

Correlations between plasma irisin and dementia biomarkers in a Brazilian cohort

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Introduction

- **Dementia, a global challenge:** Affects ~50 million people worldwide, expected to triple by 2050
- **Risk factors:** Lifestyle and environmental factors (low education, obesity, inactivity) increase dementia risk and ATN biomarkers.
- **Biomarkers:** CSF and PET scans detect Alzheimer’s pathology (Aβ and tau), but are invasive and costly → need for blood-based alternatives.
- **Exercise and cognition:** Physical activity reduces amyloid burden, brain atrophy, and tau deposition; improves cognitive functions.
- **Irisin:** Exercise-induced myokine, linked to BDNF expression, memory, and synaptic plasticity; lower in AD patients and associated with Aβ and cognition.
- **Study aim:** Investigate associations between blood-based AD biomarkers and plasma irisin levels in a Brazilian cohort.

Methods

Participants and ethics
Approved by the IDOR Ethics Committee. All participants provided written consent. From 300 recruited at IDOR’s Memory Clinic (Rio de Janeiro, Brazil), 242 with available plasma and biomarker data were classified as cognitively unimpaired (CU) or impaired (aMCI/AD).
Plasma biomarkers
Blood (3 mL, EDTA) was processed within 2 h, stored at –80 °C, and analyzed on the SIMOA HD-X platform (Quanterix) using Neurology 3-Plex A, pTau181, and pTau217 kits. Assays included calibrators, controls, and local QC (CV < 10%).
Statistics
Data were collected in REDCap and analyzed in RStudio. Sample size was determined by biomarker availability.

Results

Hierarchical linear regression models predicting plasma irisin levels

term	statistic	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7
(Intercept)	estimate	-0.090 [-0.369, 0.189]	-0.086 [-0.373, 0.201]	0.030 [-0.255, 0.315]	0.113 [-0.250, 0.476]	0.227 [-0.213, 0.666]	0.240 [-0.236, 0.717]	0.509 [-0.035, 1.052]
AB 42/40 Ratio	estimate	0.144 [-0.258, 0.546]	0.139 [-0.275, 0.553]	0.117 [-0.284, 0.518]	0.126 [-0.280, 0.532]	0.204 [-0.237, 0.644]	0.198 [-0.291, 0.686]	0.239 [-0.225, 0.703]
Age	estimate		-0.028 [-0.344, 0.287]	0.071 [-0.242, 0.384]	0.108 [-0.224, 0.440]	0.181 [-0.187, 0.549]	0.186 [-0.248, 0.621]	0.122 [-0.296, 0.539]
IPAQ	estimate			0.327 [0.004, 0.650]	0.346 [0.015, 0.676]	0.352 [0.020, 0.684]	0.356 [0.004, 0.708]	0.287 [-0.054, 0.629]
Sex M	estimate				-0.226 [-0.829, 0.377]	-0.392 [-1.095, 0.311]	-0.368 [-1.127, 0.391]	-0.467 [-1.194, 0.259]
Education	estimate					0.152 [-0.174, 0.478]	0.157 [-0.206, 0.519]	0.277 [-0.092, 0.645]
BMI	estimate						0.074 [-0.419, 0.567]	0.118 [-0.351, 0.587]
Diagnosis CU	estimate							-0.661 [-1.412, 0.090]
Num.Obs.		30	30	27	27	27	26	26
R2		0.019	0.020	0.179	0.201	0.235	0.239	0.361
R2 Adj.		-0.016	-0.052	0.072	0.056	0.053	-0.001	0.112
RMSE		0.71	0.71	0.64	0.63	0.61	0.62	0.57

term	statistic	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7
(Intercept)	estimate	-0.179 [-0.434, 0.077]	-0.164 [-0.420, 0.091]	-0.053 [-0.298, 0.191]	0.033 [-0.272, 0.338]	0.080 [-0.279, 0.439]	0.048 [-0.342, 0.439]	0.183 [-0.327, 0.692]
pTau181/AB42 Ratio	estimate	0.291 [0.052, 0.530]	0.339 [0.087, 0.591]	0.334 [0.106, 0.561]	0.338 [0.109, 0.566]	0.333 [0.100, 0.566]	0.359 [0.098, 0.619]	0.312 [0.026, 0.598]
Age	estimate		-0.172 [-0.466, 0.122]	-0.061 [-0.337, 0.216]	-0.024 [-0.311, 0.264]	0.006 [-0.308, 0.321]	-0.035 [-0.396, 0.326]	-0.051 [-0.418, 0.316]
IPAQ	estimate			0.362 [0.087, 0.637]	0.383 [0.104, 0.663]	0.388 [0.103, 0.673]	0.381 [0.082, 0.680]	0.347 [0.033, 0.660]
Sex M	estimate				-0.243 [-0.752, 0.266]	-0.314 [-0.899, 0.271]	-0.342 [-0.964, 0.281]	-0.372 [-1.006, 0.261]
Education	estimate					0.068 [-0.191, 0.328]	0.047 [-0.233, 0.327]	0.103 [-0.210, 0.416]
BMI	estimate						-0.077 [-0.511, 0.356]	-0.028 [-0.482, 0.426]
Diagnosis CU	estimate							-0.307 [-1.044, 0.430]
Num.Obs.		30	30	27	27	27	26	26
R2		0.181	0.223	0.405	0.430	0.438	0.450	0.473
R2 Adj.		0.152	0.165	0.327	0.327	0.304	0.276	0.267
RMSE		0.64	0.63	0.54	0.53	0.53	0.53	0.52

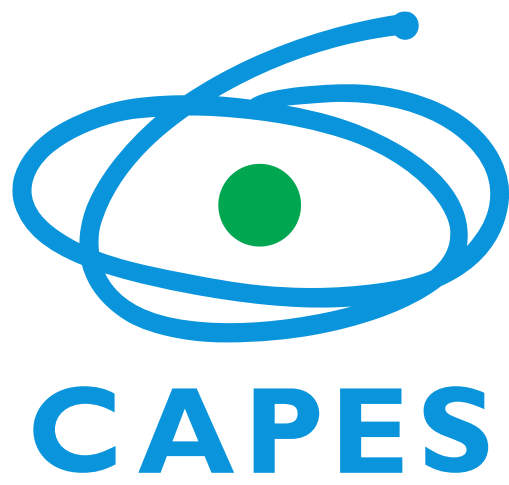
term	statistic	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6	Model 7
(Intercept)	estimate	-0.200 [-0.456, 0.057]	-0.189 [-0.441, 0.064]	-0.082 [-0.319, 0.155]	-0.028 [-0.331, 0.275]	0.022 [-0.332, 0.377]	-0.002 [-0.390, 0.386]	0.115 [-0.404, 0.634]
pTau217/AB42 Ratio	estimate	0.317 [0.070, 0.563]	0.386 [0.124, 0.647]	0.391 [0.159, 0.624]	0.385 [0.148, 0.622]	0.381 [0.140, 0.623]	0.397 [0.131, 0.662]	0.353 [0.055, 0.651]
Age	estimate		-0.206 [-0.500, 0.088]	-0.092 [-0.360, 0.176]	-0.067 [-0.353, 0.219]	-0.035 [-0.346, 0.277]	-0.065 [-0.421, 0.291]	-0.075 [-0.438, 0.288]
IPAQ	estimate			0.379 [0.115, 0.643]	0.391 [0.120, 0.663]	0.396 [0.119, 0.673]	0.391 [0.099, 0.683]	0.361 [0.053, 0.670]
Sex M	estimate				-0.144 [-0.640, 0.351]	-0.221 [-0.791, 0.349]	-0.238 [-0.844, 0.368]	-0.275 [-0.900, 0.350]
Education	estimate					0.073 [-0.178, 0.324]	0.058 [-0.214, 0.330]	0.103 [-0.202, 0.409]
BMI	estimate						-0.058 [-0.474, 0.359]	-0.019 [-0.456, 0.419]
Diagnosis CU	estimate							-0.255 [-0.988, 0.477]
Num.Obs.		30	30	27	27	27	26	26
R2		0.198	0.255	0.454	0.463	0.472	0.479	0.494
R2 Adj.		0.170	0.200	0.383	0.366	0.347	0.314	0.297
RMSE		0.64	0.61	0.52	0.51	0.51	0.52	0.51

Table 1. Hierarchical linear regression models predicting plasma irisin levels. Each model incrementally adds a new predictor to examine its contribution to the explained variance. The dependent variable in all models is plasma irisin. (A) The Aβ42/40 ratio, (B) pTau181/ Aβ42, (C) pTau217/ Aβ42 ratios were included as a baseline predictor. Additional covariates were added sequentially in the following order: age, physical activity (IPAQ), sex (male), education, body mass index (BMI), and clinical diagnosis (CU as reference).

Conclusion

Our findings indicate that irisin was not directly associated with ATN biomarkers. When physical activity was included, it emerged as a relevant factor contributing to irisin variability alongside biomarker profiles. However, physical activity alone does not fully account for the observed variation in plasma irisin levels.

Acknowledgments



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