

# Supplementary Material

## Diet Effects on Cerebrospinal Fluid Amino Acids Levels in Adults with Normal Cognition and Mild Cognitive Impairment

**Supplementary Table 1.** Baseline values (mean and standard error) of CSF amino acids ( $\mu\text{M}$ ) and AD biomarkers (pg/ml) by cognitive status for all participants who provided a sample at week 0 (n=40).<sup>1</sup>

Analyte	NC (n=16)	MCI (n=24)	p for diagnosis
Alanine	30.03 (1.91)	28.60 (1.56)	0.57
Arginine	13.12 (0.83)	13.09 (0.68)	0.98
Asparagine	5.99 (0.35)	6.47 (0.28)	0.30
Glutamine	490.87 (15.85)	477.90 (12.88)	0.53
Glycine <sup>2</sup>	0.72 (0.03)	0.75 (0.02)	0.34
Histidine <sup>3</sup>	4.85 (0.44)	3.79 (0.36)	<b>0.07+</b>
Isoleucine <sup>2</sup>	0.61 (0.03)	0.60 (0.03)	0.80
Leucine <sup>2</sup>	1.03 (0.03)	1.04 (0.02)	0.71
Lysine	23.33 (1.32)	25.59 (1.08)	0.19
Methionine	3.39 (0.17)	3.24 (0.13)	0.47
Phenylalanine <sup>2</sup>	0.95 (0.02)	0.92 (0.02)	0.30
Serine	25.45 (0.95)	24.76 (0.78)	0.55
Threonine	27.50 (1.18)	25.53 (0.96)	0.21
Tryptophan <sup>2</sup>	0.25 (0.02)	0.23 (0.02)	0.42
Tyrosine <sup>2</sup>	0.93 (0.02)	0.91 (0.02)	0.44
Valine <sup>2</sup>	1.15 (0.03)	1.17 (0.02)	0.59
A $\beta$ <sub>42</sub>	1176.52 (115.28)	1134.26 (99.46)	0.77
Tau	77.44 (11.00)	95.60 (9.53)	0.23
Ptau 181	61.59 (7.92)	78.33 (6.72)	0.10

<sup>1</sup>Data are presented as least squares means with standard errors of the mean. A mixed model was used to assess the differences in means at baseline for each amino acid by cognitive diagnosis. Gender, ApoE4 status, age, and BMI at baseline were included as covariates and dropped if they were not substantively related to the model ( $p > 0.15$ ). The non-normally distributed amino acids aspartic acid, cysteine, glutamic acid, and proline were not normally distributed after transformations and were removed from the mixed model analyses of baseline differences. p-values in bold indicate significance or trend toward significance; +  $p \leq 0.15$ , \*  $p \leq 0.05$ .

<sup>2</sup> Amino acid value presented as the log transformation.

<sup>3</sup> There was a trend toward a higher baseline histidine concentration in NC versus MCI. MCI, mild cognitive impairment; NC, normal cognition

**Supplementary Table 2.** Change scores in CSF amino acids ( $\mu\text{M}$ ) after four weeks of consumption of the LOW or HIGH diet interventions by cognitive status.

	LOW Diet		HIGH Diet	
	NC (n=6)	MCI (n=8)	NC (n=5)	MCI (n=12)
<b>Amino Acids<sup>1</sup></b>				
Alanine	0.80 (2.24)	1.53 (0.61)	0.15 (1.38)	1.21 (1.72)
Arginine	-0.19 (0.64)	-0.34 (0.86)	-0.21 (0.83)	-3.06 (0.82)
Asparagine	0.25 (0.18)	0.26 (0.12)	-0.20 (0.16)	0.12 (0.34)
Aspartic acid	0.01 (0.01)	0.05 (0.05)	-0.07 (0.13)	0.01 (0.04)
Cystine	-0.01 (0.03)	-0.01 (0.03)	0 (0)	-0.00 (0.0)
Glutamic acid	0.01 (0.02)	0.10 (0.12)	-0.21 (0.21)	-0.06 (0.09)
Glutamine	-16.49 (15.57)	8.64 (10.64)	12.42 (17.6)	17.68 (11.87)
Glycine	-0.44 (0.29)	0.07 (0.28)	-0.14 (0.54)	-0.04 (0.40)
Histidine	0.00 (0.55)	0.21 (0.37)	2.30 (0.58)	-0.10 (0.24)
Isoleucine	0.33 (0.31)	0.35 (0.11)	0.28 (0.17)	0.44 (0.34)
Leucine	0.22 (0.45)	0.45 (0.32)	0.56 (0.41)	0.78 (0.75)
Lysine	0.99 (0.50)	0.81 (0.64)	2.30 (0.93)	1.05 (0.82)
Methionine	0.18 (0.11)	0.36 (0.09)	0.14 (0.12)	0.05 (0.14)
Phenylalanine	0.25 (0.14)	0.77 (0.19)	-0.14 (0.26)	0.35 (0.41)
Proline	0.06 (0.07)	0.02 (0.04)	0.02 (0.05)	-0.01 (0.07)
Serine	-1.19 (0.62)	-0.95 (0.49)	1.10 (0.83)	1.20 (0.59)
Threonine	2.05 (1.54)	0.59 (0.97)	3.14 (0.62)	2.56 (1.40)
Tryptophan	-0.09 (0.08)	0.10 (0.05)	-0.03 (0.11)	0.11 (0.08)
Tyrosine	-0.06(0.22)	0.41 (0.33)	0.25 (0.55)	0.04 (0.45)
Valine	1.15 (0.91)	0.54 (0.47)	1.56 (0.48)	2.04 (1.16)
<b>Amino Acid Metabolites<sup>1</sup></b>				
Citrulline	-0.14 (0.14)	0.04 (0.07)	0.03 (0.10)	-0.12(0.12)
Ornithine	-0.10 (0.30)	-0.19 (0.19)	0.29 (0.19)	-0.01 (0.28)
$\alpha$ -aminoadipic acid	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.00 (0.01)

<sup>1</sup> Data are presented as means with standard errors of the means.

MCI, mild cognitive impairment; NC, normal cognition; NS, not significant.