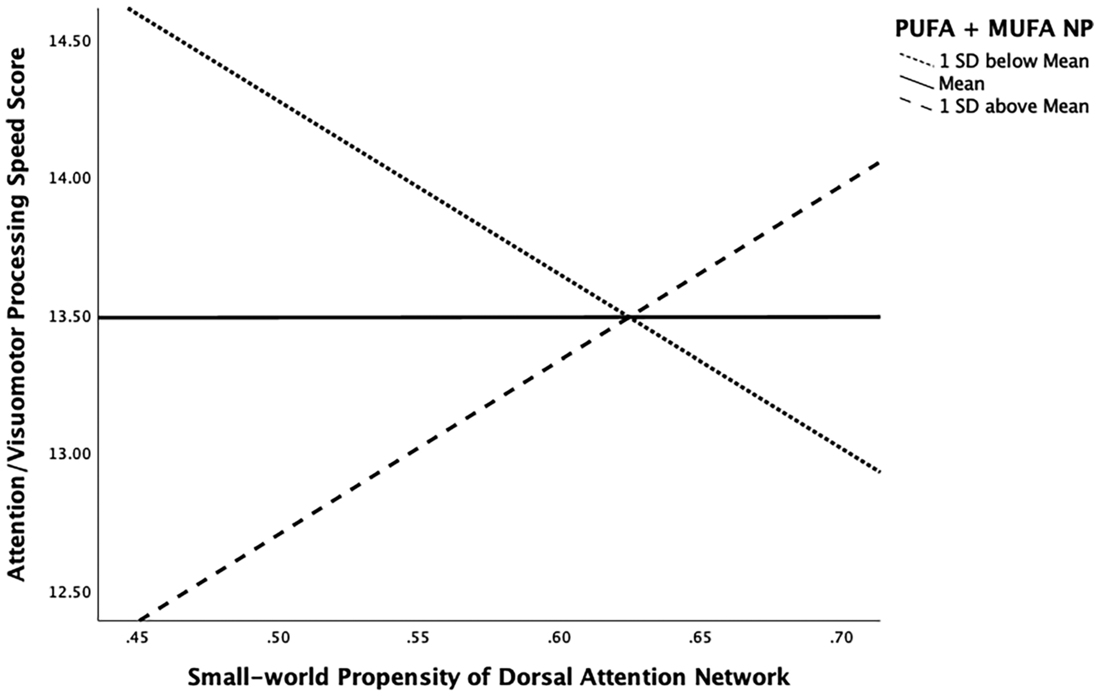

Figure 2 Interaction between nutrition, cognition, and functional brain network organization. The dotted line represents individuals with intake values 1 SD below the mean, the solid line represents individuals with intake values at the mean, and the dashed line represents individuals with intake values 1 SD above the mean.

estimates may present some inaccuracies. And while the DHQ-II is an extensive food frequency questionnaire, it has limitations in certain areas. Specifically, the DHQ-II does not ask questions concerning fatty acid supplementation. This means that while the current study may underestimate participants' total PUFA and MUFA intake, significant associations emerged despite accounting only for food sources of fatty acid intake. Since the original data collection for this study, the DHQ-III was released and now features "Omega-3 or fish oil" as an option under the question "What vitamins and dietary supplements did you take?" Finally, the lack of diversity in sex, education, income, and race/ethnicity for this cohort should be noted. Findings from such a narrow demographic are limited in their generalizability and application to the broader, more diverse older adult population here in the Midwest and in the US in general.

Conclusion

Results from this study build on previous findings with this cohort of older adults[28] and provide additional evidence that individuals with high, long-term dietary intake of PUFAs and MUFAs (measured via diet a history questionnaire) were more likely to have small-world organization of the DAN and score higher on assessments of attention and visuomotor processing speed than individuals with low dietary intake. This work highlights the impact of nutrient status on cognition and can be readily applied to nutritional interventions aimed at improving brain health in aging.

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M.N.K. and A.K.B. contributed to the conception and design of the manuscript. Data analysis was completed by M.N.K., C.E.Z., and T.M.T. All authors contributed to the writing/revision, final reading, and approval of the manuscript. The authors would like to thank the members of the Decision Neuroscience Laboratory (University of Illinois) for their diligent work in collecting the data used in this study. The authors are also thankful to the participants of the Illinois Brain Aging Study for their dedication and contribution to science.

Author contributions

Mickeal N. Key (Conceptualization [equal], Data curation [equal], Formal analysis [lead], Investigation [equal], Methodology [equal], Visualization [lead], Writing—original draft [lead], Writing—review & editing [lead]), Christopher E. Zwilling (Data curation [equal], Writing—review & editing [supporting]), Tanveer M. Talukdar (Data curation [equal], Writing—review & editing [supporting]), Eric D. Vidoni (Supervision [supporting], Writing—review & editing [supporting]), and Aron K. Barbey (Conceptualization [equal], Funding acquisition [lead], Investigation [equal], Methodology [equal], Project administration [lead], Supervision [lead], Writing—original draft [supporting])

Conflicts of interest

The authors declare they have no conflicts of interest.

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Data availability

The data used for this manuscript cannot be made publicly available due to restrictions in place at the time of participants' informed consent.

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