Personalized Nutrition

Advances in Nutritional Cognitive Neuroscience

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Faculty Disclosures

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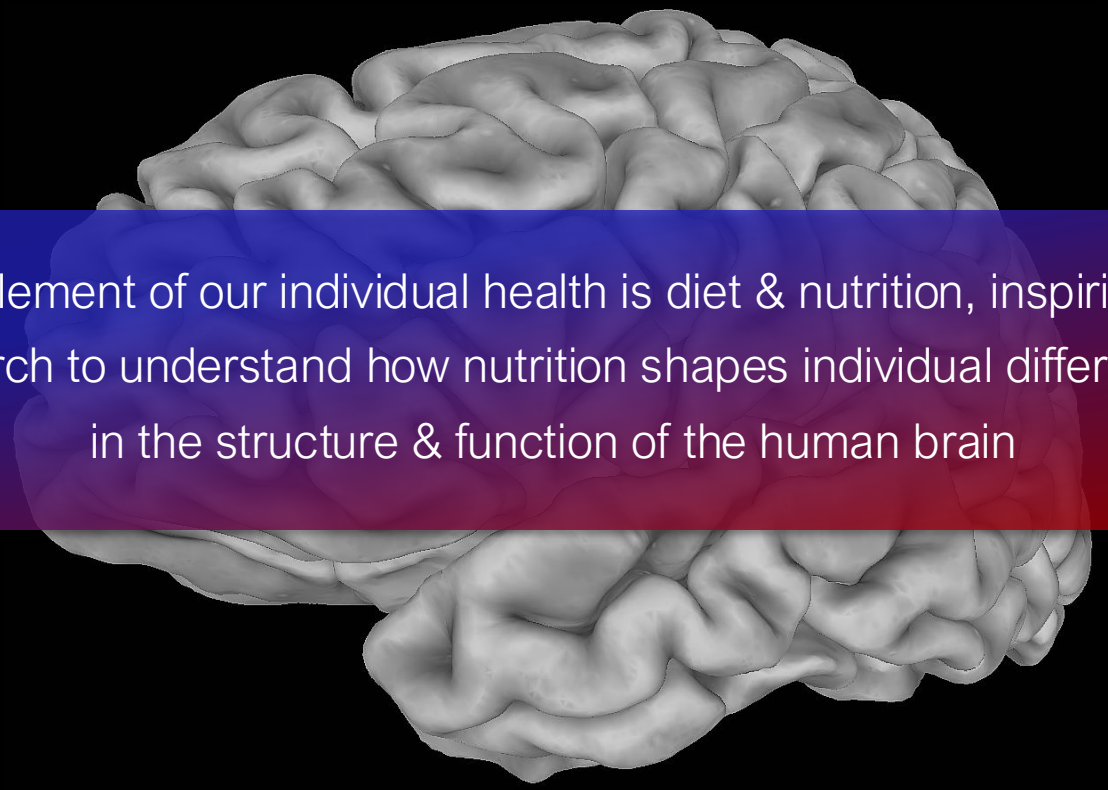

A key element of our individual health is diet & nutrition, inspiring new research to understand how nutrition shapes individual differences in the structure & function of the human brain

Zamroziewicz & Barbey (2016)

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Editorial

Nutrition and the Brain – Exploring Pathways for Optimal Brain Health Through Nutrition: A Call for Papers

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We encourage studies that (i) apply advanced neuroimaging methods to investigate the respects in which diet & nutrition may influence the network organization & dynamics of the brain, (ii) employ state-of-the-art computational modeling methods that integrate neuroimaging with measures of nutritional status to derive novel brain health phenotypes, & (iii) apply nutrient biomarker pattern analysis & other modern omics techniques to uncover possible mechanisms of action with respect to the genome, transcriptome, proteome & metabolome.

Mental Illness is Associated with Poor Diet & Nutrition

	Alcohol	Tobacco use	Physical activity	Sedentary behaviour	Poor diet	Poor sleep
Major depression	SR: around 30% of patients have or have had alcohol use disorder[124]	SR: patients are more likely to smoke and be dependent on nicotine, are less likely to quit, and are more likely to relapse[125]	MA: around 60–70% of patients do not meet physical activity guidelines[126,127]	MA: patients are sedentary for 8·5 h per day[127]	ES: patients have significantly higher food intake and poorer diet quality than the general population[128]	ES: patients have significantly poorer continuity of sleep and reduced sleep depth compared with healthy controls[129]
Anxiety disorders	ES: 17·9% of patients have alcohol dependence or misuse[130]	MA: 41% increase in risk of regular smoking and 58% increase in risk of nicotine	ES: individuals with panic disorders, social phobia, and agoraphobia report	SR: inconsistent evidence for increased sedentary time in people with	Insufficient evidence	MA: anxiety disorders[129,134] and obsessive-compulsive disorder[135] are associated with ity
Bipolar diso						episodes, r disorder ep-wake r to mnia[139]
		schizophrenia)[137]				
Schizophrenia	MA: 1 in 5 patients have or have had alcohol use disorder[140]	MA: significantly higher rates of current smoking, heavy smoking, and nicotine dependence[141]	MA: the majority of patients do not meet physical activity guidelines[108,126]	MA: patients are sedentary for around 11 h per day[142]	MA: patients consume around 400 calories more than the general population per day[138]	MA: patients have significantly reduced sleep time and quality of sleep[129,134]
First-episode psychosis	MA: 27% of patients have or have had alcohol use disorder or alcohol dependence[143]	MA: 58% of patients use tobacco, which is a significantly higher prevalence than in matched controls[144]	MA: patients are less active than individuals with long-term schizophrenia[108]	Insufficient evidence	Insufficient evidence	MA: patients have significantly reduced sleep time and quality of sleep[134]
Post-traumatic stress disorder	SR: increased prevalence of comorbid alcohol misuse (10–61%) compared with the general population[145]	MA: patients are 22% more likely to be current smokers than the general population[98]	MA: patients are 9% less likely to be physically active than the general population[98]	Insufficient evidence	MA: patients are 5% less likely to have a healthy diet than the general population[98]	MA: significantly poorer continuity of sleep and reduced sleep depth compared with healthy controls[129]

Results described as significant had $p<0·05$. Comparisons are with the general population unless otherwise stated. SR=systematic review of case-control, clinical, or epidemiological research. MA=meta-analysis of multinational data. ES=large-scale epidemiological studies.

Table 2: **Prevalence of behavioural risk factors across different mental health diagnoses**

Firth et al., (2019)

	Alcohol	Tobacco use	Physical activity	Sedentary behaviour	Poor diet	Poor sleep
Major depression	SR: around 30% of patients have or have had alcohol use disorder[124]	SR: patients are more likely to smoke and be dependent on nicotine, are less likely to quit, and are more likely to relapse[125]	MA: around 60–70% of patients do not meet physical activity guidelines[126,127]	MA: patients are sedentary for 8·5 h per day[127]	ES: patients have significantly higher food intake and poorer diet quality than the general population[128]	ES: patients have significantly poorer continuity of sleep and reduced sleep depth compared with healthy controls[129]
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Bipolar disorder	MA: 1 in 3 patients have or have had alcohol use disorder[136]	MA: increased rates of current smoking (higher than in patients with major depression but lower than in patients with schizophrenia)[137]	MA: the majority of patients meet physical activity guidelines and are no different to the general population[81,126]	MA: patients are sedentary for more than 10 h per day[81,126]	MA: patients consume around 200 calories more than the general population per day[138]	MA: even between episodes, people with bipolar disorder have increased sleep-wake disturbance, similar to patients with insomnia[139]
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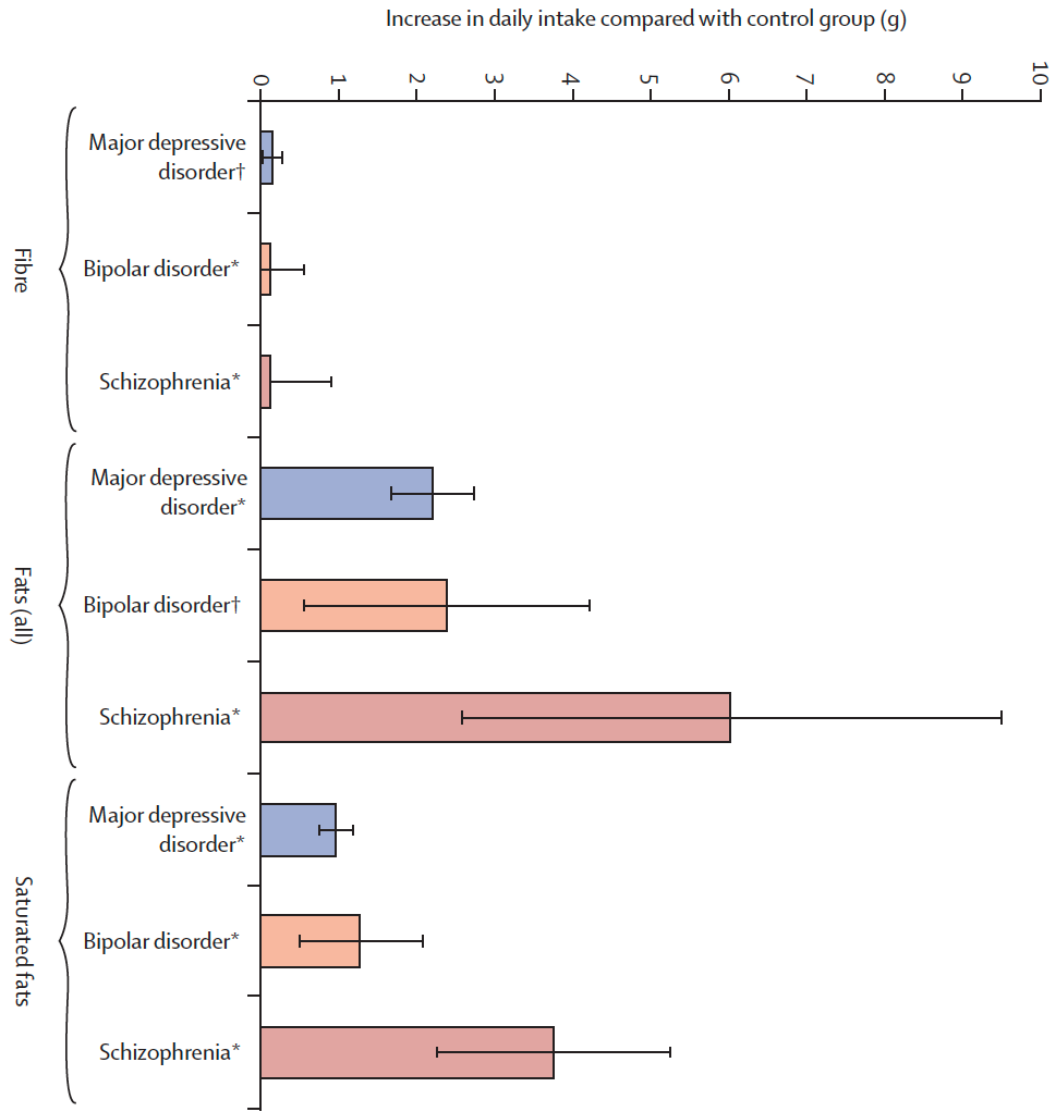

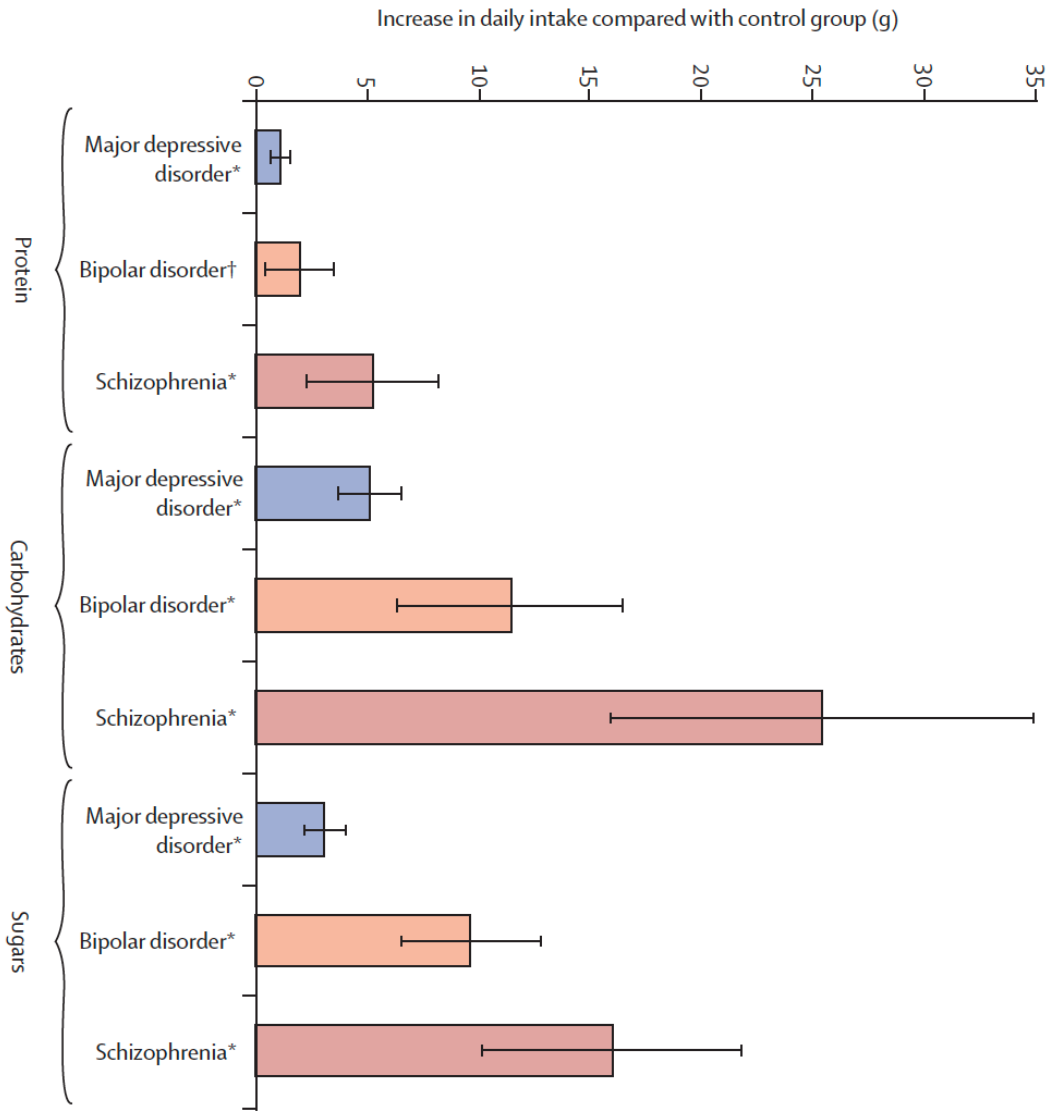

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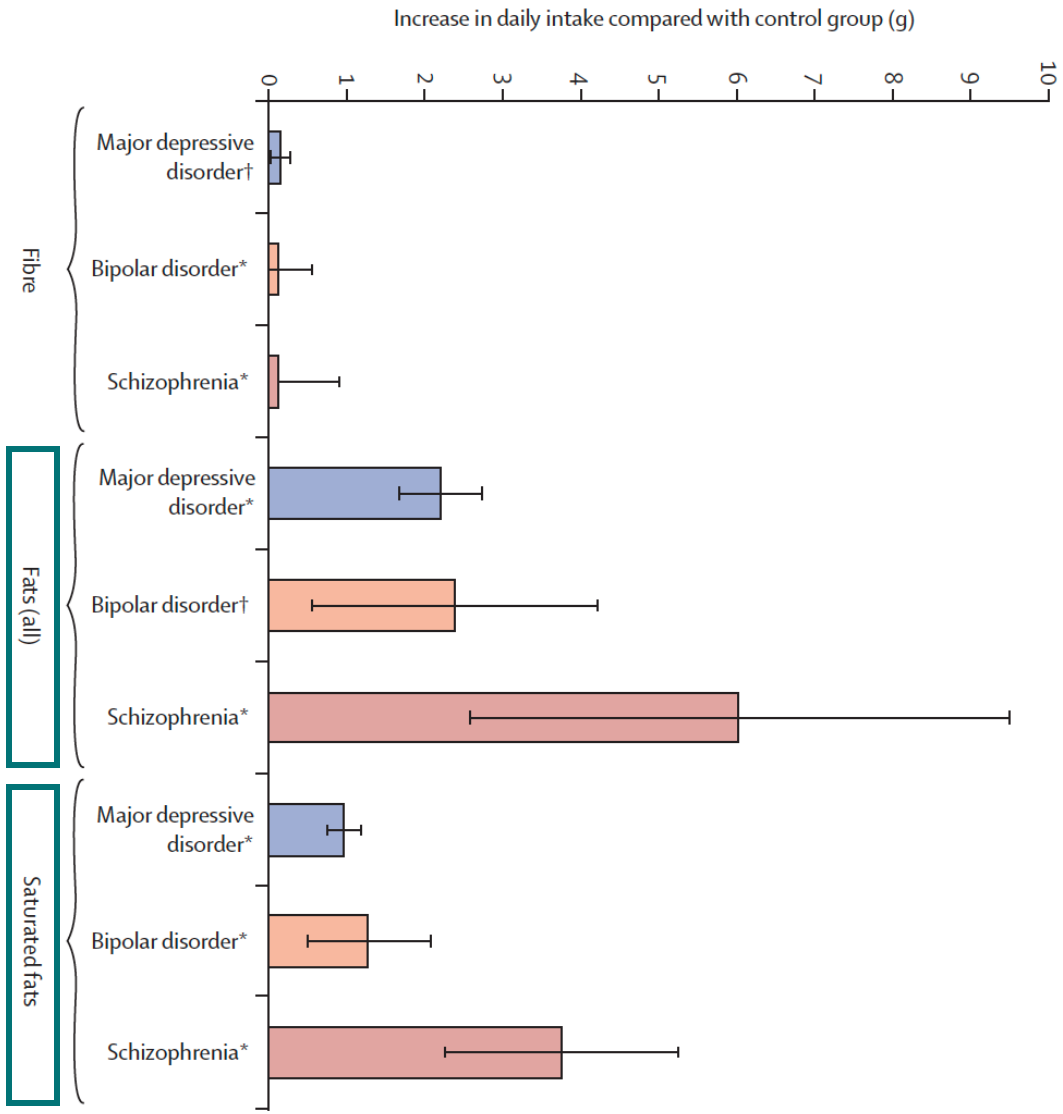

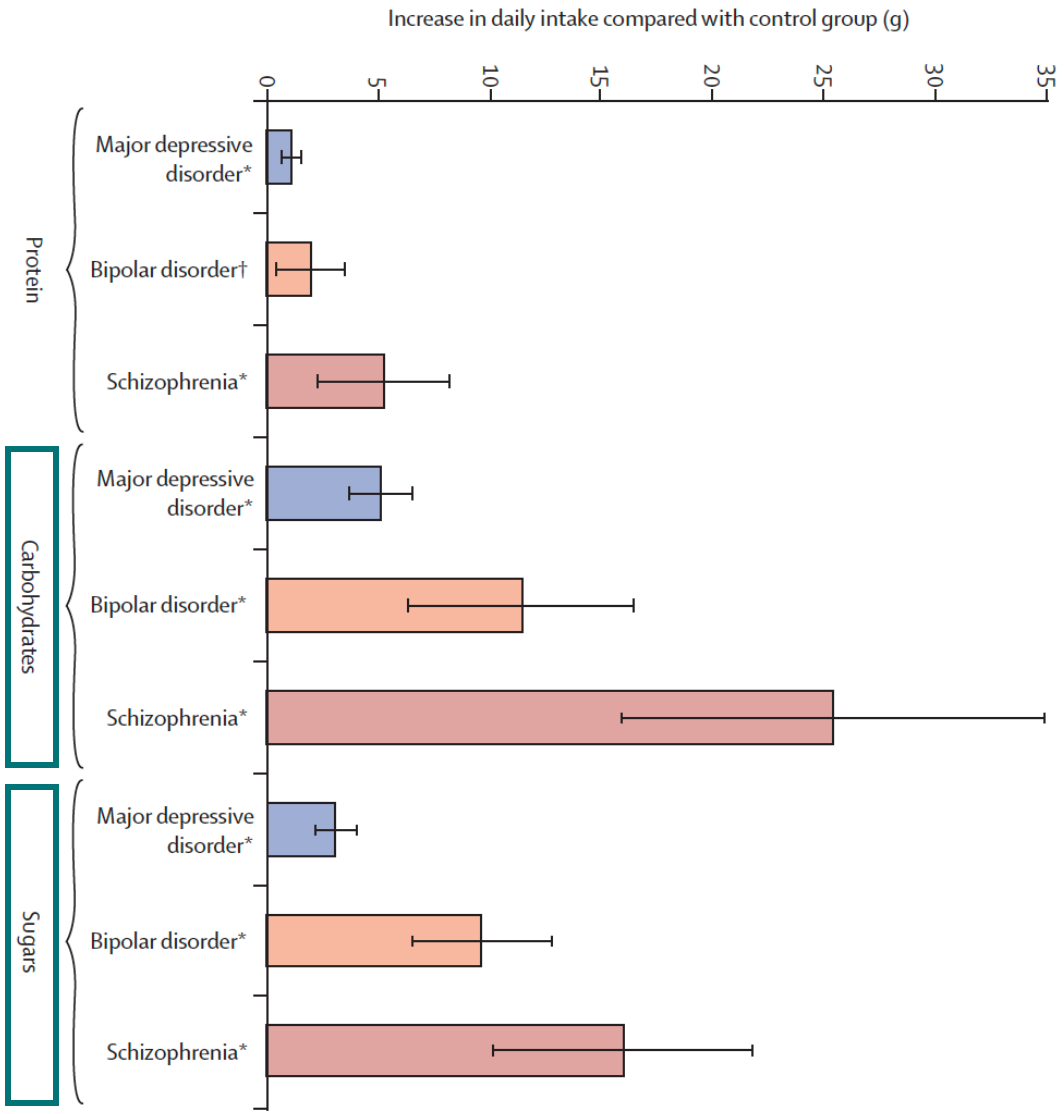

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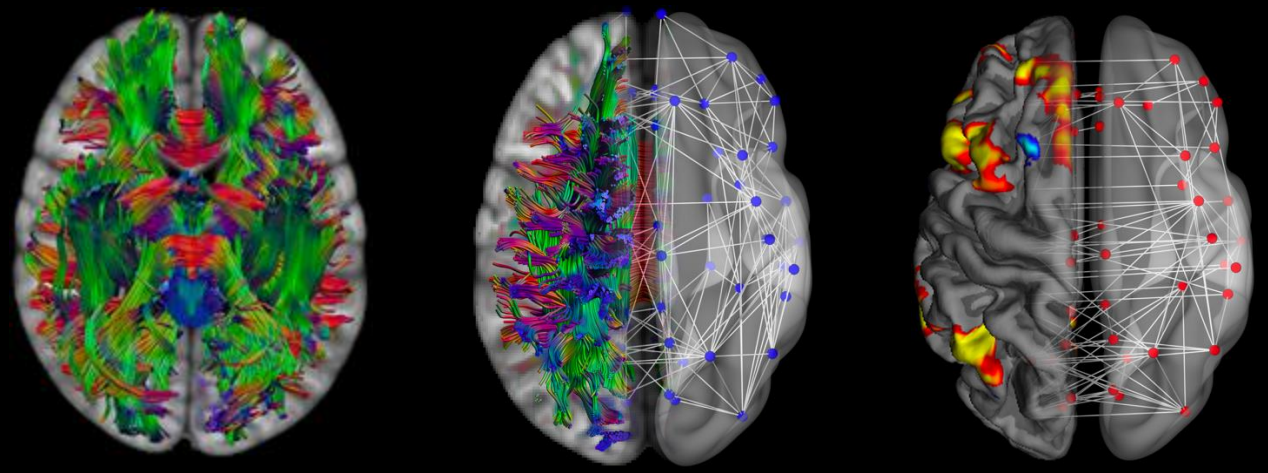


Our recent work investigates how diet & nutrition
may promote resilience in the aging brain

npj | aging

Article

nature portfolio

Investigating nutrient biomarkers of healthy brain aging: a multimodal brain imaging study

Christopher E. Zwilling [1,2], Jisheng Wu [3,4,5] & Aron K. Barbey [1,2,3,4,5,6]

The emerging field of Nutritional Cognitive Neuroscience aims to uncover specific foods and nutrients that promote healthy brain aging. Central to this effort is the discovery of nutrient profiles that can be targeted in nutritional interventions designed to promote brain health with respect to multimodal neuroimaging measures of brain structure, function, and metabolism. The present study therefore conducted one of the largest and most comprehensive nutrient biomarker studies examining multimodal neuroimaging measures of brain health within a sample of 100 older adults. To assess brain health, a comprehensive battery of well-established cognitive and brain imaging measures was administered, along with 13 blood-based biomarkers of diet and nutrition. The findings of this study revealed distinct patterns of aging, categorized into two phenotypes of brain health based on hierarchical clustering. One phenotype demonstrated an accelerated rate of aging, while the other exhibited slower-than-expected aging. A t-test analysis of dietary biomarkers that distinguished these phenotypes revealed a nutrient profile with higher concentrations of specific fatty acids, antioxidants, and vitamins. Study participants with this nutrient profile demonstrated better cognitive scores and delayed brain aging, as determined by a t-test of the means. Notably, participant characteristics such as demographics, fitness levels, and anthropometrics did not account for the observed differences in brain aging. Therefore, the nutrient pattern identified by the present study motivates the design of neuroscience-guided dietary interventions to promote healthy brain aging.

Table 1 | Summary of MRI measures used to derive brain health phenotypes

Brain structure[a]		**Functional connectivity**[b]	
banks superior temporal	para hippocampal	Graph Theory Metrics	Brain Network
caudal anterior cingulate	pars opercularis	Global Efficiency	default mode
caudal middle frontal	pars orbitalis	Local Efficiency	dorsal attention
Cuneus	pars triangularis	Small World Propensity	frontoparietal
Entorhinal	pericalcarine	Strength	limbic
frontal pole	postcentral		motor
Fusiform	posterior cingulate		ventral attention
inferior parietal	precentral		visual
inferior temporal	precuneus		whole brain
Insula	rostral anterior cingulate		
isthmus cingulate	rostral middle frontal	**Brain metabolism**[c]	
lateral occipital	superior frontal	Metabolite	Region
lateral orbitofrontal	superior parietal	Choline	Anterior and Posterior Cingulate Cortex
Lingual	superior temporal	Creatine	
medial orbitofrontal	supramarginal	NAA	
middle temporal	temporal pole		
para central	transverse temporal		

[a]The structural regions were measured for both volumetrics (right and left hemispheres measured separately) and white matter.

[b]Functional connectivity included eight brain networks measured by four separate graph theory metrics.

[c]The concentrations of the three brain metabolites were measured in the same region of the brain. *NAA* is N-acetyl aspartate.

Table 2 | Average brain measurement values for the Accelerated and Delayed Aging phenotypes of brain health

Domain	Measure	Accelerated Aging	Delayed Aging
Brain Structure	Volumetric Regions	0.43	0.48
	Diffusion Tensor Imaging Tracts	0.49	0.61
Brain Metabolism	Magnetic Resonance Spectroscopy	0.441	0.443
Functional Connectivity	Whole Brain	0.45	0.51
	Small World Propensity (network)	0.43	0.52
	Strength (network)	0.57	0.45
	Local efficiency (network)	0.52	0.47
	Global efficiency (network)	0.55	0.43

Values were averaged across all variables listed in Table 1. Before averaging, values for each variable were scaled between 0 and 1.

Table 3 | Nutrient profile of the Delayed Brain Aging phenotype

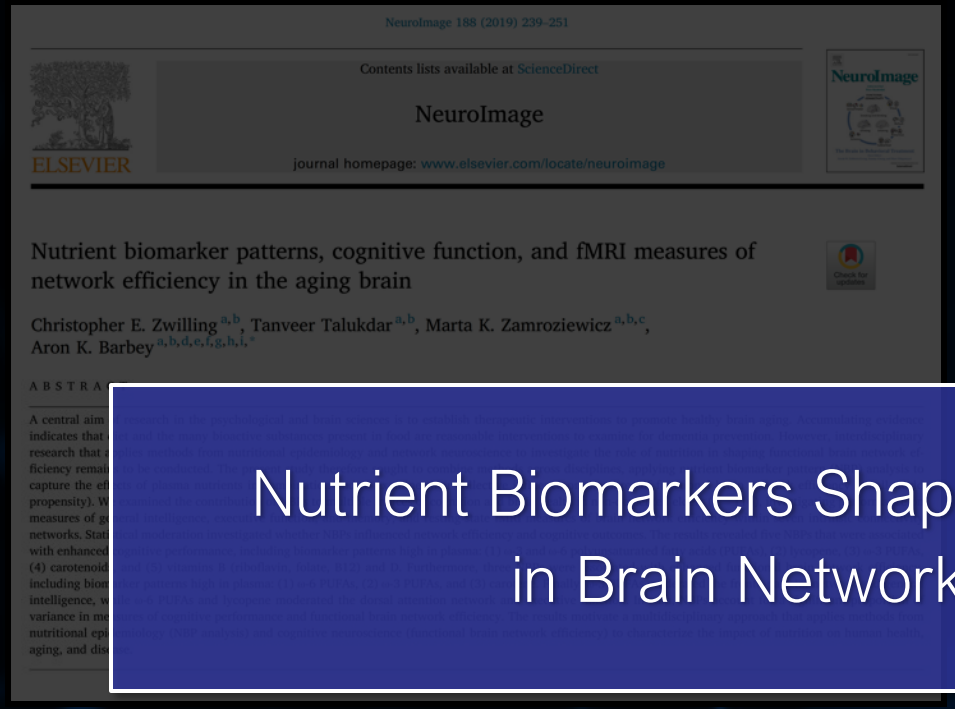
Nutrient Category	Nutrient	Name
Fatty Acids	C18:1n-7	Vaccenic Acid
	C20:1n-9	Gondoic Acid
	C18:3n-3	Alpha Linolenic Acid (ALA)
	C20:5n-3	Eicosapentaenoic Acid (EPA)
	C22:2n-6	Docosadienoic Acid
	C20:2n-6	Eicosadienoic Acid
	C24:0	Lignoceric Acid
Antioxidants and Carotenoids	cis-lutein	Lutein
	trans-lutein	Lutein
	zeaxanthin	Zeaxanthin
Vitamins and Vitamin-Like Compounds	α-tocopherol	Vitamin E
	γ-tocopherol	Vitamin E
	Choline	Choline

These 5 foods can slow aging in your brain, new study finds

A new study published in the journal Nature Aging points to specific nutrients that can contribute to slower aging in the brain. The 100 participants between 65 and 75 years old completed questionnaires, underwent various physical and cognitive tests, MRI scans and had their blood plasma drawn after fasting.

Poll Question 1

Nutrient Biomarkers Shape Individual Differences in Brain Network Organization



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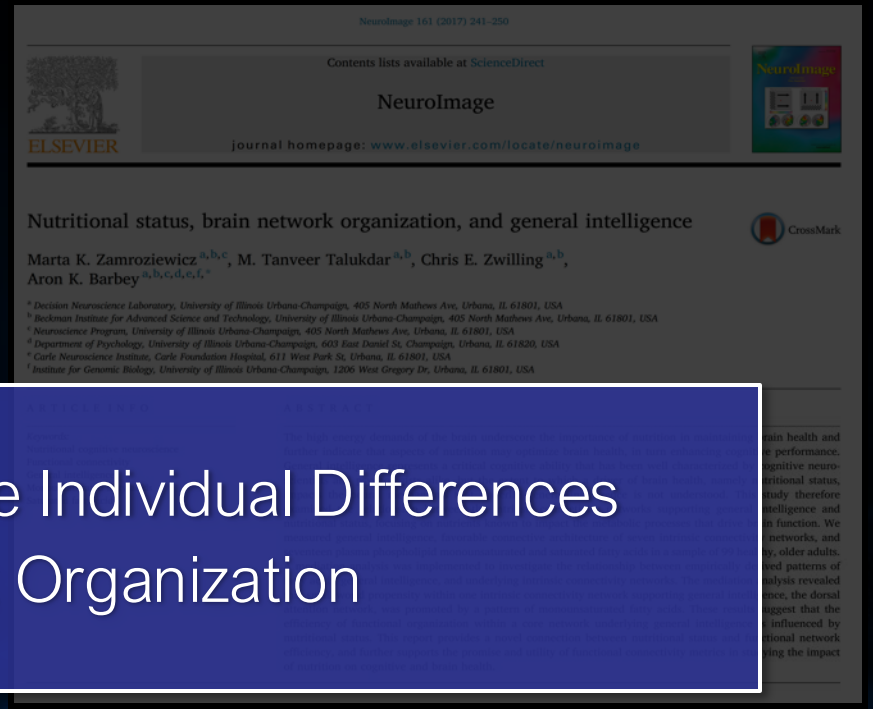

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Nutritional status, brain network organization, and general intelligence

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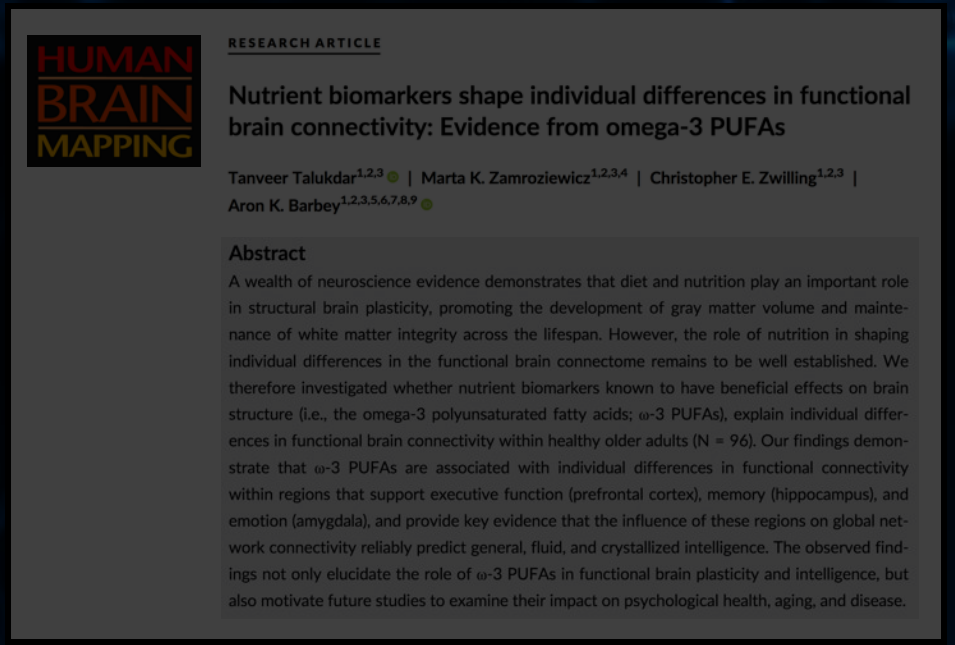

HUMAN BRAIN MAPPING

RESEARCH ARTICLE

Nutrient biomarkers shape individual differences in functional brain connectivity: Evidence from omega-3 PUFAs

Tanveer Talukdar[1,2,3] | Marta K. Zamroziewicz[1,2,3,4] | Christopher E. Zwilling[1,2,3] | Aron K. Barbey[1,2,3,5,6,7,8,9]

Abstract

A wealth of neuroscience evidence demonstrates that diet and nutrition play an important role in structural brain plasticity, promoting the development of gray matter volume and maintenance of white matter integrity across the lifespan. However, the role of nutrition in shaping individual differences in the functional brain connectome remains to be well established. We therefore investigated whether nutrient biomarkers known to have beneficial effects on brain structure (i.e., the omega-3 polyunsaturated fatty acids; ω-3 PUFAs), explain individual differences in functional brain connectivity within healthy older adults (N = 96). Our findings demonstrate that ω-3 PUFAs are associated with individual differences in functional connectivity within regions that support executive function (prefrontal cortex), memory (hippocampus), and emotion (amygdala), and provide key evidence that the influence of these regions on global network connectivity reliably predict general, fluid, and crystallized intelligence. The observed findings not only elucidate the role of ω-3 PUFAs in functional brain plasticity and intelligence, but also motivate future studies to examine their impact on psychological health, aging, and disease.

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Biochemical, Molecular, and Genetic Mechanisms in Nutrition

Integrating Nutrient Biomarkers, Cognitive Function, and Structural MRI Data to Build Multivariate Phenotypes of Healthy Aging

Tanveer Talukdar [1], Christopher E. Zwilling [1], Aron K. Barbey [1,2,3,4,5,6,*]

[1] Decision Neuroscience Laboratory, Beckman Institute, University of Illinois, Urbana, IL, USA; [2] Department of Psychology, University of Illinois, Urbana, IL, USA; [3] Carl R. Woese Institute for Genomic Biology, University of Illinois, Champaign, IL, USA; [4] Department of Bioengineering, University of Illinois, Champaign, IL, USA; [5] Division of Nutritional Sciences, University of Illinois, Champaign, IL, USA; [6] Neuroscience Program, University of Illinois, Champaign, IL, USA

ABSTRACT

Background: Research in the emerging field of nutritional cognitive neuroscience demonstrates that many aspects of nutrition—from entire diets to specific nutrients—affect cognitive performance and brain health.
Objectives: Although previous research has primarily examined the bivariate relationship between nutrition and cognition or nutrition and brain health, this study sought to investigate the joint relationship between these essential and interactive elements of human health.
Methods: We applied a state-of-the-art data fusion method, coupled matrix tensor factorization, to characterize the joint association between measures of nutrition (52 nutrient biomarkers), cognition (Wechsler Abbreviated Test of Intelligence and Wechsler Memory Scale), and brain health (high-resolution MRI measures of structural brain volume) within a cross-sectional sample of 111 healthy older adults, with an average age of 69.1 y, 62% being female, and an average body mass index of 26.0 kg/m^2.
Results: Data fusion uncovered latent factors that capture the joint association between specific nutrient profiles, cognitive measures, and cortical volumes, demonstrating the respects in which these health domains are coupled. A hierarchical cluster analysis further revealed systematic differences between a subset of variables contributing to the underlying latent factors, providing evidence for multivariate phenotypes that represent high and low levels of performance across multiple health domains. The primary features that distinguish between each phenotype were as follows: *1*) nutrient biomarkers for monounsaturated and polyunsaturated fatty acids; *2*) cognitive measures of immediate, auditory, and delayed memory; and *3*) brain volumes within frontal, temporal, and parietal cortexes.
Conclusions: By incorporating innovations in nutritional epidemiology (nutrient biomarker analysis), cognitive neuroscience (high-resolution structural brain imaging), and statistics (data fusion), this study provides an interdisciplinary synthesis of methods that elucidate how nutrition, cognition, and brain health are integrated through lifestyle choices that affect healthy aging.

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ABSTRACT

A central aim of research in the psychological and brain sciences is to establish therapeutic interventions to promote healthy brain aging. Accumulating evidence indicates that diet and the many bioactive substances present in food are reasonable interventions to examine for dementia prevention. However, interdisciplinary research that applies methods from nutritional epidemiology and network neuroscience to investigate the role of nutrition in shaping functional brain network efficiency remains to be conducted. The present study therefore sought to combine methods across disciplines, applying nutrient biomarker pattern (NBP) analysis to capture the effects of plasma nutrients in combination and to examine their collective influence on measures of functional brain network efficiency (small-world propensity). We examined the contribution of NBPs to multiple indices of cognition and brain health in non-demented elders ($n = 116$), investigating performance on measures of general intelligence, executive function, and memory, and resting-state fMRI measures of brain network efficiency within seven intrinsic connectivity networks. Statistical moderation investigated whether NBPs influenced network efficiency and cognitive outcomes. The results revealed five NBPs that were associated with enhanced cognitive performance, including biomarker patterns high in plasma: (1) ω-3 and ω-6 polyunsaturated fatty acids (PUFAs), (2) lycopene, (3) ω-3 PUFAs, (4) carotenoids, and (5) vitamins B (riboflavin, folate, B12) and D. Furthermore, three NBPs were associated with enhanced functional brain network efficiency, including biomarker patterns high in plasma: (1) ω-6 PUFAs, (2) ω-3 PUFAs, and (3) carotene. Finally, ω-3 PUFAs moderated the fronto-parietal network and general intelligence, while ω-6 PUFAs and lycopene moderated the dorsal attention network and executive function. In sum, NBPs account for a significant proportion of variance in measures of cognitive performance and functional brain network efficiency. The results motivate a multidisciplinary approach that applies methods from nutritional epidemiology (NBP analysis) and cognitive neuroscience (functional brain network efficiency) to characterize the impact of nutrition on human health, aging, and disease.

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Saturated fatty acids

ABSTRACT

The high energy demands of the brain underscore the importance of nutrition in maintaining brain health and further indicate that aspects of nutrition may optimize brain health, in turn enhancing cognitive performance. General intelligence represents a critical cognitive ability that has been well characterized by cognitive neuroscientists and psychologists alike, but the extent to which a driver of brain health, namely nutritional status, impacts the neural mechanisms that underlie general intelligence is not understood. This study therefore examined the relationship between the intrinsic connectivity networks supporting general intelligence and nutritional status, focusing on nutrients known to impact the metabolic processes that drive brain function. We measured general intelligence, favorable connective architecture of seven intrinsic connectivity networks, and seventeen plasma phospholipid monounsaturated and saturated fatty acids in a sample of 99 healthy, older adults. A mediation analysis was implemented to investigate the relationship between empirically derived patterns of fatty acids, general intelligence, and underlying intrinsic connectivity networks. The mediation analysis revealed that small world propensity within one intrinsic connectivity network supporting general intelligence, the dorsal attention network, was promoted by a pattern of monounsaturated fatty acids. These results suggest that the efficiency of functional organization within a core network underlying general intelligence is influenced by nutritional status. This report provides a novel connection between nutritional status and functional network efficiency, and further supports the promise and utility of functional connectivity metrics in studying the impact of nutrition on cognitive and brain health.

HUMAN BRAIN MAPPING

RESEARCH ARTICLE

Nutrient biomarkers shape individual differences in functional brain connectivity: Evidence from omega-3 PUFAs

Tanveer Talukdar[1,2,3] | Marta K. Zamroziewicz[1,2,3,4] | Christopher E. Zwilling[1,2,3] | Aron K. Barbey[1,2,3,5,6,7,8,9]

Abstract

A wealth of neuroscience evidence demonstrates that diet and nutrition play an important role in structural brain plasticity, promoting the development of gray matter volume and maintenance of white matter integrity across the lifespan. However, the role of nutrition in shaping individual differences in the functional brain connectome remains to be well established. We therefore investigated whether nutrient biomarkers known to have beneficial effects on brain structure (i.e., the omega-3 polyunsaturated fatty acids; ω-3 PUFAs), explain individual differences in functional brain connectivity within healthy older adults (N = 96). Our findings demonstrate that ω-3 PUFAs are associated with individual differences in functional connectivity within regions that support executive function (prefrontal cortex), memory (hippocampus), and emotion (amygdala), and provide key evidence that the influence of these regions on global network connectivity reliably predict general, fluid, and crystallized intelligence. The observed findings not only elucidate the role of ω-3 PUFAs in functional brain plasticity and intelligence, but also motivate future studies to examine their impact on psychological health, aging, and disease.

ASN American Society for Nutrition

JN THE JOURNAL OF NUTRITION

journal homepage: www.journals.elsevier.com/the-journal-of-nutrition

Biochemical, Molecular, and Genetic Mechanisms in Nutrition

Integrating Nutrient Biomarkers, Cognitive Function, and Structural MRI Data to Build Multivariate Phenotypes of Healthy Aging

Tanveer Talukdar[1], Christopher E. Zwilling[1], Aron K. Barbey[1,2,3,4,5,6,*]

[1] Decision Neuroscience Laboratory, Beckman Institute, University of Illinois, Urbana, IL, USA; [2] Department of Psychology, University of Illinois, Urbana, IL, USA; [3] Carl R. Woese Institute for Genomic Biology, University of Illinois, Champaign, IL, USA; [4] Department of Bioengineering, University of Illinois, Champaign, IL, USA; [5] Division of Nutritional Sciences, University of Illinois, Champaign, IL, USA; [6] Neuroscience Program, University of Illinois, Champaign, IL, USA

ABSTRACT

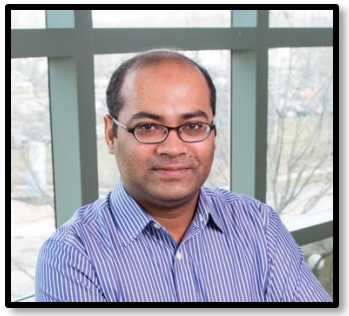
Background: Research in the emerging field of nutritional cognitive neuroscience demonstrates that many aspects of nutrition—from entire diets to specific nutrients—affect cognitive performance and brain health.
Objectives: Although previous research has primarily examined the bivariate relationship between nutrition and cognition or nutrition and brain health, this study sought to investigate the joint relationship between these essential and interactive elements of human health.
Methods: We applied a state-of-the-art data fusion method, coupled matrix tensor factorization, to characterize the joint association between measures of nutrition (52 nutrient biomarkers), cognition (Wechsler Abbreviated Test of Intelligence and Wechsler Memory Scale), and brain health (high-resolution MRI measures of structural brain volume) within a cross-sectional sample of 111 healthy older adults, with an average age of 69.1 y, 62% being female, and an average body mass index of 26.0 kg/m^2.
Results: Data fusion uncovered latent factors that capture the joint association between specific nutrient profiles, cognitive measures, and cortical volumes, demonstrating the respects in which these health domains are coupled. A hierarchical cluster analysis further revealed systematic differences between a subset of variables contributing to the underlying latent factors, providing evidence for multivariate phenotypes that represent high and low levels of performance across multiple health domains. The primary features that distinguish between each phenotype were as follows: *1*) nutrient biomarkers for monounsaturated and polyunsaturated fatty acids; *2*) cognitive measures of immediate, auditory, and delayed memory; and *3*) brain volumes within frontal, temporal, and parietal cortexes.
Conclusions: By incorporating innovations in nutritional epidemiology (nutrient biomarker analysis), cognitive neuroscience (high-resolution structural brain imaging), and statistics (data fusion), this study provides an interdisciplinary synthesis of methods that elucidate how nutrition, cognition, and brain health are integrated through lifestyle choices that affect healthy aging.

RESEARCH ARTICLE

HUMAN BRAIN MAPPING

Nutrient biomarkers shape individual differences in functional brain connectivity: Evidence from omega-3 PUFAs

Tanveer Talukdar[1,2,3] | Marta K. Zamroziewicz[1,2,3,4] | Christopher E. Zwilling[1,2,3] | Aron K. Barbey[1,2,3,5,6,7,8,9]



TANVEER TALUKDAR
Research Scientist

Abstract

A wealth of neuroscience evidence demonstrates that diet and nutrition play an important role in structural brain plasticity, promoting the development of gray matter volume and maintenance of white matter integrity across the lifespan. However, the role of nutrition in shaping individual differences in the functional brain connectome remains to be well established. We therefore investigated whether nutrient biomarkers known to have beneficial effects on brain structure (i.e., the omega-3 polyunsaturated fatty acids; ω-3 PUFAs), explain individual differences in functional brain connectivity within healthy older adults (N = 96). Our findings demonstrate that ω-3 PUFAs are associated with individual differences in functional connectivity within regions that support executive function (prefrontal cortex), memory (hippocampus), and emotion (amygdala), and provide key evidence that the influence of these regions on global network connectivity reliably predict general, fluid, and crystallized intelligence. The observed findings not only elucidate the role of ω-3 PUFAs in functional brain plasticity and intelligence, but also motivate future studies to examine their impact on psychological health, aging, and disease.

ω-3 PUFAS

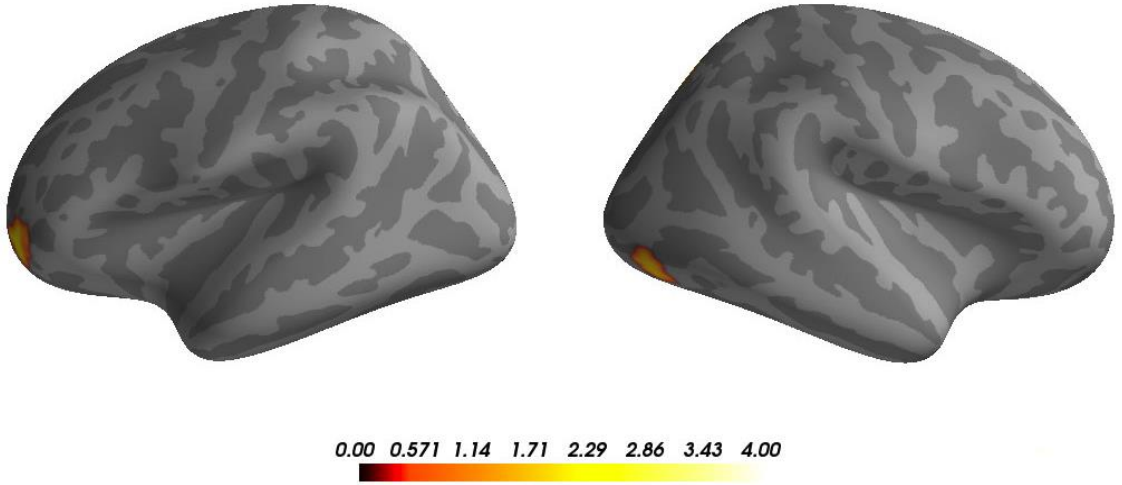
- Evidence suggests that ω-3's may have beneficial effects on cognitive aging

- ω-3's PUFAs are known to contribute to:
  - Structural integrity of neuronal membranes
  - Control inflammation & oxidation
  - Promote energy metabolism

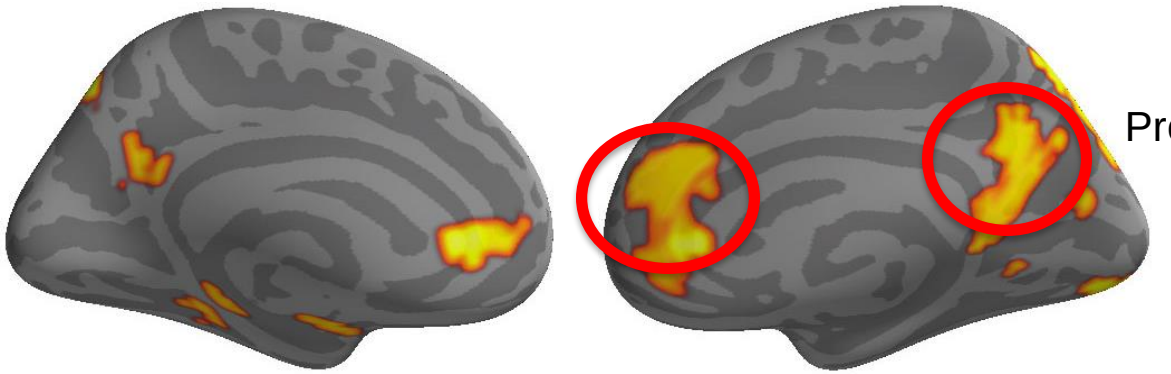
- PUFAs enable the myelination of white matter (Fields, 2005), which is critical for information transmission & synaptic response across long fiber tracks underlying brain networks

- Long chain fatty acids may be critical for healthy lipid composition in myelin & therefore may support information transfer in brain networks

Omega-3 Sensitive Regions (*n* = 96)



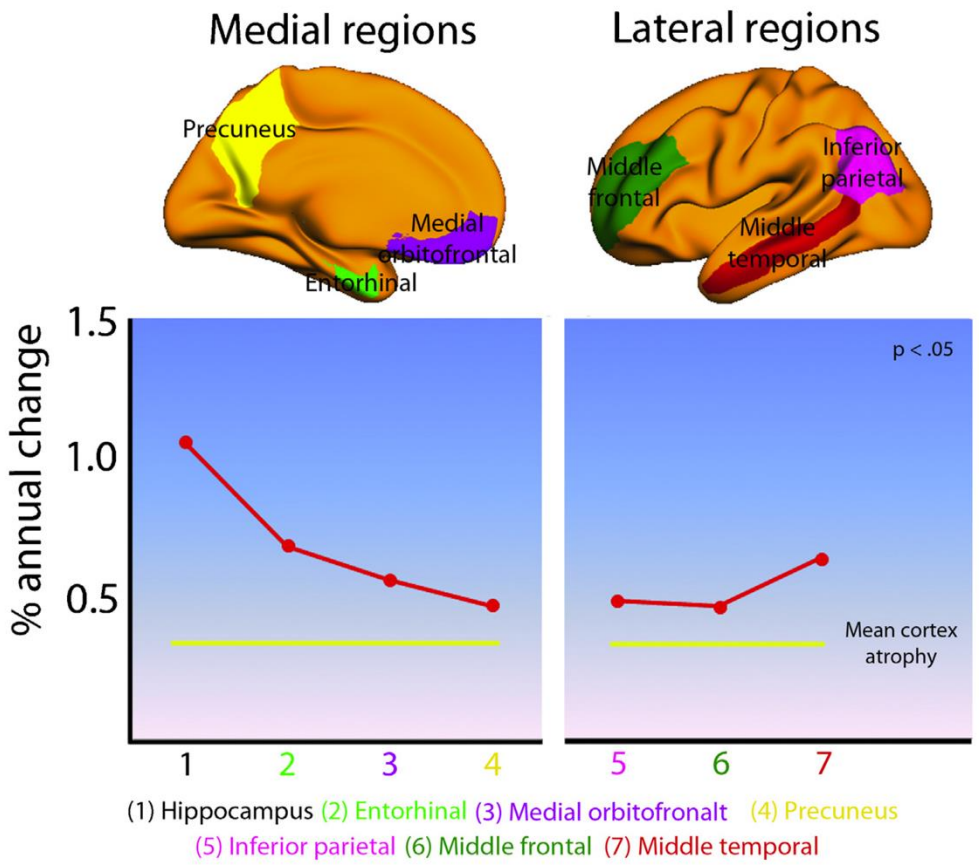
(*p < 0.05; corrected for multiple comparisons*)



Precuneus

Medial Prefrontal Cortex

Age-Related Cortical Atrophy



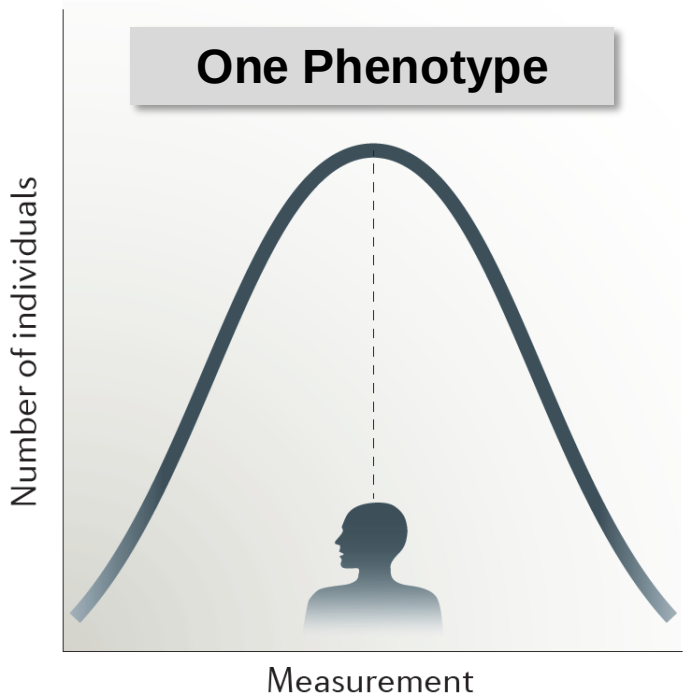
Fjell et al., (2013)

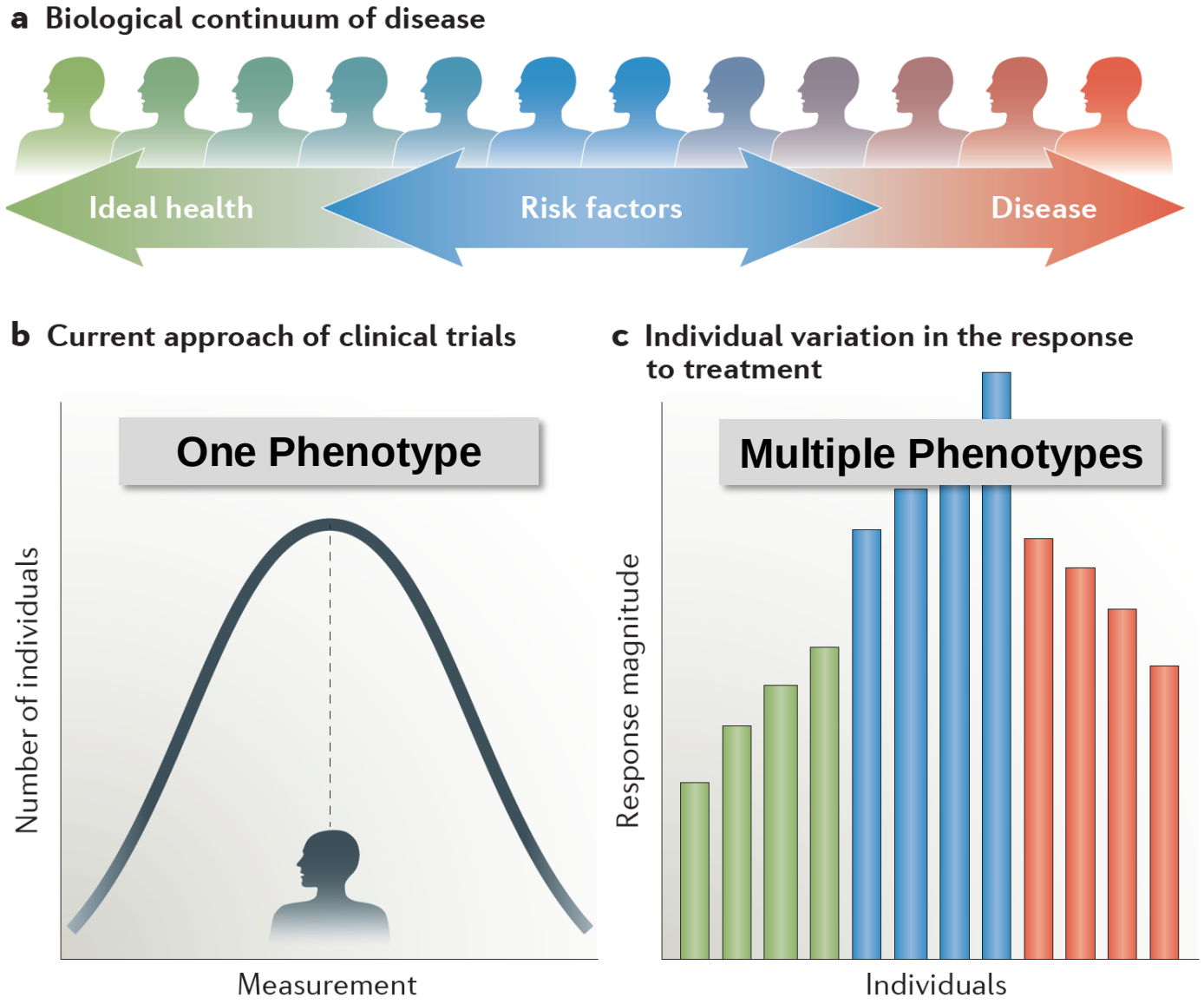
The role of diet & nutrition in shaping individual differences in brain connectivity suggests that the effects of nutrition on brain health are personalized

a Biological continuum of disease

a Biological continuum of disease

b Current approach of clinical trials





Antman & Loscalzo, 2016

Individual Difference Phenotypes

Environments
- Behavioral
- Economic
- Physical
- Social

Raiten et al., 2021

Individual Difference Phenotypes

Environments
- Behavioral
- Economic
- Physical
- Social

Nutrition
- Food Systems
- Nutrient Exposure & Status

Raiten et al., 2021

Individual Difference Phenotypes

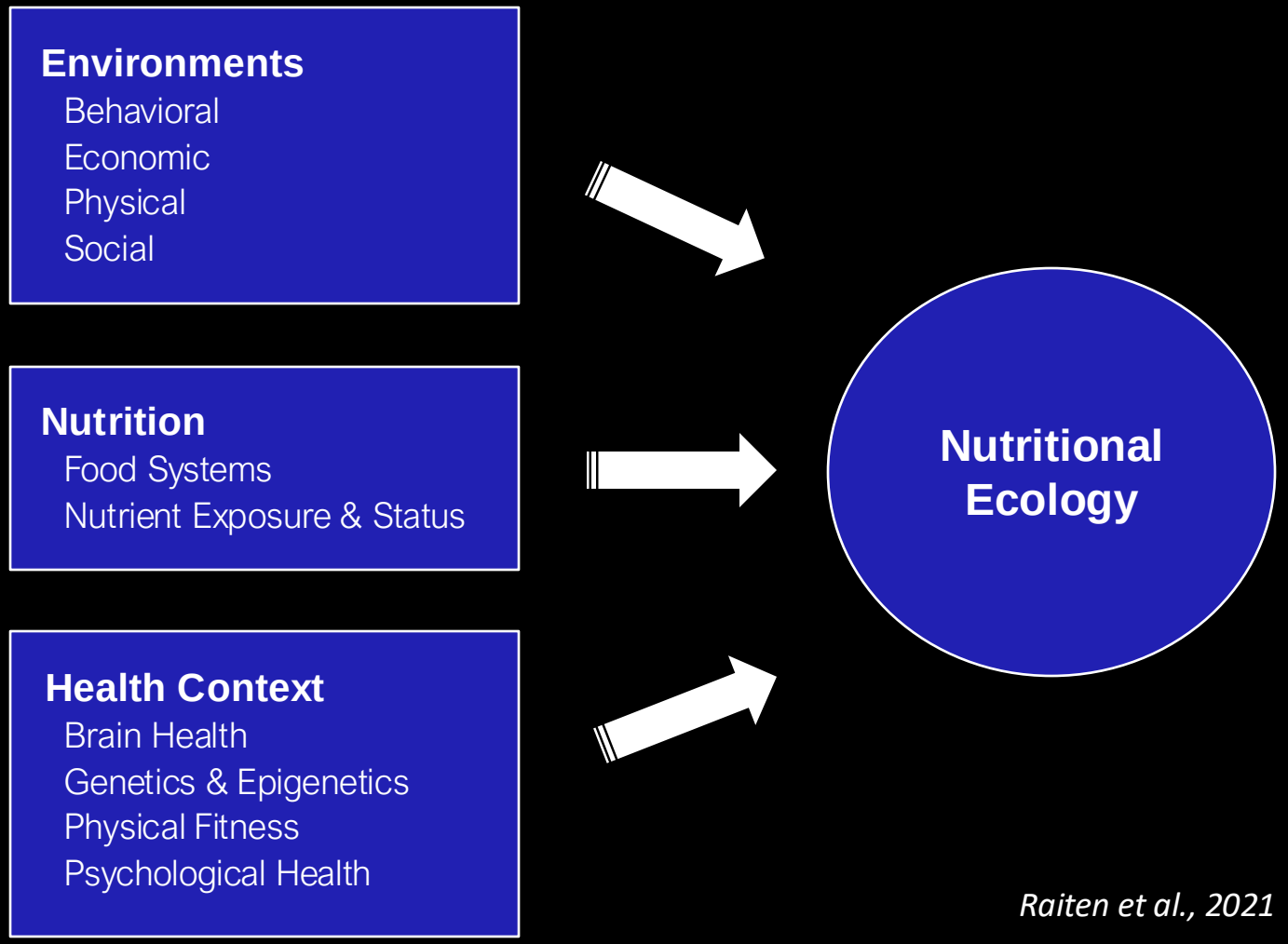
Environments
- Behavioral
- Economic
- Physical
- Social

Nutrition
- Food Systems
- Nutrient Exposure & Status

Health Context
- Brain Health
- Genetics & Epigenetics
- Physical Fitness
- Psychological Health

Raiten et al., 2021

Individual Difference Phenotypes



Raiten et al., 2021

Poll Question 2

We need to build a sound foundation for
personalized solutions to healthy brain aging

Personalized Nutrition

- Step 1: Moderating Factors
  - Approach: Building a Knowledge Base
  - Deliverable: Map of Nutrients & Ecological Factors that Moderate Brain Health

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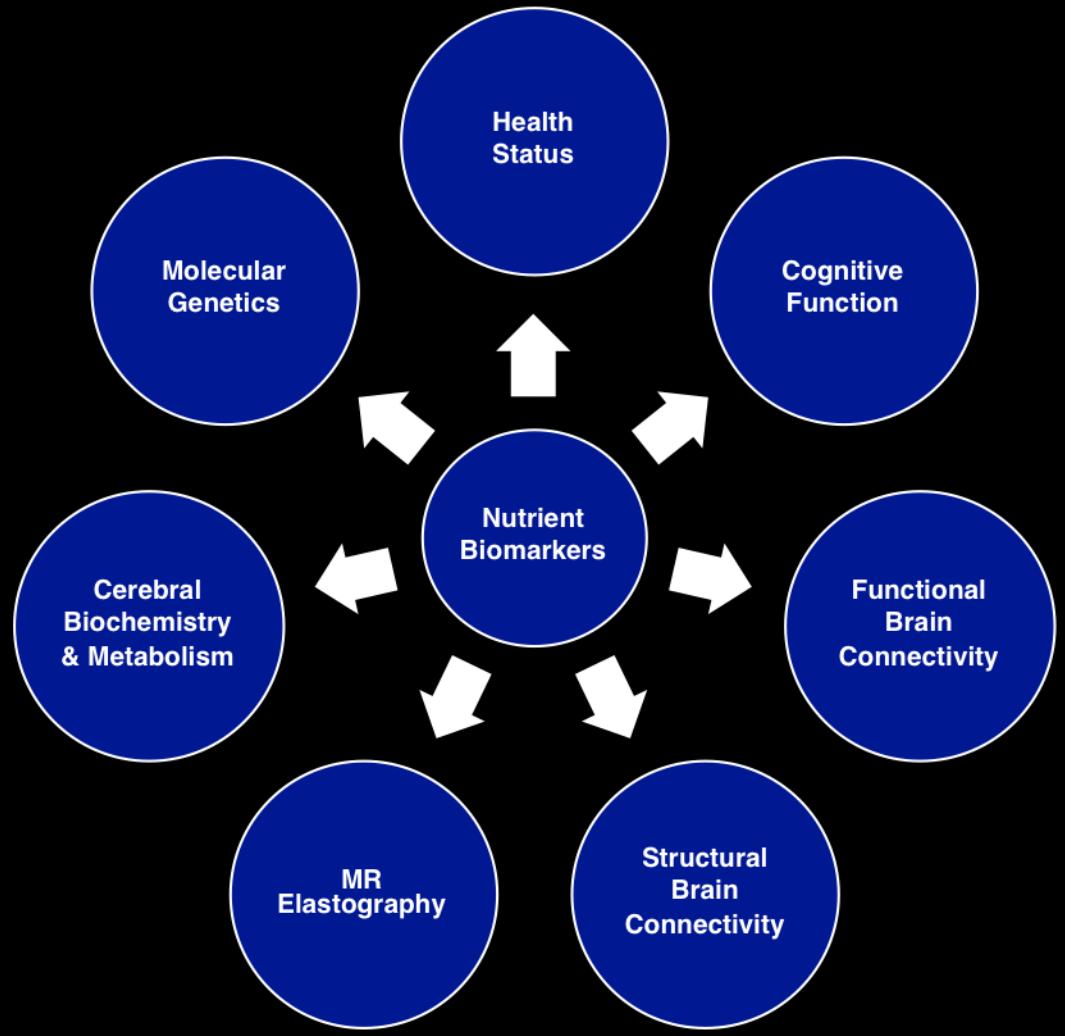
  - Approach: Apply Moderating Factors for Personalized Nutrition
  - Deliverable: Customization Trees for Selected Benefits

  - Approach: Data Science Methods (Machine Learning & AI)
  - Deliverable: Predictive Algorithm with Deeper Personalization Capacity

Building a Knowledge Base for Personalized Nutrition



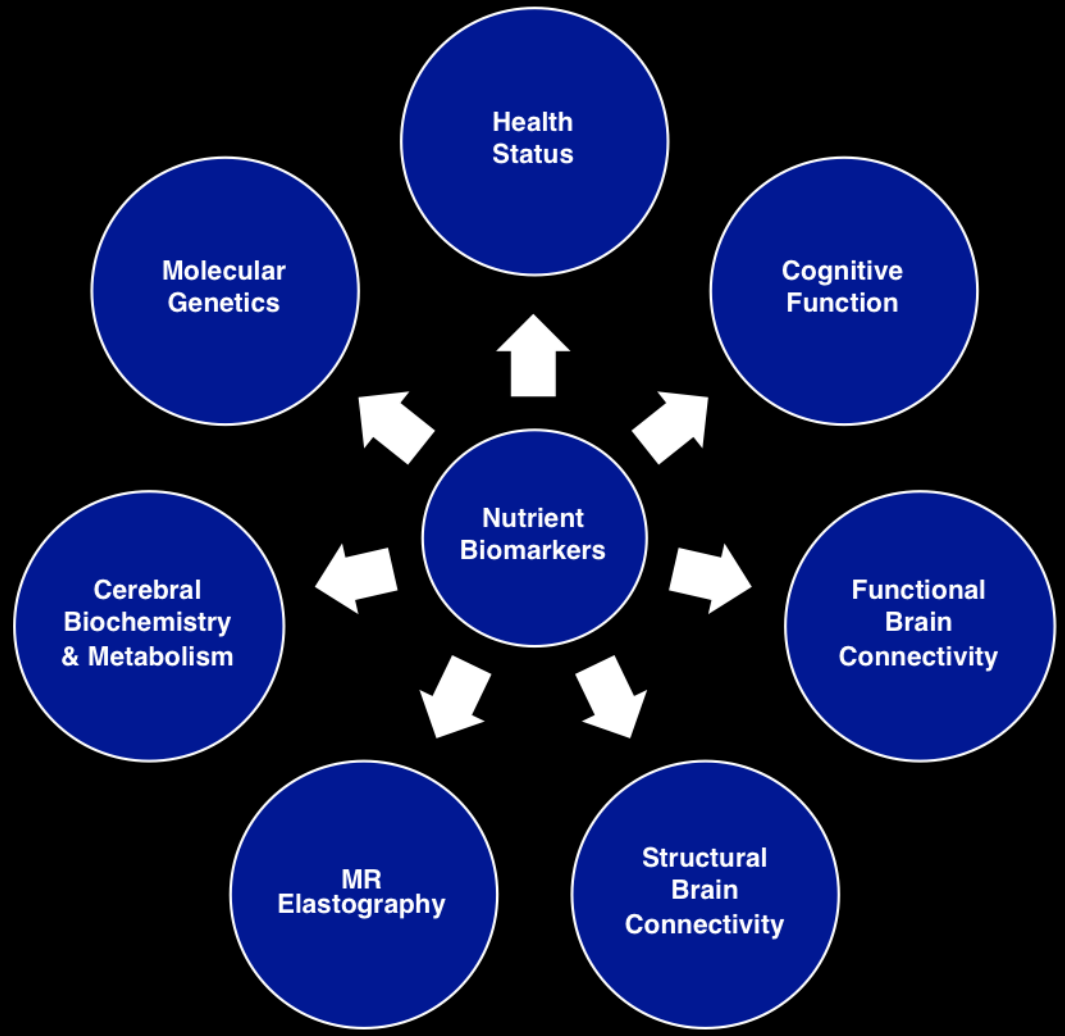
ILLINOIS Nutrition & Healthy Brain Aging Project

- A longitudinal cohort study in healthy older adults (*n* ~ 120; age 65-75)

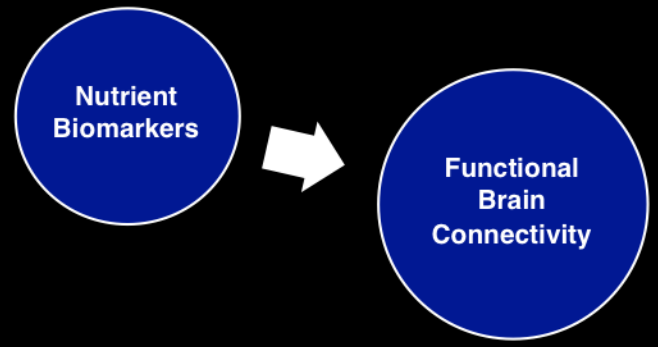
ILLINOIS Nutrition & Healthy Brain Aging Project

- A longitudinal cohort study in healthy older adults (*n* ~ 120; age 65-75)
    1. Nutritional Status: ~ 70 Blood-based biomarkers of nutrition & dietary history questionnaire
    2. Health Status: Physical fitness, daily exercise, social function, & mental health
    3. Cognitive Function: Executive function, learning, & memory
    4. Functional Brain Connectivity: Resting-state functional connectivity
    5. Structural Brain Connectivity: Diffusion tensor imaging of white matter fiber tracts
    6. Cortical Thickness & Brain Volume: Voxel-based morphometry
    7. Cerebral Biochemistry & Metabolism: MR Spectroscopy
    8. Cytoarchitecture Integrity: MR Elastography
    9. Molecular Genetics: Genetic risk factors for cognitive impairment (ApoE4)
    10. Inflammatory Markers: ~ 74 Blood-based biomarkers of inflammation

Building a Knowledge Base for Personalized Nutrition



Building a Knowledge Base for Personalized Nutrition



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CHRIS ZWILLING
Postdoctoral Fellow

Nutrient biomarker patterns, cognitive function, and fMRI measures of network efficiency in the aging brain

Christopher E. Zwilling [a,b], Tanveer Talukdar [a,b], Marta K. Zamroziewicz [a,b,c], Aron K. Barbey [a,b,d,e,f,g,h,i,*]

ABSTRACT

A central aim of research in the psychological and brain sciences is to establish therapeutic interventions to promote healthy brain aging. Accumulating evidence indicates that diet and the many bioactive substances present in food are reasonable interventions to examine for dementia prevention. However, interdisciplinary research that applies methods from nutritional epidemiology and network neuroscience to investigate the role of nutrition in shaping functional brain network efficiency remains to be conducted. The present study therefore sought to combine methods across disciplines, applying nutrient biomarker pattern (NBP) analysis to capture the effects of plasma nutrients in combination and to examine their collective influence on measures of functional brain network efficiency (small-world propensity). We examined the contribution of NBPs to multiple indices of cognition and brain health in non-demented elders ($n = 116$), investigating performance on measures of general intelligence, executive function, and memory, and resting-state fMRI measures of brain network efficiency within seven intrinsic connectivity networks. Statistical moderation investigated whether NBPs influenced network efficiency and cognitive outcomes. The results revealed five NBPs that were associated with enhanced cognitive performance, including biomarker patterns high in plasma: (1) ω-3 and ω-6 polyunsaturated fatty acids (PUFAs), (2) lycopene, (3) ω-3 PUFAs, (4) carotenoids, and (5) vitamins B (riboflavin, folate, B12) and D. Furthermore, three NBPs were associated with enhanced functional brain network efficiency, including biomarker patterns high in plasma: (1) ω-6 PUFAs, (2) ω-3 PUFAs, and (3) carotene. Finally, ω-3 PUFAs moderated the fronto-parietal network and general intelligence, while ω-6 PUFAs and lycopene moderated the dorsal attention network and executive function. In sum, NBPs account for a significant proportion of variance in measures of cognitive performance and functional brain network efficiency. The results motivate a multidisciplinary approach that applies methods from nutritional epidemiology (NBP analysis) and cognitive neuroscience (functional brain network efficiency) to characterize the impact of nutrition on human health, aging, and disease.

Nutrient Biomarkers

Table 2
Study sample serum concentration mean ± standard deviation for 32 Mediterranean Diet nutrients. Units are in μmol/L.

Carotenoids	Vitamins	Fatty Acids
α-Carotene 200 ± 170	A1 (Retinol) 2885 ± 854	Alpha Linolenic Acid (C18.3n.3) 6 ± 3
β-carotene-13-cis 49 ± 26	B2 (Riboflavin) 3.5 ± 3	Stearidonic Acid (C18.4n.3) 2.4 ± 0.9
trans-β-carotene 809 ± 616	B2 (FMN/FAD) 15 ± 6	Sciadonic Acid (C20.3n.3) 1.4 ± 0.6
Cryptoxanthin 172 ± 136	B6 (Plp) 157 ± 161	Eicosapentaenoic Acid (EPA, C20.5n.3) 26 ± 17
trans-Lutein 392 ± 253	B9 (Folate) 21 ± 13	Docosapentaenoic Acid (DPA, C22.5n.3) 23 ± 7
Lycopene-9-cis 229 ± 109	B12 (Cobalamin) 670 ± 600	Docosahexaenoic Acid (DHA, C22.6n.3) 80 ± 33
Lycopene-13-cis 453 ± 236	D 38 ± 13	Linoleic Acid (C18.2n.6) 606 ± 162
trans-Lycopene 883 ± 421	E (α-Tocopherol) 44314 ± 17606	Dihomolinoleic Acid (C20.2n.6) 10 ± 3
Zeaxanthin 85 ± 67	E (γ-Tocopherol) 4891 ± 3302	Dihomo-γ-Linolenic (C20.3n.6) 72 ± 26
		Arachidonic Acid (C20.4n.6) 301 ± 79
		Docosadienoic Acid (C22.2n.6) 0.3 ± 0.1
		Adrenic Acid (C22.4n.6) 11 ± 4
		Docosapentanoic Acid (22.5n.6) 6 ± 3
		MUFA:SFA Ratio 0.3 ± 0.0

Nutrient Biomarker Patterns

Table 3
Factor loadings of 32 Mediterranean Diet nutrients on 10 components.

	ω3/ω6 mix	Lycopene	ω6	ω3	Carotenoid	Carotene	BD	MUFA :SFA	AB	B6
Linoleic Acid (C18.2n.6)	0.82									
Dihomolinoleic Acid (C20.2n.6)	0.80									
Alpha Linolenic Acid (C18.3n.3)	0.78									
Stearidonic Acid (C18.4n.3)	0.63									
Sciadonic Acid (C20.3n.3)	0.57									
Docosadienoic Acid (C22.2n.6)	0.39									
Lycopene-9-cis		0.93								
trans-Lycopene		0.92								
Lycopene-13-cis		0.90								
Docosapentanoic (22.5n.6)			0.87							
Adrenic Acid (C22.4n.6)			0.85							
Arachidonic Acid (C20.4n.6)			0.76							
Dihomo-γ-Linolenic (C20.3n.6)			0.55							
Eicosapentaenoic Acid (EPA)				0.86						
Docosahexaenoic Acid (DHA)				0.76						
Docosapentaenoic Acid (DPA)				0.72						
Zeaxanthin					0.86					
trans-Lutein					0.71					
Cryptoxanthin					0.64					
Vitamin E (α-Tocopherol)					0.48					
trans-β-carotene						0.76				
α-Carotene						0.75				
β-carotene-13-cis						0.61				
Vitamin B12 (Cobalamin)							0.76			
Vitamin D							0.69			
Vitamin B2 (Riboflavin)							0.59			
Vitamin B9 (Folate)							0.57			
MUFA:SFA Ratio								0.77		
Vitamin E (γ-Tocopherol)								−0.58		
Vitamin B2 (FMN/FAD)									0.80	
Vitamin A1 (Retinol)									0.48	
Vitamin B6 (Plp)										0.79
Cumulative Variance	0.11	0.22	0.32	0.40	0.48	0.56	0.63	0.68	0.72	0.76
Proportion Explained	0.15	0.14	0.13	0.12	0.11	0.11	0.09	0.06	0.05	0.05
Cumulative Proportion	0.15	0.29	0.42	0.53	0.64	0.74	0.83	0.90	0.95	1.00

EPA = C20.5n.3; DHA = C22.6n.3; DPA = C22.5n.3; MUFA:SFA = ratio of monounsaturated to saturated fatty acids.

Functional Brain Networks

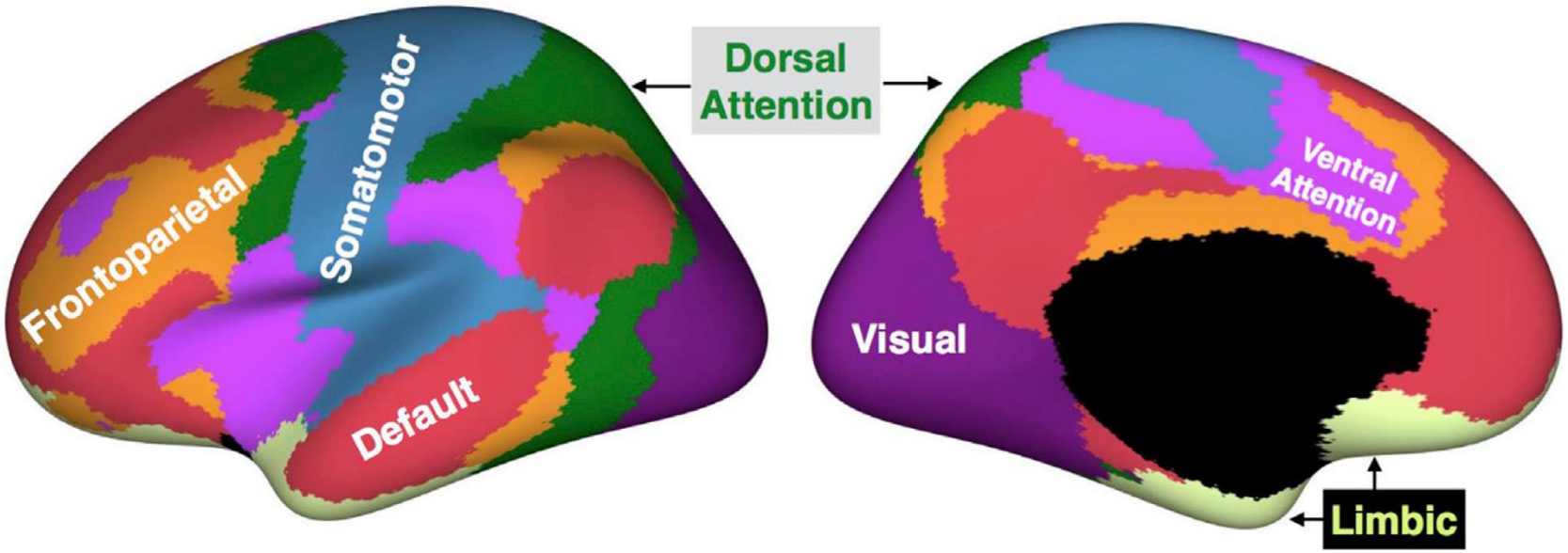

Fig. 1. Seven brain networks for which small-world propensity was computed (Yeo et al., 2011a).

Lycopene Moderates the Association between Dorsal Attentional Network Efficiency & Executive Functions

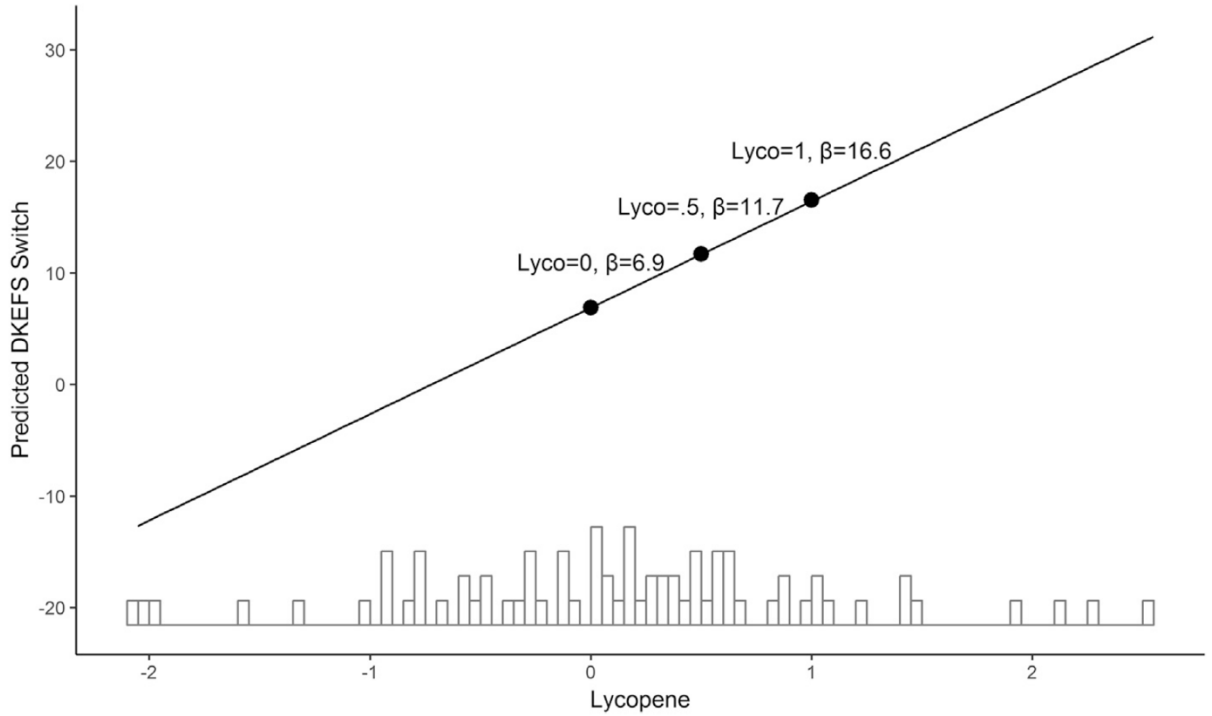

Fig. 5. Conditional coefficients plot illustrating the linear predictive relationship between DKEFS Switch score and dorsal attention network efficiency, for a given level of lycopene. The three dots on the line represent lycopene values of 0, 0.5 and 1.0 and the associated conditional predicted value for the DKEFS. The histogram along the x-axis represents the distribution of lycopene in the sample.

Nutrient Biomarker Patterns

Table 3
Factor loadings of 32 Mediterranean Diet nutrients on 10 components.

	ω3/ω6 mix	Lycopene	ω6	ω3	Carotenoid	Carotene	BD	MUFA :SFA	AB	B6
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EPA = C20.5n.3; DHA = C22.6n.3; DPA = C22.5n.3; MUFA:SFA = ratio of monounsaturated to saturated fatty acids.

Lycopene-9-cis
trans-Lycopene
Lycopene-13-cis

ω-6 PUFAs Moderate the Association between Dorsal Attentional Network Efficiency & Executive Functions

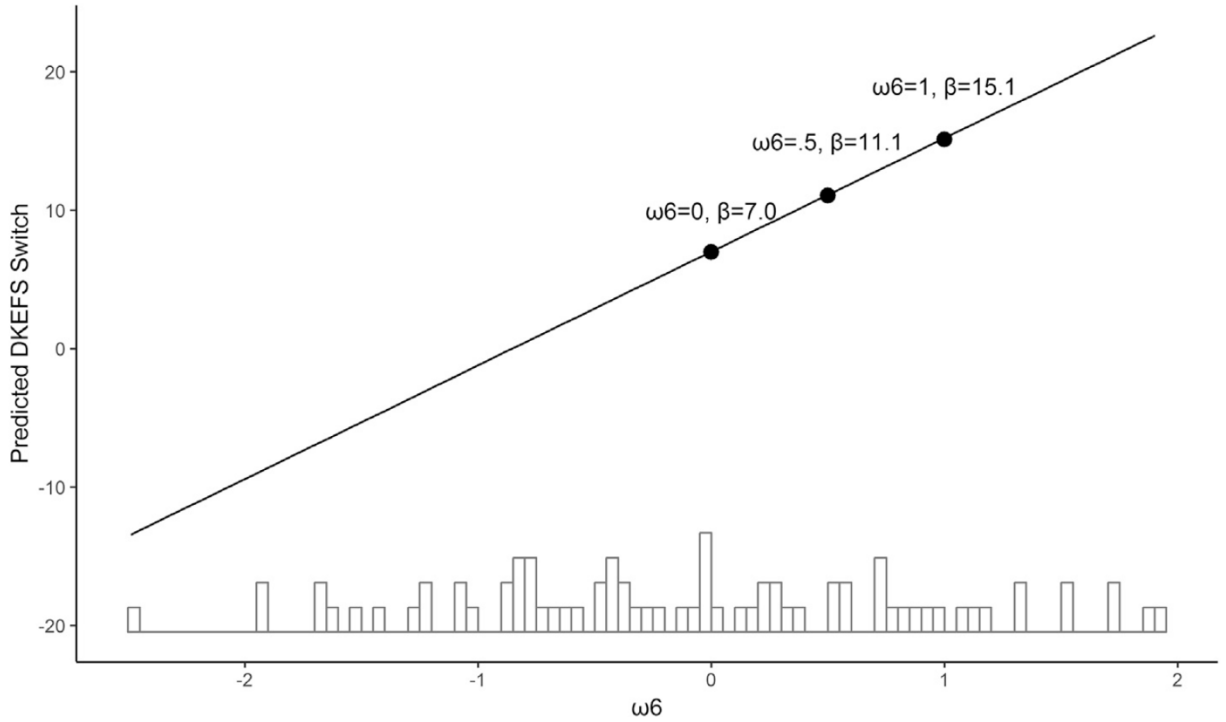

Fig. 4. Conditional coefficients plot illustrating the linear predictive relationship between DKEFS Switch score and dorsal attention network efficiency, for a given level of ω-6. The three dots on the line represent ω-6 values of 0, 0.5 and 1.0 and the associated conditional predicted value for the DKEFS. The histogram along the x-axis represents the distribution of ω-6 in the sample.

Nutrient Biomarker Patterns

Table 3
Factor loadings of 32 Mediterranean Diet nutrients on 10 components.

	ω3/ω6 mix	Lycopene	ω6	ω3	Carotenoid	Carotene	BD	MUFA :SFA	AB	B6
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Adrenic Acid (C22.4n.6)										
Arachidonic Acid (C20.4n.6)										
Dihomo-γ-Linolenic (C20.3n.6)										
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EPA = C20.5n.3; DHA = C22.6n.3; DPA = C22.5n.3; MUFA:SFA = ratio of monounsaturated to saturated fatty acids.

ω-3 PUFAs Moderate the Association between Frontoparietal Network Efficiency & General Intelligence

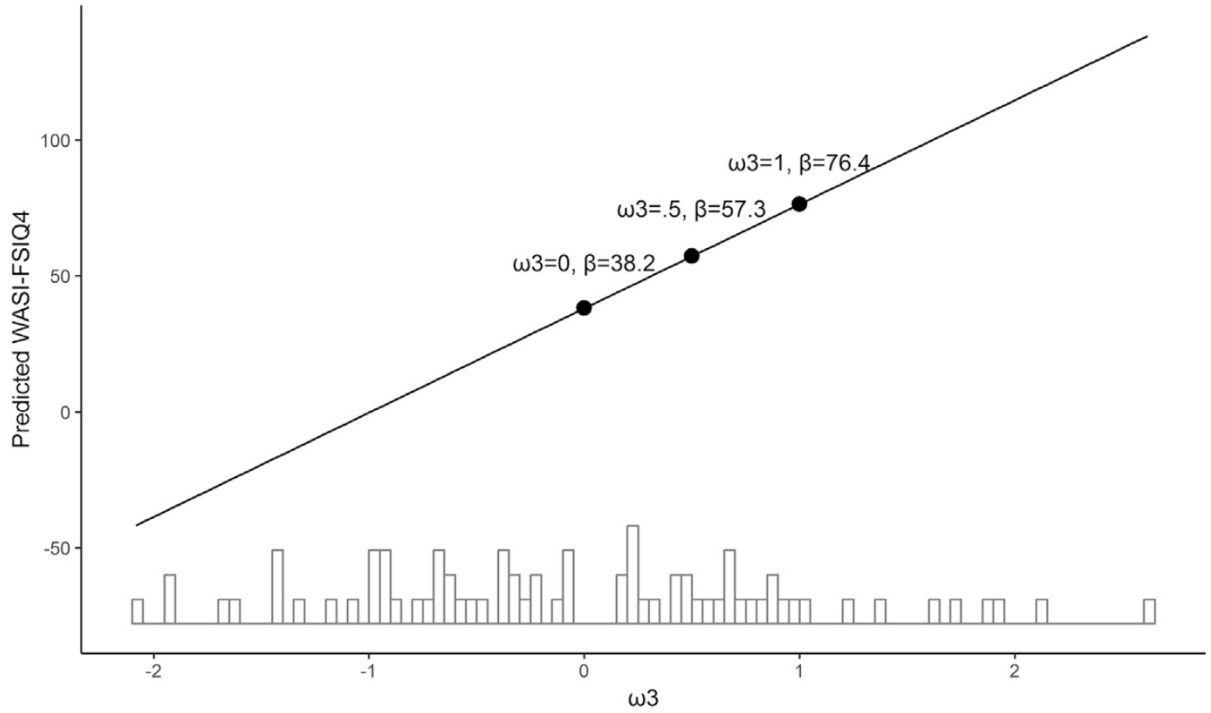

Fig. 3. Conditional coefficients plot illustrating the linear predictive relationship between WASI-FSIQ4 and fronto-parietal network efficiency, for a given level of ω-3. The three dots on the line represent ω-3 values of 0, 0.5 and 1.0 and the associated conditional predicted value for the WASI-FSIQ4. The histogram along the x-axis represents the distribution of ω-3 in the sample.

Nutrient Biomarker Patterns

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Factor loadings of 32 Mediterranean Diet nutrients on 10 components.

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Eicosapentaenoic Acid (EPA)
Docosahexaenoic Acid (DHA)
Docosapentaenoic Acid (DPA)

Nutrition & Brain Network Efficiency

- Findings motivate a multidisciplinary approach that applies methods in nutritional cognitive neuroscience to characterize the impact of nutrition on brain network efficiency in health, aging, & disease

Nutrition & Brain Network Efficiency

- Findings motivate a multidisciplinary approach that applies methods in nutritional cognitive neuroscience to characterize the impact of nutrition on brain network efficiency in health, aging, & disease

Provides a map of nutrient biomarkers that moderate the relationship between brain health & cognition

Poll Question 3

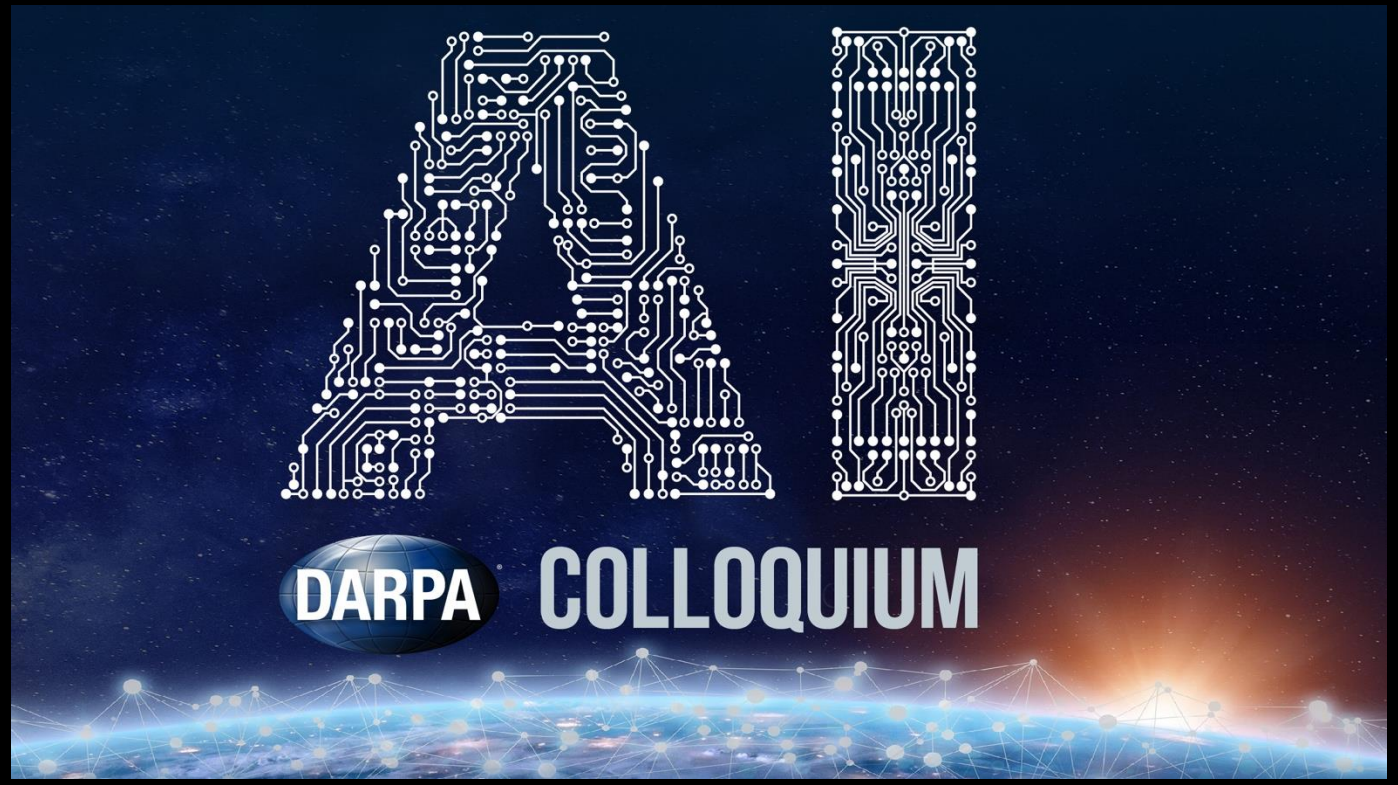
Personalized Nutrition

- Step 1: Moderating Factors
  - Approach: Building a Knowledge Base
  - Deliverable: Map of Nutrients & Ecological Factors that Moderate Brain Health

- Step 2: Personalization
  - Approach: Apply Moderating Factors for Personalized Nutrition
  - Deliverable: Customization Trees for Selected Benefits

  - Approach: Data Science Methods (Machine Learning & AI)
  - Deliverable: Predictive Algorithm with Deeper Personalization Capacity

DARPA's AI Next Campaign



Teaching AI to Leverage Overlooked Residuals (TAILOR)

Dr. Adam Russell

A key challenge for optimizing human performance is the “tyranny of averages:” a common experimental approach that uses between-subject outcomes and group averages (means) to make conclusions about the efficacy of a given intervention. This approach frequently (mis)characterizes individual variance as statistical “noise,” “residuals,” or “error.” The resulting interventions (e.g., diet, physical training regimen, brain stimulation) are, at best, suboptimal and, at worst, deleterious for each person.

Personalized Interventions

To establish & validate a novel modeling framework for the selection & design of personalized training, readiness, & recovery programs that are optimized for an individual's cognitive, nutritional, & neurobiological phenotype

INFERENCE

Intelligent Forecasting through Explanatory Reasoning & Contextual Learning

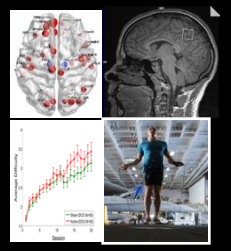
BECKMAN INSTITUTE
University of Illinois

Georgia Tech

http://www.Beckman.Illinois.edu

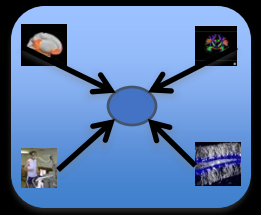
Modeling Approach

Multi-modal data



fMRI, cognitive training, fitness, nutrition, etc.

Dimensionality reduction

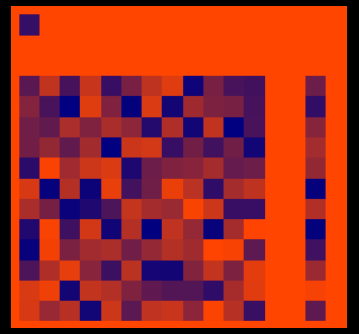


Model common variance across modalities

Identify relationships among factors

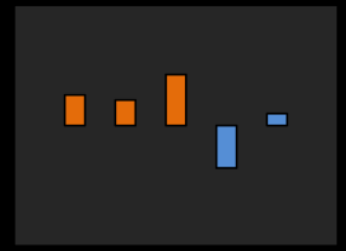
Examine relationships between cognition and underlying biology

Neural network models

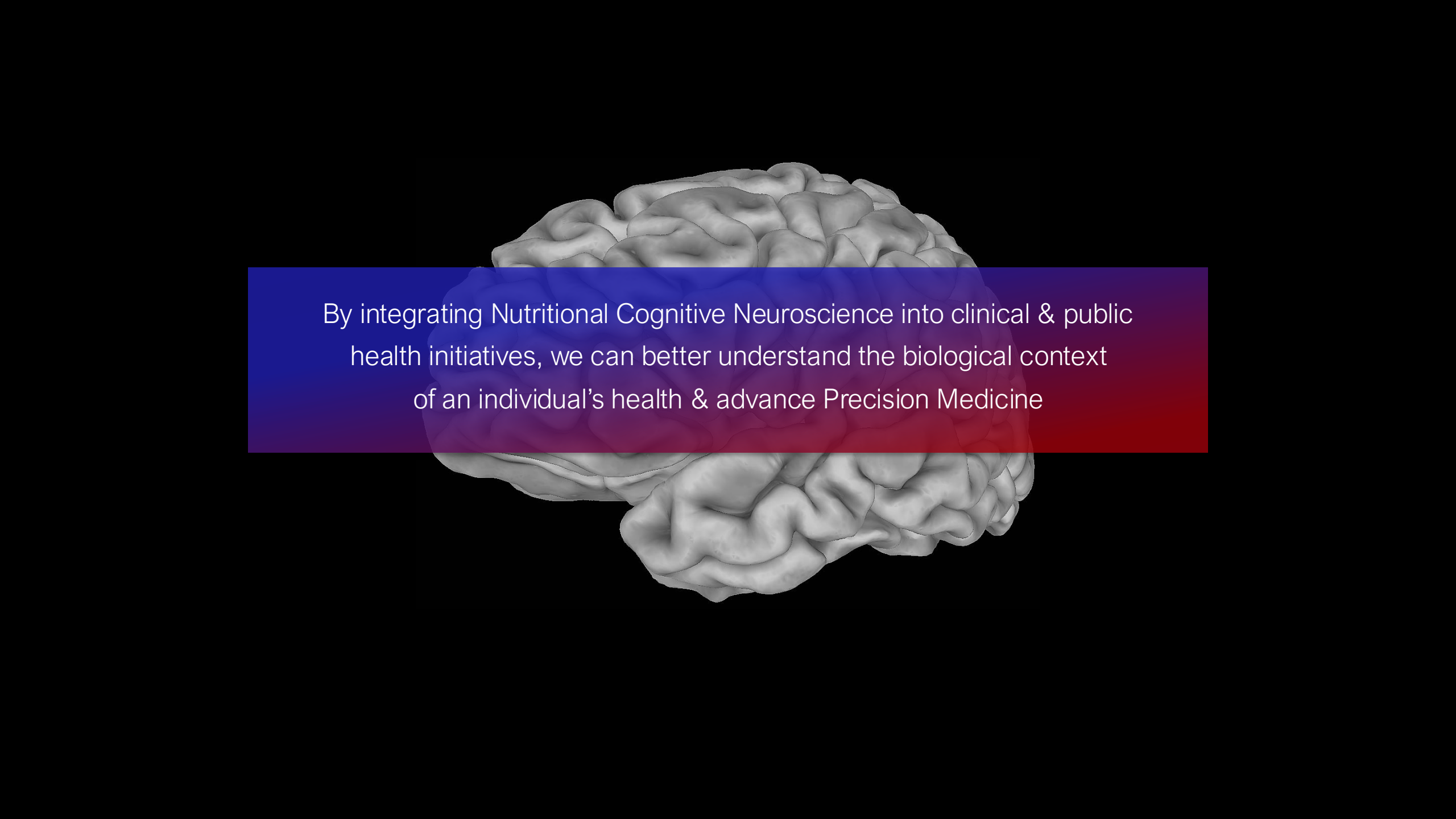


Train to predict individual outcomes

Model effect of interventions



Simulate impact of each intervention on each participant


By integrating Nutritional Cognitive Neuroscience into clinical & public health initiatives, we can better understand the biological context of an individual's health & advance Precision Medicine

Thank You

MoCA Cognition

Session Organizers, Steven Ricciardi & Eduard Coman

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