eAppendix

Sensitivity analysis

Power calculations

Since we generally did not find significant associations of physical activity and intellectual activity with biomarker values, we wanted to ensure that our null findings were not primarily attributable to our sample size. To do so, we utilized a series of simulations to estimate minimum sample sizes required to detect our observed effect sizes at an alpha level of 0.05 (two-tailed).

Holding the observed variability constant as well as the influence of all other variables in our full model, we found that physical activity only predicted .12% of unique variance in FDG changes overtime. This corresponded to an f^2 effect size of 0.0012. Based on the observed effect size, we estimated that 6,535 participants would be needed to obtain 80% power to detect significant associations between physical activity and FDG changes.

Additionally, with the same model specifications described above, we found that intellectual activity only accounted for .09% of unique variance in FDG changes overtime. This corresponded to an f^2 effect size of 0.0009. Based on the observed effect size, we estimated that 8,716 participants would be needed to obtain 80% power to detect significant associations between intellectual activity and FDG changes over 3 years.

In contrast to these results, MeDi scores uniquely predicted 8.83% of the variance in FDG changes over time. This corresponded to an f^2 effect size of 0.097. Based on the observed effect size, we estimated that as few as 84 participants are needed to obtain 80% power to detect significant associations between MeDi adherence and FDG changes over 3 years.

Given the small magnitude of the observed effect sizes of physical and intellectual activity, as well as the unrealistically large sample sizes required to obtain satisfactory power of detecting significant differences, we conclude that our null results are not attributable to sample size concerns. Lack of associations between physical activity, intellectual activity, and AD biomarker changes are also consistent with previous studies in the elderly.

Breaking down global cognition

Global cognition was the main cognitive outcome measure in this study. We then conducted an exploratory analysis to independently assess domain-specific associations (i.e. association with memory, executive function and language scores) using the same procedures as with the global cognition scores and $p<0.05$.

Longitudinal results are summarized in the tables below.

None of the predictors were directly associated with changes in memory (Table 1) and executive function (Table 2).

As shown in table 3, after accounting for baseline language, higher baseline plasma homocysteine was negatively, though marginally associated with faster rates of decline in language scores in the full model (model 1 $p=0.076$), in the reduced model (model 2, $p=0.069$), and reached significance in the model with vascular variables only (model 4, $p=0.036$). Additionally, MeDi scores were positively, though marginally associated with language in the model with lifestyle variables only (model 3, $p=0.063$).

Table 1. Prediction of changes in memory.

	Model 1[a]	**Model 2[b]**	**Model 3[c]**	**Model 4[d]**
Mediterranean diet	.025 (.065)	.027 (.066)	.038 (.060)	
Physical activity	-.000 (.011)	-.002 (.012)	-.002 (.012)	
Intellectual activity	-.044 (.172)	-.058 (.175)	-.063 (.168)	
Plasma homocysteine	.022 (.046)	.009 (.045)		.008 (.044)
Plasma cholesterol	.000 (.003)	.000 (.003)		.000 (.003)
Body mass index	-.007 (.020)	-.005 (.021)		-.005 (.021)
QUICKI scores	-6.940 (5.867)	-4.758 (5.800)		-5.306 (5.637)
Hypertension	-.077 (.154)	-.083 (.148)		-.085 (.146)
Memory at baseline	.666 (.137)***	.677 (.149)***	.652 (.144)***	.672 (.148)***
Sex	-.108 (.114)			
APOE status	.051 (.105)			
Age	-.010 (.016)			
Time to follow-up	-.001 (.000)			
Constant	1.062 (.983)	.725 (.969)	-.002 (.094)	.816 (.944)

*p<0.05; **p<0.01; ***p<0.001; †0.05<p<0.10

Values are presented as unstandardized beta coefficients (standard error).
[a]Model 1: full model with all variables examined
[b]Model 2: full model without non-significant adjustment variables

[c]Model 3: model with lifestyle variables only, and without non-significant adjustment variables
[d]Model 4: model with vascular variables only, and without non-significant adjustment variables
Abbreviations: QUICKI, Quantitative Insulin Sensitivity Check Index.

Table 2. Prediction of changes in executive function (EF).

	Model 1[a]	**Model 2[b]**	**Model 3[c]**	**Model 4[d]**
Mediterranean diet	.019 (.044)	.022 (.044)	.015 (.042)	
Physical activity	-.000 (.009)	-.002 (.009)	-.002 (.009)	
Intellectual activity	.218 (.133)	.173 (.132)	.193 (.130)	
Plasma homocysteine	-.032 (.038)	-.027 (.034)		-.030 (.035)
Plasma cholesterol	.000 (.003)	.000 (.002)		.000 (.002)
Body mass index	.012 (.014)	.012 (.014)		.010 (.014)
QUICKI scores	2.367 (4.078)	2.623 (4.006)		2.346 (3.921)
Hypertension	-.024 (.121)	-.036 (.108)		-.062 (.110)
EF at baseline	.861 (.082)***	.849 (.084)***	.842 (.080)***	.885 (.085)***
Sex	-.044 (.087)			
APOE status	.086 (.078)			
Age	.005 (.012)			
Time to follow-up	.000 (.000)			
Constant	-.337 (.674)	-.389 (.662)	.071 (.071)	-.360 (.649)

*p<0.05; **p<0.01; ***p<0.001; †0.05<p<0.10
See legend to Table 1.

Table 3. Prediction of changes in language.

	Model 1[a]	**Model 2[b]**	**Model 3[c]**	**Model 4[d]**
Mediterranean diet	.115 (.073)	.116 (.072)	.134 (.070)†	
Physical activity	-.002 (.014)	-.002 (.009)	-.007 (.013)	
Intellectual activity	.189 (.203)	.173 (.132)	.180 (.189)	
Plasma homocysteine	-.087 (.048)†	-.027 (.034) †		-.098 (.046)*
Plasma cholesterol	-.000 (.004)	.000 (.002)		.001 (.004)
Body mass index	.013 (.021)	.012 (.014)		.014 (.021)
QUICKI scores	1.254 (7.056)	2.623 (4.006)		3.486 (6.308)
Hypertension	.006 (.177)	-.036 (.108)		.061 (.157)

Language at baseline	.737 (.143)***	.849 (.084)***	.717 (.139)***	.731 (.134)***
Sex	-.032 (.136)			
APOE status	.078 (.120)			
Age	.003 (.015)			
Time to follow-up	-.000 (.001)			
Constant	-.249 (1.154)	-.389 (.662)	-.050 (.106)	-.582 (1.019)

*p<0.05; **p<0.01; ***p<0.001; †0.05<p<0.10

See legend to Table 1.