

As shown in Supplementary table 1, there were significant differences ( $P<0.05$ ) in the average daily total energy intake and STT-A score among MCI patients with different levels of E-DII, and the trend from T1 (anti-inflammatory diet group) to T3 (pro-inflammatory diet group) was towards low total energy intake and high STT-A score. There was no statistically significant difference in MMSE, MoCA, VFT, and BNT scores among the MCI patients in each group ( $P>0.05$ ), but MMSE, MoCA, VFT, and BNT scores showed a gradually decreasing trend from T1 to T3. There were no significant statistical differences ( $P>0.05$ ) in other variables at different levels of E-DII.

**Supplementary table 1 Basic characteristics of MCI patients with different E-DII levels**

Variables	N=60	T1(n=60)	T2(n=60)	T3(n=60)	<i>P</i>
		<0.11	0.11~1.04	≥1.04	
Age(years)	71.2±7.40	69.9±7.41	70.7±8.14	72.9±6.61	0.408
BMI(kg/m <sup>2</sup> )	23.8±3.24	24.2±2.86	24.5±4.01	22.7±2.50	0.158
Energy intake(kcal/day)	1433.2±468.55	1651.3±514.41	1373.1±444.31	1275.4±373.63	0.028*
MMSE	26.6±1.96	26.8±1.76	26.6±2.09	26.4±2.08	0.773
MoCA	21.2±2.52	21.6±2.28	21.4±2.60	20.7±2.69	0.514
AVLT-IR	12.3±4.13	12.4±4.59	12.1±4.40	12.3±3.54	0.980
AVLT-LR	2.5 ( 1.0-4.0 )	3.0 ( 1.0-4.0 )	2.0 ( 1.0-4.0 )	2.5 ( 1.0-4.5 )	0.796
AVLT-REC	20.0 (17.0-22.0)	21.0 (18.0-21.0)	20.0 (16.0-21.5)	20.5 (17.0-22.0)	0.470
VFT	12.9±3.71	13.8±3.11	13.2±4.59	11.9±3.17	0.294
BNT	20.3±4.55	21.6±3.60	20.6±4.29	18.6±5.28	0.104
STT-A	89.3±37.88	73.2±23.83	93.2±45.01	101.5±37.59	0.049*
STT-B	253.9±122.66	226.1±66.21	260.8±139.66	274.9±146.63	0.439
Sex, n(%)					0.243
Male	27 ( 45.0 )	11 ( 55.0 )	6 ( 30.0 )	10 ( 50.0 )	0.089
Female	33 ( 55.0 )	9 ( 45.0 )	14 ( 70.0 )	10 ( 50.0 )	
Education level, n(%)					
None	2 ( 3.3 )	0 ( 0.0 )	1 ( 5.0 )	1 ( 5.0 )	
Primary school	18 ( 30.0 )	2 ( 10.0 )	6 ( 30.0 )	10 ( 50.0 )	0.335
Middle school	24 ( 40.0 )	10 ( 50.0 )	8 ( 40.0 )	6 ( 30.0 )	
High school or higher	16 ( 26.7 )	8 ( 40.0 )	5 ( 25.0 )	3 ( 15.0 )	
Income (yuan/m), n (%)					
<3000	0 ( 0.0 )	0 ( 0.0 )	0 ( 0.0 )	0 ( 0.0 )	0.761
3000-5000	10 ( 16.7 )	1 ( 5.0 )	6 ( 30.0 )	3 ( 15.0 )	
5000-10000	23 ( 38.3 )	9 ( 45.0 )	7 ( 35.0 )	7 ( 35.0 )	
>10000	27 ( 45.0 )	10 ( 50.0 )	7 ( 35.0 )	10 ( 50.0 )	
Smoking status, n(%)					0.761
Current	7 ( 11.7 )	3 ( 15.0 )	1 ( 5.0 )	3 ( 15.0 )	
Former	5 ( 8.3 )	2 ( 10.0 )	1 ( 5.0 )	2 ( 10.0 )	
Never	48 ( 80.0 )	15 ( 75.0 )	18 ( 90.0 )	15 ( 75.0 )	

Variables	N=60	T1(n=60)	T2(n=60)	T3(n=60)	p
Alcohol status, n(%)					
Current	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.490
Former	20 (20.0)	8 (25.0)	6 (25.0)	6 (10.0)	
Never	40 (13.3)	12 (15.0)	14 (5.0)	14 (20.0)	
First-degree relatives with AD, n(%)					1.000
Yes	1 (1.7)	0 (0.0)	0 (0.0)	1 (5.0)	0.415
No	59 (98.3)	20 (100.0)	20 (100.0)	19 (95.0)	
Hypertension, n(%)					
Yes	39 (65.0)	15 (75.0)	13 (65.0)	11 (55.0)	0.745
No	21 (35.0)	5 (25.0)	7 (35.0)	9 (45.0)	
Diabetes, n(%)					
Yes	96(25.8)	33(26.6)	34(27.4)	29(23.4)	0.863
No	276(74.2)	91(73.4)	90(72.6)	95(76.6)	
Hyperlipidemia, n(%)					
Yes	6 (10.0)	3 (15.0)	2 (10.0)	1 (5.0)	1.000
No	54 (90.0)	17 (85.0)	18 (90.0)	19 (95.0)	
Coronary heart disease, n(%)					
Yes	3 (5.0)	1 (5.0)	1 (5.0)	1 (5.0)	1.000
No	57 (95.0)	19 (95.0)	19 (95.0)	19 (95.0)	
Cerebrovascular disease, n(%)					
Yes	4 (6.7)	1 (5.0)	2 (10.0)	1 (5.0)	1.000
No	56 (93.3)	19 (95.0)	18 (90.0)	19 (95.0)	

Data are presented as mean  $\pm$  SD, medians (interquartile range, IQR), or numbers (%). Abbreviations: BMI, body mass index; MMSE, Mini Mental State Examination; MoCA, Montreal Cognitive Assessment; AVLT-IR, AVLT immediate recall; AVLT-LR, AVLT long-term recall; AVLT-REC, AVLT recognition; VFT, Verbal Fluency Test; BNT, Boston Naming Test; STT, shape trails test; E-DII, Energy-adjusted Dietary Inflammatory Index; P \* values were calculated with chi-squared tests for categorical variables and ANOVA tests for continuous variables. \* $P<0.05$ , \*\* $P<0.01$ .

### **DNA extraction and 16S rRNA sequencing**

DNA extraction and 16S rRNA gene amplicon sequencing DNA extraction, PCR amplification, and the sequencing of the V3–V4 hypervariable regions of the bacterial 16S rRNA gene based on gut DNA samples were undertaken at the DNA Sequencing and Genomics Laboratory of Sangon BioTech (Shanghai). Following the manufacturer's instructions, total community genomic DNA extraction was performed using an E.Z.N.A. Soil DNA Kit (Omega, USA). PCR was started immediately after the DNA was extracted. The 16S rRNA V3–V4 amplicon was amplified using KAPA HiFi Hot Start Ready Mix (2×) (TaKaRa Bio Inc., Japan). Two polyacrylamide gel electrophoresis-purified universal bacterial 16S rRNA gene amplicon PCR primers were used: the amplicon PCR forward primer (5'-CCTACGGGNGGCWGCAG-3') and the amplicon PCR reverse primer (5'-GACTACHVGGGTATCTAATCC-3'). PCR was performed using a thermal cycler (Applied Biosystems 9700, USA) using the following program: one cycle of denaturing at 95°C for 3 min; five cycles of denaturing at 95°C for 30 s, annealing at 45°C for 30 s, and elongation at 72°C for 30 s; 20 cycles of denaturing at 95°C for 30 s, annealing at 55°C for 30 s, and elongation at 72°C for 30 s; and a final extension at 72°C for 5 min. The PCR products were checked through a separation with electrophoresis in 1% (w/v) agarose gels in Tris, boric acid, and EDTA (TBE) buffer, staining with ethidium bromide, and visualizing under ultraviolet light.

Sequencing was then performed using the Illumina MiSeq system (Illumina MiSeq, California, USA). The raw sequencing reads were detected using Fast QC software to remove the primer region and low-quality sequences. The chimera sequences arising from the PCR amplification were detected and excluded using Mothur (<http://www.mothur.org>) based on the Green Genes database. The high-quality reads that reached a 97% nucleotide similarity were clustered into operational taxonomic units (OTUs) according to the Ribosomal Database Project database. Summaries of the taxonomic distributions of OTUs were constructed using these taxonomies and were used to calculate the relative abundance of microbiota at the phylum and genus taxonomic levels.

### **The calculation method of E-DII**

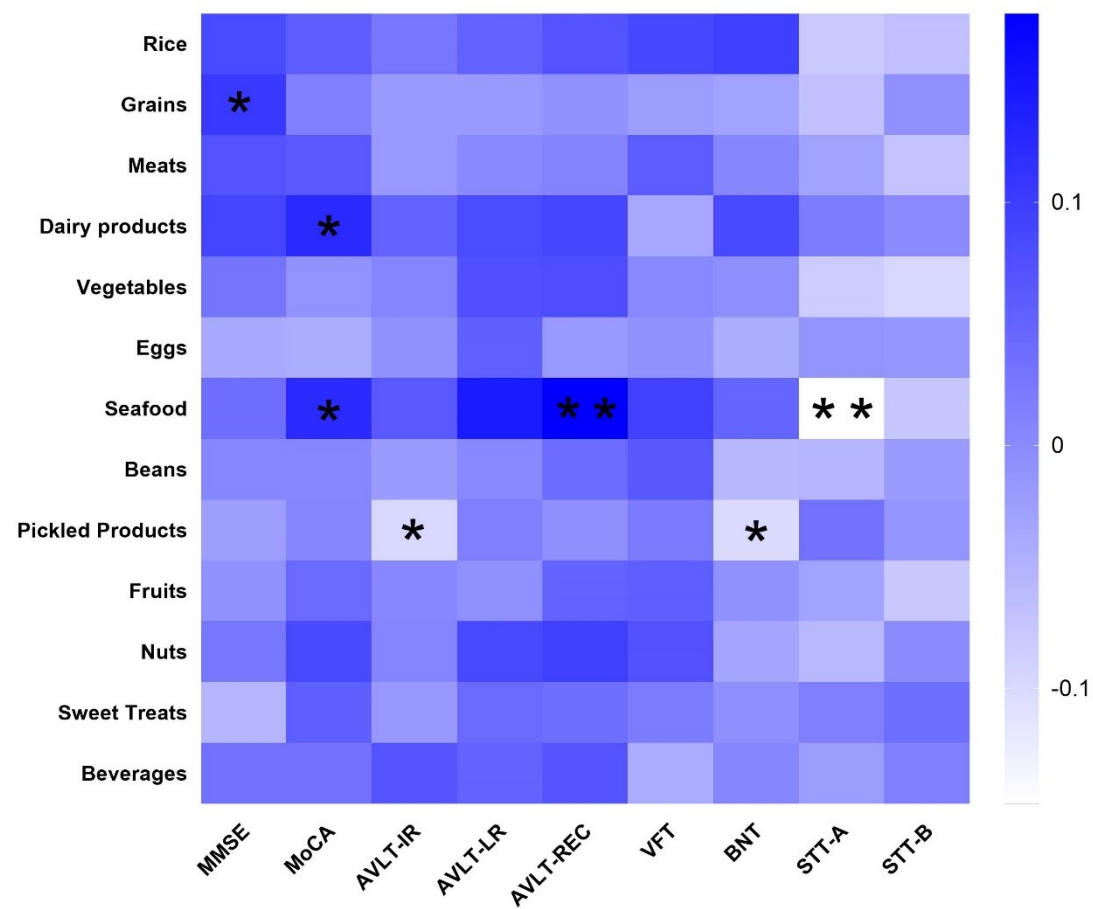
Based on the effects of dietary components on inflammatory biomarkers, they are categorized into three groups: anti-inflammatory, pro-inflammatory, and those with no significant inflammatory effect. Each dietary component is assigned a score reflecting its inflammatory potential according to its impact on inflammatory biomarkers, referred to as the inflammatory effect score.

If a dietary component significantly increases IL-1 $\beta$ , IL-6, TNF- $\alpha$ , and CRP levels or decreases IL-4 and IL-10 levels, it is assigned a score of "+1," indicating a pro-inflammatory tendency. Conversely, if a dietary component significantly reduces IL-1 $\beta$ , IL-6, TNF- $\alpha$ , and CRP levels or increases IL-4 and IL-10 levels, it is assigned a score of "-1," indicating an anti-inflammatory tendency. When a dietary component has no significant effect on inflammatory biomarkers, it is assigned a score of "0."

To minimize randomness caused by using individual baseline intake values, the actual intake of each dietary component is standardized using the mean intake and standard deviation from 11 countries worldwide, converting it into a Z-score. Subsequently, each Z-score is converted into a percentile score based on the distribution of all individual dietary component Z-scores. To minimize the influence of right-skewed distribution, the original percentile score is doubled (i.e., multiplied by 2) and then subtracted by 1 to obtain a percentile score symmetrically distributed around 0. Each symmetrically distributed percentile value is then multiplied by its corresponding inflammatory effect score to obtain the dietary inflammation index (DII) score specific to each dietary component. Finally, the DII scores of all dietary components are summed to obtain an individual's overall DII score.

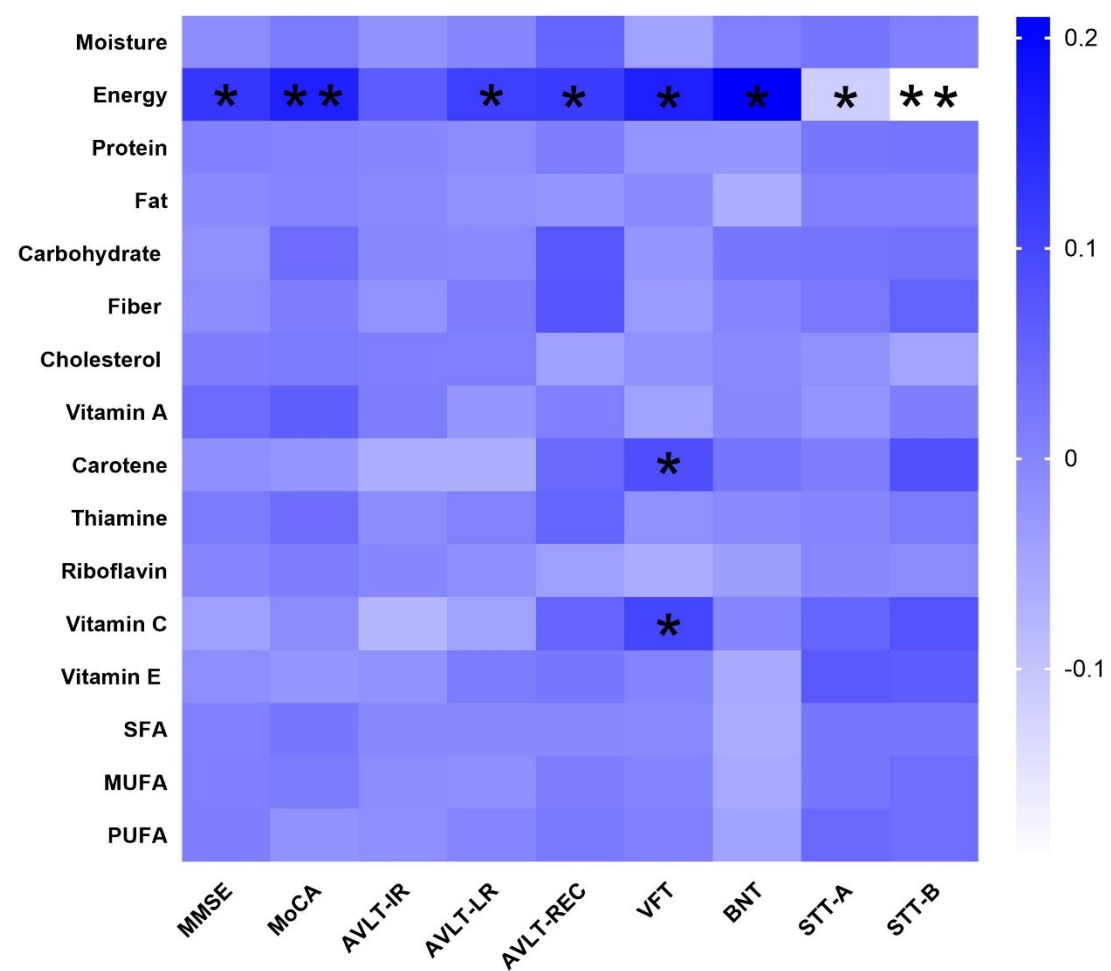
Considering that energy intake influences the amount of nutrients consumed and that total energy intake may mask the specific effects of individual nutrients, this study applied energy standardization to the DII. Before calculating Z-scores, the initial dietary intake values were adjusted to reflect intake per 1000 kcal of energy consumption.

Supplementary Figure 1 showed that the grains were positively correlated with MMSE scores ( $r=0.11$ ), and dairy products and seafood were positively correlated with MoCA scores ( $r=0.13$ ,  $r=0.12$ ), and seafood also was positively correlated with AVLT-REC scores ( $r=0.18$ ). In contrast, the pickled products were negatively correlated with AVLT-IR and BNT scores ( $r=-0.10$ ,  $r=-0.11$ ), and seafood was negatively correlated with STT-A scores ( $r=-0.15$ ).



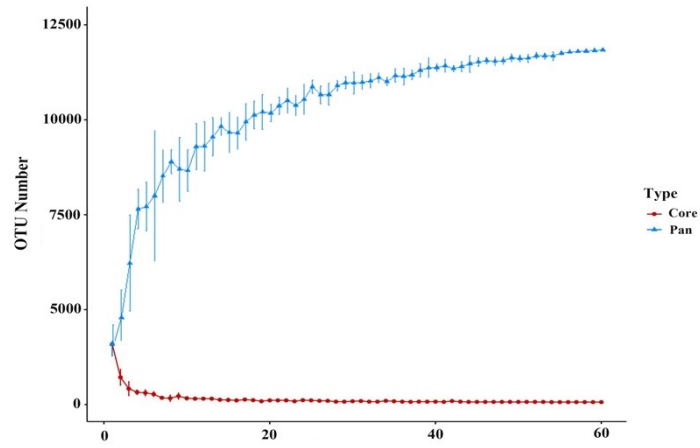
Supplementary Figure 1 Spearman analysis between major food items and cognitive function (\* $P < 0.05$ , \*\* $P < 0.01$ )

As shown in Supplementary Figure 2, energy was positively correlated with MMSE, MoCA, AVLT-LR, AVLT-REC, VFT, and BNT scores ( $r=0.13$ ,  $r=0.16$ ,  $r=0.12$ ,  $r=0.13$ ,  $r=0.16$ ,  $r=0.21$ ). Carotene and Vitamin C were positively correlated with VFT scores ( $r=0.09$ ,  $r=0.10$ ). Conversely, energy was negatively correlated with STT-A and STT-B scores ( $r=-0.12$ ,  $r=-0.20$ ).



Supplementary Figure 2 Spearman analysis between major nutrients and cognitive function  
(\* $P < 0.05$ , \*\* $P < 0.01$ )

As the Supplementary Figure 3 showed that as the sample size increased, the number of OTUs with richness in the three groups approached saturation, indicating that the sample size of this study was sufficient.



**Supplementary Figure 3 The Pan/Core curves of gut microbiota among three groups**