

Gut Microbiome Mediates the Relationship Between Healthy Diet and Larger Brain Volume

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INTRODUCTION

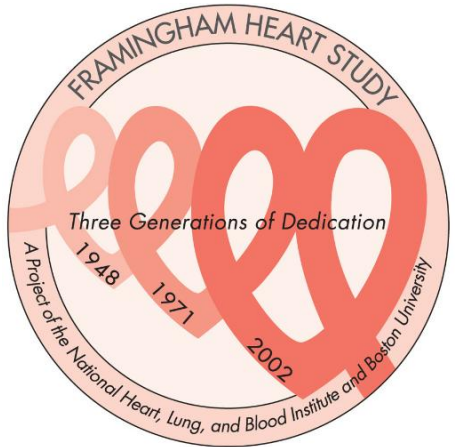
- Emerging evidence links diet and the gut microbiome to brain health, but their interplay at preclinical stages of neurodegeneration remains unclear.
- The Dietary Inflammatory Index (DII) and Dietary Index for Gut Microbiota (DIGM) quantify pro-inflammatory dietary content and microbiota-friendly dietary patterns, respectively.

OBJECTIVE

We investigated how these diet quality indices relate to gut microbial composition and total brain volume in middle-aged adults before clinical cognitive decline.

METHODS

We analyzed 972 dementia-free participants from the Framingham Heart Study (Gen 3, New Offspring Spouses, and the OMNI2 cohorts, exam 3, 2016–2019) with available dietary data, stool 16S rRNA sequencing, and brain MRI. DII and DIGM scores were computed from food-frequency questionnaires. Multivariable linear models assessed the associations between DII and DIGM scores and the relative abundance of gut bacterial genera, adjusting for potential confounders ($FDR < 0.05$). Mediation analysis tested whether specific gut genera explained the associations between DII/DIGM and total brain volume (statistical significance was set at $P < 0.05$).



RESULTS

Table 1. Baseline characteristics of the study participants (N = 972).

Variables	Overall (N = 972)
Age, years	53.2 ± 9.5
Women, n (%)	540 (55.6)
Body mass index, kg/m ²	27.9 ± 5.3
Dietary inflammation index scores	-1.6 ± 2.7
Dietary index for gut microbiota scores	6.1 ± 1.8
Total brain volume (TBV), % of intracranial volume	79.7 ± 2.2

Higher DIGM scores (microbiome-supporting diet) and lower DII scores (anti-inflammatory diet) correlated with increased abundance of putatively beneficial genera – *Faecalibacterium*, *Vitivallis*, *Oscillospira*, *Ruminococcus*, *Clostridium* (family Ruminococcaceae) – and decreased abundance of potentially deleterious genera – *Bacteroides*, *Streptococcus*, *Subdoligranulum*, *Cytophaga*. These diet-related microbial shifts significantly mediated the link between diet and brain volume.

RESULTS

Table 2. Indirect associations through gut microbiome

Exposure	Mediator	Indirect effect (95% CI)	Proportion mediated	P value
Dietary Index Gut Microbiota	<i>Faecalibacterium</i>	0.043 (0.011 to 0.080)	1.01%	0.012
	<i>Oscillospira</i>	0.016 (0.0006 to 0.040)	0.38%	0.044
	<i>Vitivallis</i>	0.020 (0.005 to 0.040)	0.48%	4e-3
	Ruminococcaceae_Ruminococcus	0.031 (0.011 to 0.050)	0.73%	0.024
	Ruminococcaceae_Clostridium	0.036 (0.009 to 0.060)	0.84%	0.012
	<i>Cytophaga</i>	-0.009 (-0.017 to -0.002)	0.21%	0.036
	<i>Streptococcus</i>	-0.094 (-0.130 to -0.065)	2.25%	<0.001
	<i>Bacteroides</i>	-0.361 (-0.059 to -0.21)	2.93%	<0.001
	<i>Subdoligranulum</i>	-0.035 (-0.058 to -0.010)	0.82%	4e-3
	<i>Faecalibacterium</i>	0.036 (0.015 to 0.060)	1.48%	<0.001
Dietary Inflammatory Index	<i>Oscillospira</i>	0.008 (0.0002 to 0.008)	0.26%	0.028
	<i>Vitivallis</i>	0.010 (0.007 to 0.020)	0.42%	<0.001
	Ruminococcaceae_Ruminococcus	0.008 (-0.003 to 0.020)	0.35%	0.190
	Ruminococcaceae_Clostridium	0.015 (0.002 to 0.020)	0.63%	4e-3
	<i>Cytophaga</i>	-0.005 (-0.013 to -0.002)	0.21%	0.048
	<i>Streptococcus</i>	-0.037 (-0.054 to -0.02)	1.49%	<0.001
	<i>Bacteroides</i>	-0.008 (-0.022 to -0.005)	0.38%	0.048
	<i>Subdoligranulum</i>	-0.013 (-0.033 to -0.002)	0.56%	0.044

CONCLUSION

Adherence to an anti-inflammatory, microbiome-friendly diet may foster a gut microbial profile that protects against brain atrophy. A replication in larger samples and representing different ethnicities are needed to explore the potential of dietary interventions targeting the gut–brain axis to preserve brain volume before clinical neurodegeneration.

RESULTS

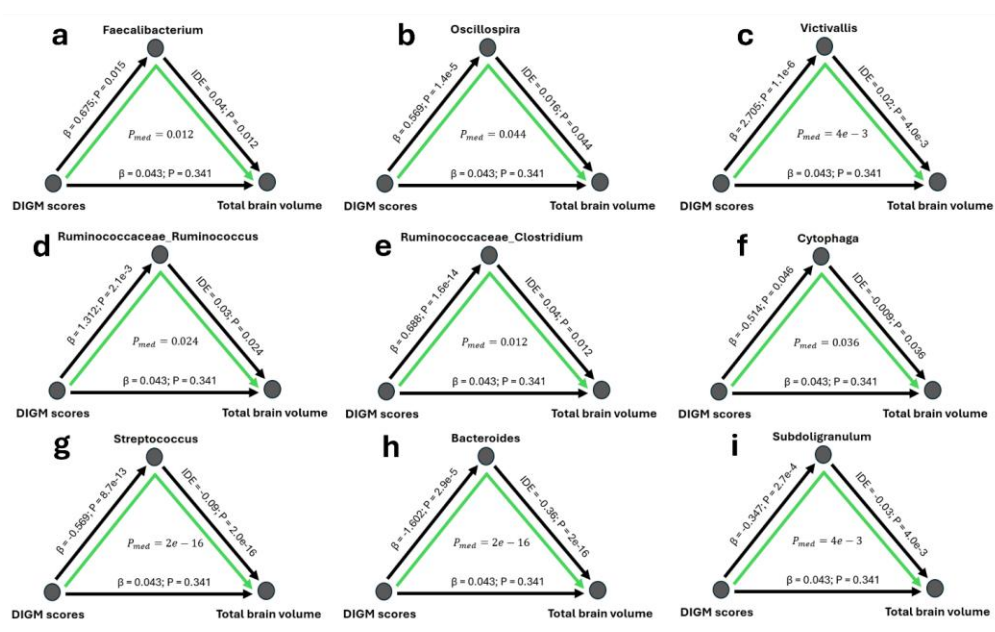


Figure 1. Indirect effect of DIGM on total brain volume via gut microbial taxa. Subpanels (a–e) illustrate that higher DIGM scores (healthier diet) are associated with increased relative abundance of *Faecalibacterium*, *Vitivallis*, *Oscillospira*, *Ruminococcus*, and *Clostridium* (family Ruminococcaceae), which in turn is linked to greater brain volume. Subpanels (f–i) show that higher DIGM scores are associated with lower abundance of *Bacteroides*, *Streptococcus*, *Subdoligranulum*, and *Cytophaga*, which corresponds to larger brain volume.

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