

Associations of Cerebrospinal Fluid Biomarkers with Hippocampal Volume in a Hispanic Cohort

Alcibiades E. Villareal^{1,2}, Anna V. Díaz- Ramírez¹, Josefina Fletcher^{4,6,7}, Aron Benzadon^{4,5}, Pahola Araujo^{4,5,6}, Ricardo Williams^{4,7}, Rainier Rodríguez^{4,5}, Nelson Navarro^{4,6}, David Dondis^{4,6}, David Anguizola^{4,6}, Judy Mendoza⁴, Verónica Billinglea⁴, Olmedo Almanza⁴, Karen Courville⁸, Sassil Z. Pitti⁸, Héctor Torres⁸, Lizzetha Y. Quintero⁸, Dámaso M. Díaz⁸, Laura M. Cerrud⁸, Bruno Hammerschlag⁵, Ariel Saldaña⁵, Alexis A. Palacios⁵, Andrés E. Bernalles⁵, Fernando Sucre¹⁰, Diana C. Oviedo^{1,2,3}, Giselle Rangel^{1,2}, Carolina E. Rodríguez¹, Sofía Rodríguez-Araña¹, Maria B. Carreira^{1,2}, Gabrielle B. Britton^{2,11}. (1) Instituto de Investigaciones Científicas y Servicios de Alta Tecnología (INDICASAT-AIP), City of Knowledge, Panamá, (2) Sistema Nacional de Investigación (SNI), Panamá, Panamá, (3) Universidad Santa María La Antigua, Panamá, Panamá, (4) Servicio de Neurología, CIDELAS-CSS, Panamá, Panamá, (5) Hospital Paitilla, Panamá, Panamá, (6) Hospital Pacífica Salud, Panamá, Panamá, (7) Hospital The Panama Clinic, Panamá, Panamá, (8) Hospital Dr. Gustavo Nelson Collado, Panamá, Panamá, (9) Servicio de Radiología Hospital Paitilla, Panamá, Panamá, (10) Caja de Seguro Social, Panamá, Panamá, (11) Centro de Vacunación Internacional Cevaxin, Panamá, Panamá.



INTRODUCTION

Alzheimer's disease (AD) is biologically determined by findings in the core biomarkers of AD neuropathologic change (ADNPC): low amyloid-beta 42 (**A β -42**) and elevated total-Tau (**t-Tau**) and phosphorylated-tau (**p-Tau**) proteins.

Hippocampal volume (HV) and atrophy are helpful AD hallmarks for disease progression.

Main Objective

To evaluate the diagnostic and prognostic value of biomarkers in cerebrospinal fluid and magnetic resonance imaging for mild cognitive impairment (MCI), Alzheimer's disease (AD) and Parkinson's disease (PD) in Panamanian older adults (≥ 65 years of age). Here we report a description of the overall correlation between CSF and MRI findings.

METHODS

Descriptive
Prospective Study ≥ 65 Panamanian Older Adults

N=86 Participants underwent clinical interviews, neuropsychological assessments, and CSF collection through lumbar puncture.

Structural magnetic resonance imaging on a 3T scanner using T1-weighted MPRAGE, T2 FLAIR, and diffusion-weighted imaging sequences.

CSF concentrations of A β 42, t-Tau, and p-Tau181 were quantified by electrochemoluminescence immunoassay (ECLIA) using the cobas® e411 analyzer and Roche Diagnostics® reagent kits.

Hippocampal volumes were obtained using the volBrain automated image analysis platform (HIPS pipeline). Correlations were evaluated using Spearman correlation analysis.

RESULTS

Table 1. Descriptive and clinical characteristics among diagnostic groups

	Total (n=86)	NCI (n=6)	MCI (n=28)	AD (n=39)	PD (n=6)	Others (n=7)
Age/Years	73.5 $\pm$ 5.7	70.6 $\pm$ 3.5	70.2 $\pm$ 5.5	75.4 $\pm$ 5.4	74.8 $\pm$ 6.8	73.6 $\pm$ 5.8
Sex, female, n(%)	47 (54.7%)	4 (66.7%)	19 (67.9%)	19 (48.2%)	1 (16.7%)	4 (57.1%)
Education, Years	13.2 $\pm$ 5.2	12.8 $\pm$ 5.4	12.9 $\pm$ 5.1	13.9 $\pm$ 5.3	12.0 $\pm$ 5.4	12.4 $\pm$ 5.2
Diabetes, n(%)	24 (27.9%)	3 (50.0%)	10 (35.7%)	7 (17.9%)	1 (16.7%)	3 (42.9%)
Hypertension, n(%)	56 (65.1%)	3 (50.0%)	20 (71.4%)	27 (69.2%)	2 (33.3%)	4 (57.1%)
Cardio-vascular Disease, n(%)	19 (22.1%)	2 (33.3%)	6 (21.4%)	8 (20.5%)	2 (33.3%)	1 (14.3%)
Cerebro-vascular Disease, n(%)	21 (24.4%)	0 (0%)	9 (32.1%)	10 (25.6%)	0 (0%)	2 (25.8%)
MMSE	23.8 $\pm$ 5.1	28.7 $\pm$ 1.0	25.9 $\pm$ 3.1	21.7 $\pm$ 5.4	26.8 $\pm$ 4.1	19.9 $\pm$ 5.0

Note: NCI=Non-Cognitively Impaired; MCI=Mild Cognitive Impairment; AD=Alzheimer's Disease; PD=Parkinson's Disease; Others=Vascular Dementia & Unspecified Dementia; MMSE=Mini Mental State Examination.

Fig 1. Correlation heatmap between CSF biomarkers and brain volumes

Whole Hippocampus
R. Hippocampus
L. Hippocampus
A β 42
p-Tau
t-Tau

A B C D E F

Note: Heatmap showing correlations between CSF biomarker concentrations and volumetric measures of the hippocampus. Spearman's correlation values (r) are displayed, with intensity representing the strength of association between specific CSF biomarkers and hippocampal sub-regions (cm³). CSF values were log-transformed to normalize their distribution. A: Whole Hippocampus; B: R. Hippocampus; C: L. Hippocampus; D: A β 42; E: p-Tau; F: t-Tau. $P < .05^*$, $p < .01^{**}$, $p < .001^{***}$.

CONCLUSIONS

Our study found **significant correlations** between A β 42 CSF biomarkers and hippocampal volumes, suggesting that brain atrophy may reflect the cumulative effect of protein alterations, subsequently impairing cognition and functional independence.

REFERENCES

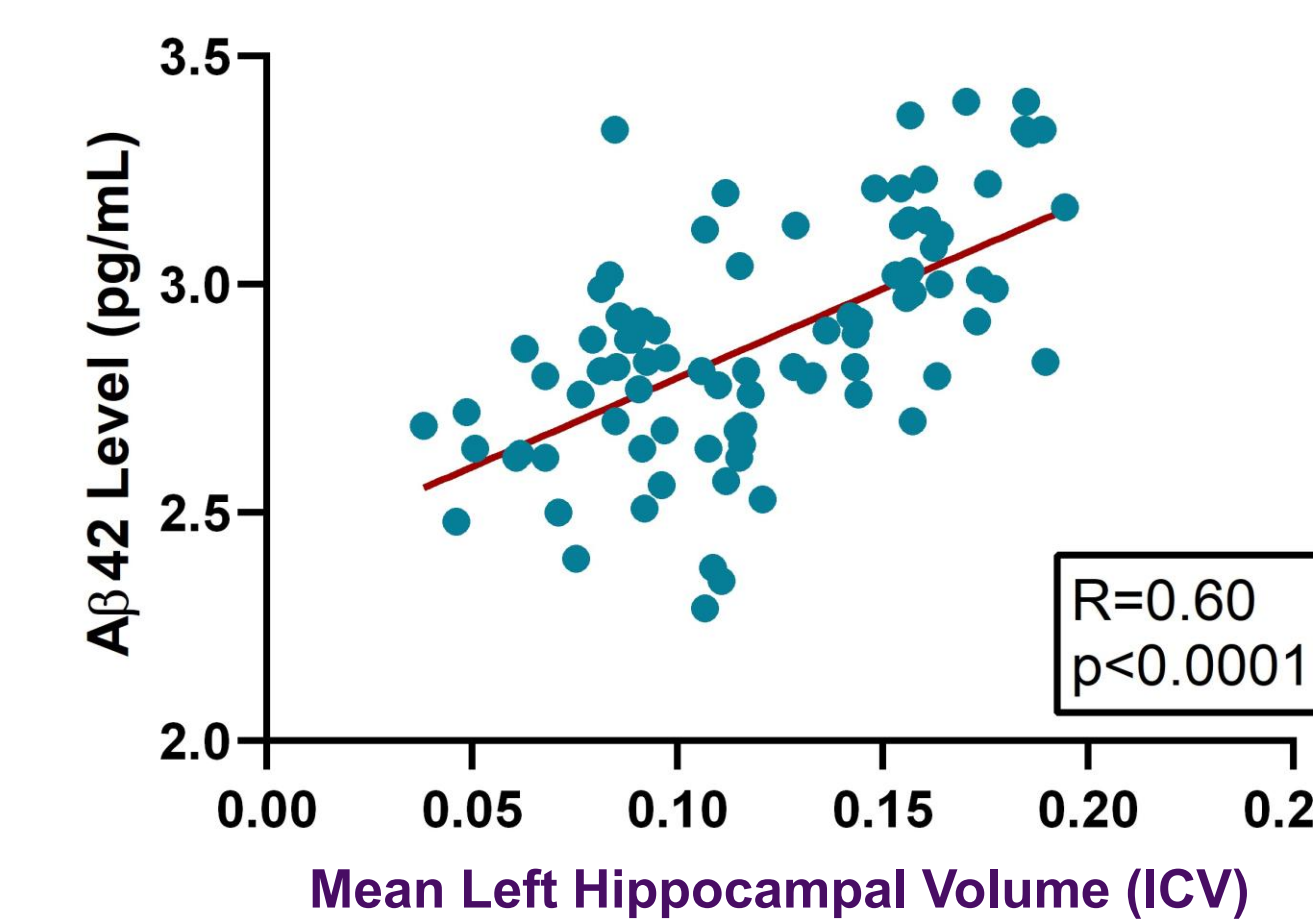
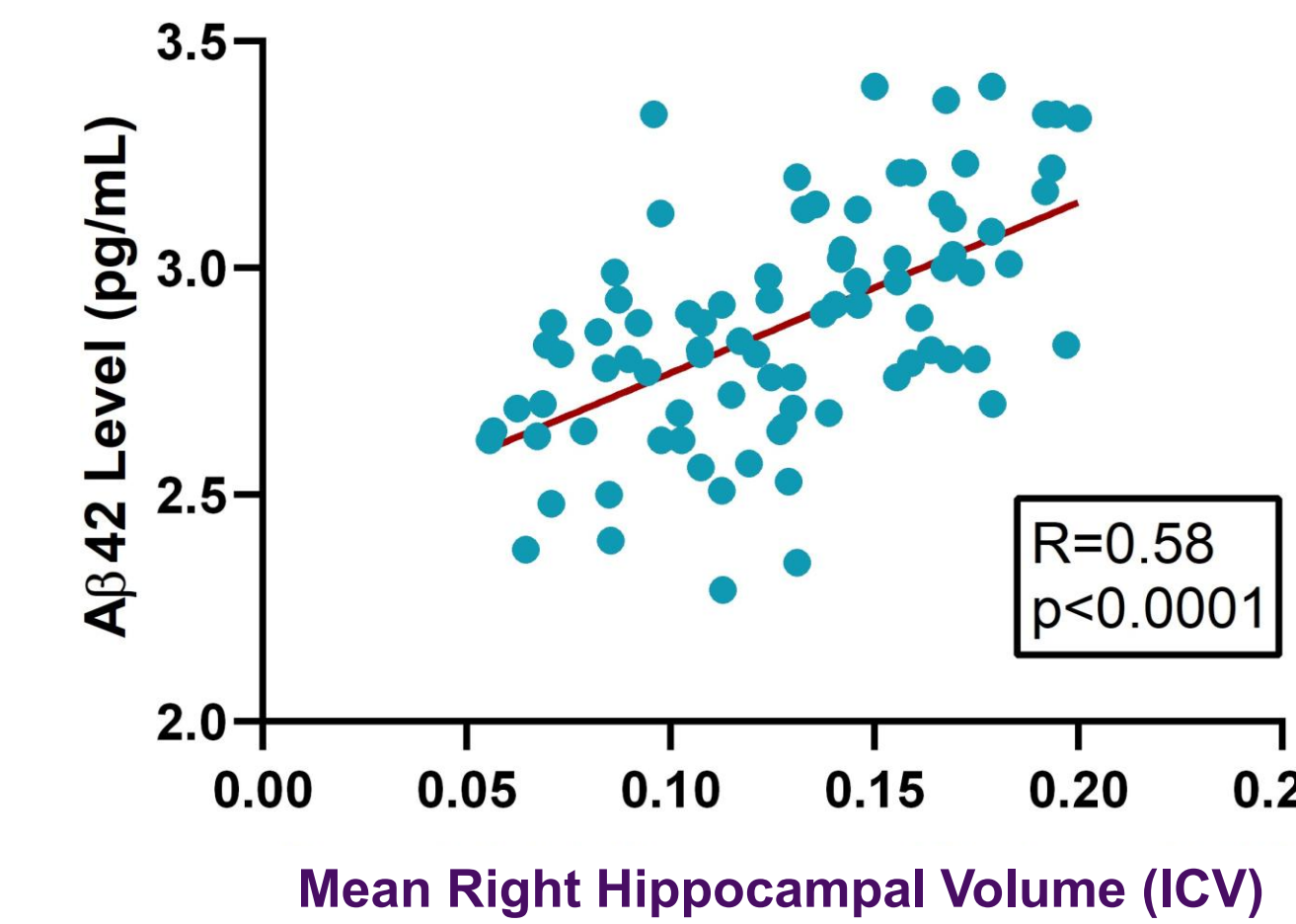
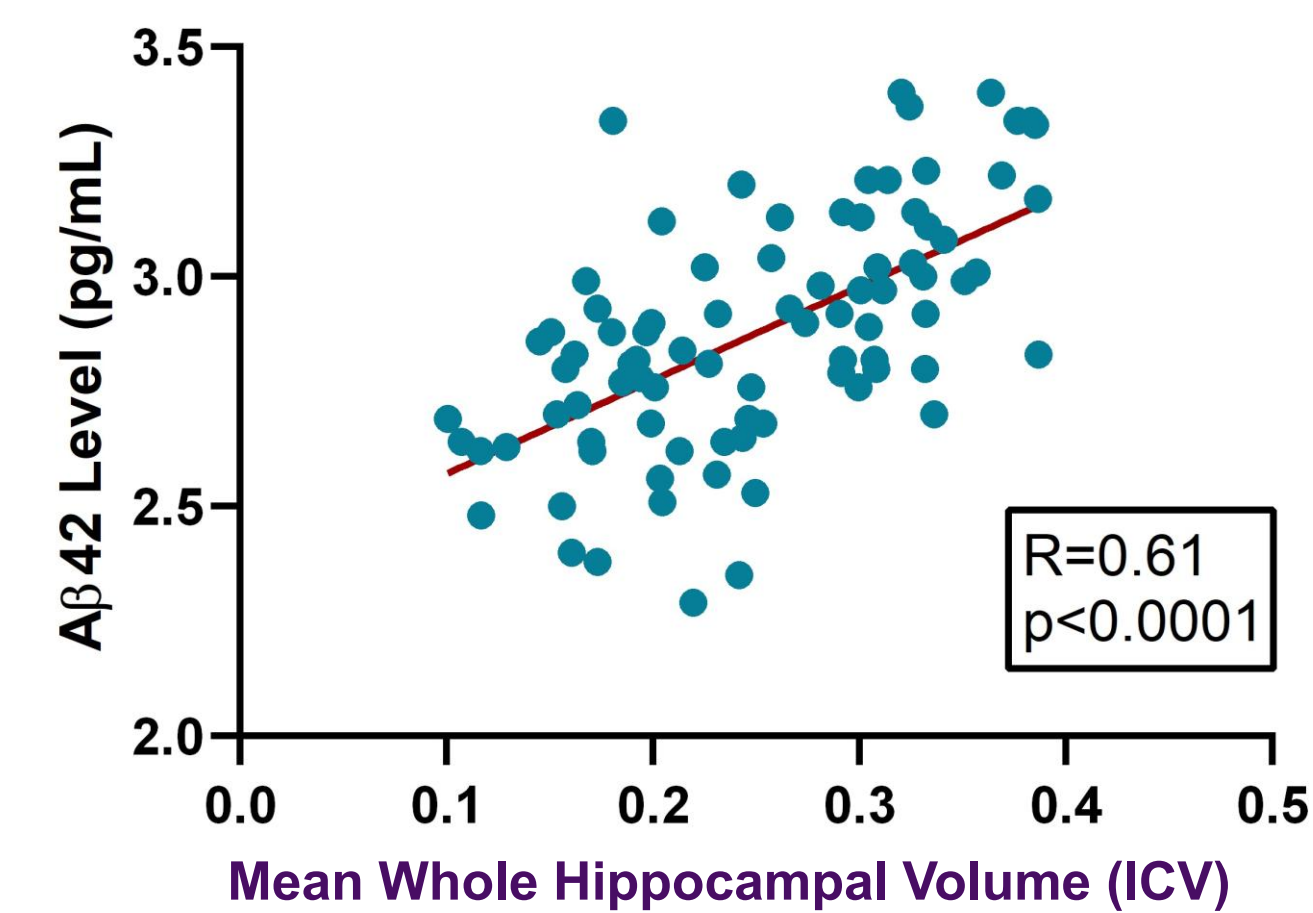
- Jack CR, Andrews JS, Beach TG, et al. Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup. *Alzheimer's Dement.* 2024;20:5143–5169. <https://doi.org/10.1002/alz.13859>.
- Rosén C, Hansson O, Blennow K, Zetterberg H. Fluid biomarkers in Alzheimer's disease: Current concepts. *Mol Neurodegener.* 2013;8:20. Yang X, Tan MZ, Qiu A. CSF and Brain Structural Imaging Markers of the Alzheimer's Pathological Cascade. *PLoS One.* 2012;7(12):e47406.
- Romero J, Coupé P, Manjón J. HIPS: A new hippocampus subfield segmentation method. *NeuroImage.* 163:286–295, 2017

CONTACT

Alcibiades Villarreal, T.M., PhD., PI
INDICASAT-AIP, Panama City, Panama
avillarreal@indicasat.org.pa

ALZHEIMER'S ASSOCIATION | **AAIC Neuroscience Next**

Figures 2-4. Correlation analysis of CSF A β 42 and hippocampal volumes.



Note: Plots demonstrate the positive association between A β 42 and volumes for the whole hippocampus, as well as the right and left hemispheres. Solid line represents the linear regression fit. Spearman's correlation coefficient (r) and p values are displayed for each analysis. Values were adjusted for intracranial volume (ICV). CSF values were log-transformed to normalize their distribution.