

## Supplementary Material

### An Inflammation-related Nutrient Pattern is Associated with Both Brain and Cognitive Measures in a Multiethnic Elderly Population

Yian Gu<sup>a,b,c,\*</sup>, Jennifer J. Manly<sup>a,b,d</sup>, Richard P. Mayeux<sup>a,b,c,d</sup> and Adam M. Brickman<sup>a,b,d</sup>

<sup>a</sup>The Taub Institute for Research in Alzheimer's Disease and the Aging Brain, Columbia University, New York, NY, 10032, USA; <sup>b</sup>The Department of Neurology, Columbia University, New York, NY, 10032, USA; <sup>c</sup>The Department of Epidemiology, Joseph P. Mailman School of Public Health, Columbia University, New York, NY, 10032, USA; <sup>d</sup>The Gertrude H. Sergievsky Center, Columbia University, New York, NY, 10032, USA

**Table e1.** Factor loadings of nutrients associated with various nutrient patterns from the reduced rank regression model.

Nutrients in the RRR model <sup>#</sup>	INP*	IL6_NP	CRP_NP	INP32
Pantothenic acid (vitamin B5, mg)	-0.42	-0.38	-0.41	-0.37
Thiamin (vitamin B1, mg)	-0.39	-0.32	-0.35	-0.34
Calcium (mg)	-0.36	-0.26	-0.34	-0.31
Vitamin E (mg)	-0.31	-0.37	-0.28	-0.27
Riboflavin (vitamin B2, mg)	-0.29	-0.14	-0.28	-0.25
Vitamin B6 (mg)	-0.23	-0.10	-0.27	-0.21
Vitamin D (IU)	-0.20	-0.18	-0.16	-0.17
Vitamin A (IU)	-0.18	-0.01	-0.25	-0.17
Total folate (µg)	-0.18	-0.08	-0.21	-0.16
Ω-3 Polyunsaturated fatty acid (PUFA) (g)	-0.16	-0.38	0.00	-0.12
Niacin (vitamin B3, mg)	-0.16	-0.10	-0.17	-0.14
Vitamin C (mg)	-0.11	-0.13	0.00	-0.08
β Carotene (µg)	-0.10	0.05	-0.23	-0.10
β Cryptoxanthin (µg)	-0.09	-0.15	0.04	-0.06
Total carbohydrates (g)	-0.05	-0.01	-0.10	-0.05
Ω-6 PUFA (g)	-0.03	-0.32	0.15	0.00
Iron (mg)	-0.01	0.08	-0.08	-0.02
Lycopene (µg)	0.01	0.03	0.01	0.01
Total protein (g)	0.03	0.06	0.02	0.03
Lutein (µg)	0.05	0.19	-0.12	0.03
Saturated fatty acid (g)	0.07	0.09	0.07	0.06
Monounsaturated fatty acid (MUFA) (g)	0.07	-0.10	0.18	0.07
Vitamin B12 (mg)	0.07	0.12	0.07	0.06

Nutrients in the RRR model <sup>#</sup>	INP*	IL6_NP	CRP_NP	INP32
<b>Cholesterol (mg)</b>	<b>0.31</b>	<b>0.32</b>	<b>0.23</b>	<b>0.26</b>

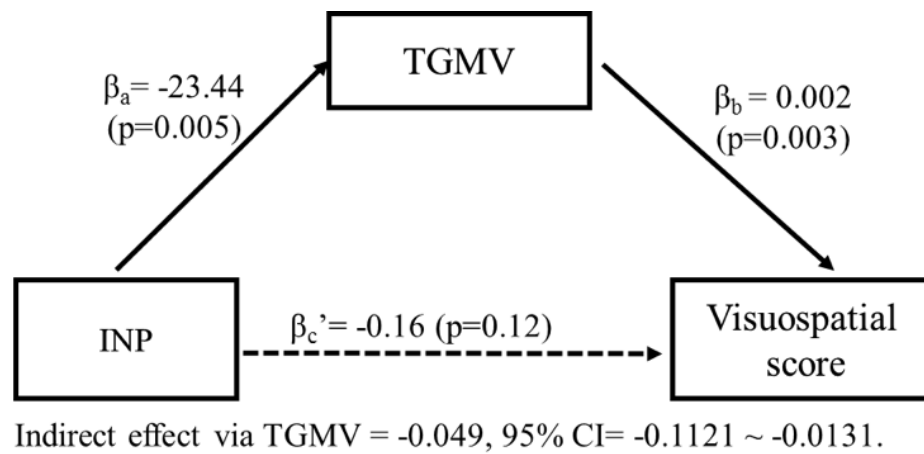
<sup>#</sup>The INP and INP32 were derived with reduced rank regression with both CRP and IL6 entered into the model as the response variables, and with 24 or 32 nutrients as the independent variables, respectively. The CRP\_INP and IL6\_INP were derived with reduced rank regression with CRP and IL6 entered into the model as the response variables, respectively, and with 24 nutrients as the independent variables. \* Factor loadings represent the magnitude and direction of each food group's contribution to a specific dietary pattern score. A positive factor loading indicates that a higher intake of the nutrient contributes to a higher pattern score, while a negative loading indicates a higher intake of the nutrient contributes to a lower pattern score. Factor loadings <0.15 or > 0.15 are highlighted in bold and indicate the corresponding nutrients are the key nutrients for each pattern. Additional nutrients including zinc, manganese, phosphorous, potassium, magnesium, and sodium also contributed to the INP32, all with loadings <-0.15.

Table e2. Sensitivity analyses.

All subjects		INP		CRP_NP		IL6_NP		INP32	
		b	p	b	p	b	p	b	p
Cognition	Mean Cognition	-0.16	0.136	-0.12	0.210	-0.18	0.096	-0.13	0.400
	Language	-0.11	0.372	-0.06	0.549	-0.14	0.232	-0.17	0.341
	Memory	-0.05	0.771	-0.06	0.688	-0.11	0.481	-0.07	0.779
	Speed/executive	-0.28	0.198	-0.22	0.265	-0.22	0.308	-0.18	0.575
	Visuospatial	<b>-0.21</b>	<b>0.038</b>	-0.13	0.137	<b>-0.22</b>	<b>0.027</b>	-0.09	0.553
Brain	TBV (cm <sup>3</sup> )	<b>-36.79</b>	<b>0.023</b>	<b>-40.31</b>	<b>0.004</b>	-21.48	0.175	<b>-52.72</b>	<b>0.027</b>
	TGMV (cm <sup>3</sup> )	<b>-22.90</b>	<b>0.005</b>	<b>-16.70</b>	<b>0.019</b>	<b>-21.69</b>	<b>0.007</b>	<b>-34.96</b>	<b>0.004</b>
	TWMV (cm <sup>3</sup> )	<b>-22.76</b>	<b>0.030</b>	<b>-19.23</b>	<b>0.037</b>	<b>-24.59</b>	<b>0.016</b>	<b>-36.51</b>	<b>0.019</b>
	Mean cortical thickness (cm)	-0.04	0.116	-0.02	0.420	-0.05	0.072	<b>-0.09</b>	<b>0.021</b>
	WMHV (cm <sup>3</sup> )	0.22	0.177	0.08	0.592	<b>0.40</b>	<b>0.013</b>	<b>0.50</b>	<b>0.034</b>
Limited to 248 non-MCI subjects		INP		CRP_NP		IL6_NP		INP32	
		b	p	b	p	b	p	b	p
Cognition	Mean Cognition	<b>-0.28</b>	<b>0.011</b>	<b>-0.21</b>	<b>0.040</b>	<b>-0.26</b>	<b>0.018</b>	<b>-0.34</b>	<b>0.046</b>
	Language	-0.19	0.128	-0.12	0.295	-0.17	0.160	-0.34	0.067
	Memory	-0.30	0.079	-0.29	0.064	-0.25	0.136	-0.41	0.110
	Speed/executive	-0.36	0.127	-0.27	0.212	-0.30	0.205	-0.28	0.437
	Visuospatial	<b>-0.30</b>	<b>0.003</b>	<b>-0.19</b>	<b>0.041</b>	<b>-0.34</b>	<b>0.001</b>	-0.29	0.055
Brain	TBV (cm <sup>3</sup> )	-26.13	0.140	-26.57	0.096	-17.87	0.298	-43.06	0.107
	TGMV (cm <sup>3</sup> )	<b>-19.85</b>	<b>0.027</b>	-12.63	0.120	<b>-21.99</b>	<b>0.013</b>	<b>-30.95</b>	<b>0.022</b>
	TWMV (cm <sup>3</sup> )	-9.17	0.427	-5.21	0.617	-13.63	0.218	-17.09	0.327
	Mean cortical thickness (cm)	-0.06	0.055	-0.04	0.128	-0.05	0.070	<b>-0.12</b>	<b>0.008</b>
	WMHV (cm <sup>3</sup> )	0.30	0.109	0.19	0.242	<b>0.44</b>	<b>0.016</b>	<b>0.63</b>	<b>0.022</b>

Abbreviations: intracranial volume (ICV); total brain volume (TBV); total gray matter volume (TGMV); total white matter volume (TWMV); white matter hyperintensity volume (WMHV).

All cognitive scores were z-scores; brain volumes were adjusted for intracranial volume using a regression model, and residuals were used in the analysis; for WMHV, the Log10(WMHV/ICV) was used. All results were from a model adjusted for Model 3 covariates including age, sex, education, ethnicity, caloric intake, APOE ε4, vascular burden and BMI. All models additional adjusted for ICV for MRI outcome variables. Bold numbers indicate significant associations.



**Fig. (e1). Indirect effect of INP on visuospatial cognition via total gray matter volume.**

Standardized beta weights ( $\beta$ ) were estimated from models adjusted for age, sex, education, ethnicity, APOE genotype, caloric intake, BMI, and vascular burden. Bias-corrected bootstrap 95%CI confidence intervals (95%CI) were estimated from 10000 bootstrap samples using Preacher and Hayes's[1] PROCESS SPSS macro. A 95%CI that does not include 0 is considered as statistically significant, and suggesting that a significant mediating role of brain measures on the relationship between INP on visuospatial cognition. Significant associations are marked using solid lines and dotted lines indicate the association is not significant.

## REFERENCE

- [1] Preacher KJ, Hayes AF. Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. Behavior research methods. 2008; 40(3): 879-91.