

MARIA APARECIDA CAMARGOS BICALHO^{1,2,6}, Joice Coutinho de Alvarenga¹, Bernardo de Mattos Viana^{1,2,6}, Engelmann Tomé Gabriela¹, Jonas Jardim de Paula^{1,6}, Natalia Dias Silva¹, Hansen de Oliveira Erika², Rafaela Ávila³, Andréa Teixeira Carvalho⁴, Pilar Freccero⁵, Julio Fernandez Campuzano⁵, Daniela Valadão Rosa⁶, Anja Schneider⁷, Debora Marques De Miranda^{1,6}, Michaela Thoenes⁸, Maria Barbara Postillone⁵, Hanna Huber⁷, Michael Wagner⁷, Michael Pentzek⁹, Martin Scherer¹⁰, Luca Kleineidam¹¹, Marco Aurélio Angelo¹², Marco Aurélio Romano-Silva^{1,6}, Luiz Armando Cunha De Marco^{1,6}, Maria Carolina DALMASSO¹³,Pamela Martino-Adami⁸, Alfredo Ramirez⁸

1. Federal University of Minas Gerais (UFMG), Belo Horizonte, Brazil; 2 University Hospital of the Federal University of Minas Gerais (UFMG), Belo Horizonte, Brazil; 3. FUMEC, Belo Horizonte, Brazil; 4. FIOCRUZ- Minas Gerais, Belo Horizonte, Brazil; 5. CONICET, Buenos Aires, Argentina; 6. National Institute of Science and Technology - Neurotec R, Belo Horizonte, Brazil; 7. DZNE, Bonn, Germany; 8. University of Cologne, Cologne, Germany; 9. University of Duisburg-Essen, Essen, Germany; 10. University Medical Center Hamburg-Eppendorf, Hamburg, Germany; 11. University of Bonn, Germany; 12. Minas Gerais State Health Department, Brazil; 13- CONICET, Florencio Varela, Argentina.

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BACKGROUND

Plasma pTau217 is a promising biomarker for Alzheimer’s disease. However, its performance in South American populations remains insufficiently characterized. This study aimed to evaluate cerebrospinal fluid (CSF) and blood-based biomarkers (BBB), as well as APOE4 genomic ancestry, in older adults from two Latin American cohorts: Brazil (Cog-Aging Study (CAS), n=353) and Argentina (GeNED.ar (GND), n=134 (Table1).

METHODS

Data-driven cut-offs were derived using Gaussian mixture models (GMM). In the CAS, logistic regression combined with Youden’s index was applied to cognitively unimpaired (CU) and dementia of Alzheimer’s disease (DAT) groups to define clinically based cut-offs. Associations between BBB and clinical covariates were examined using separate regression models. Interactions between APOEε4 and global African ancestry were evaluated for their effects on biomarker levels.



CONTACT INFORMATION

Maria Aparecida Bicalho, MD, Ph.D
Email: macbicalho@gmail.com

pTau217-based biomarkers demonstrated good performance in admixed South American populations, supporting their implementation in LMICs.

RESULTS

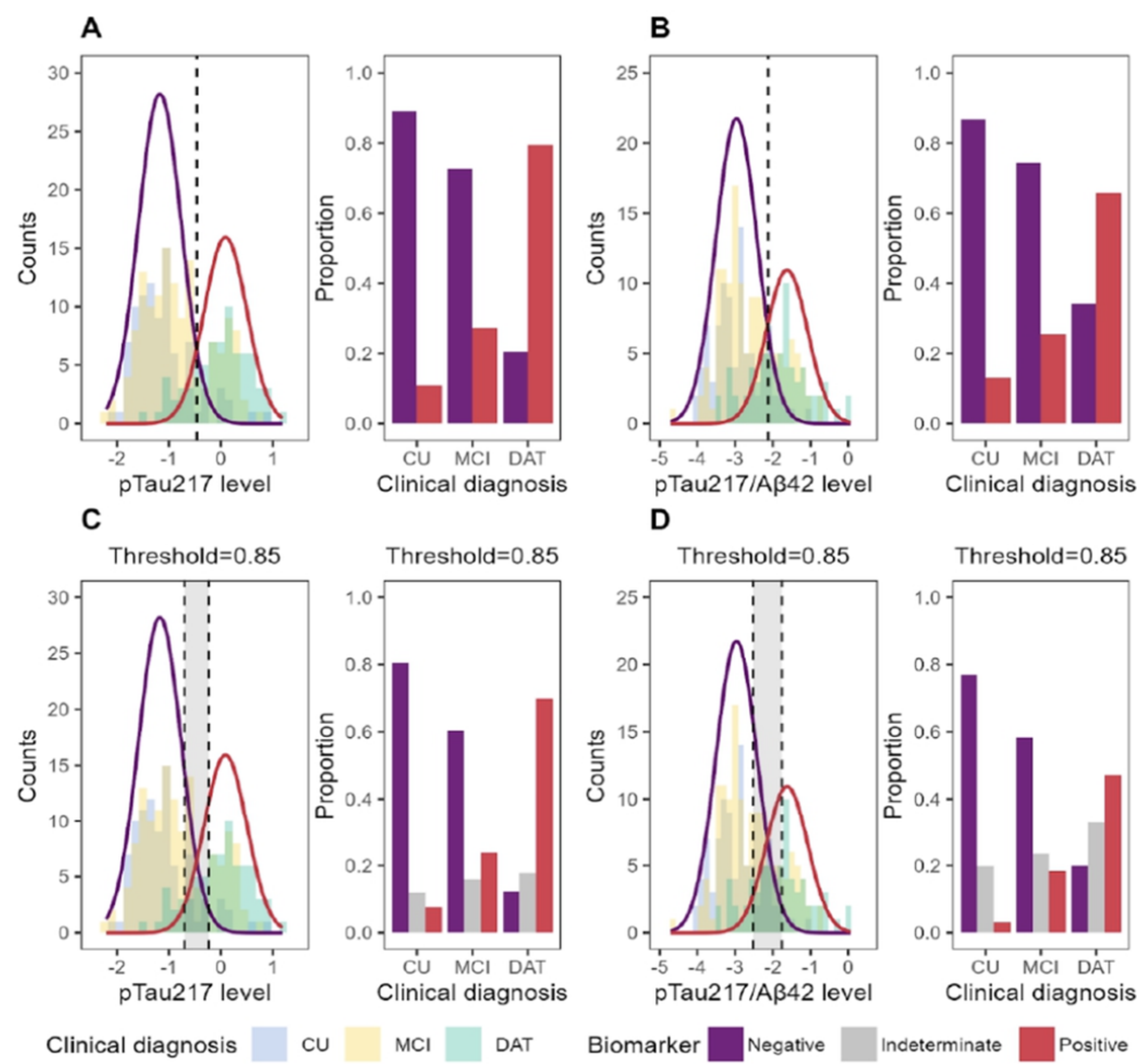


Figure 1. Data-driven cut-offs for plasma pTau217 and pTau217/Aβ42 in Cog-Aging-Study–Brazil. Histograms showing the distribution of biomarker levels across clinical diagnostic groups, with overlap curves representing the modelled distributions of normal and abnormal values. In panels A–B, values left of the dashed line indicate normal biomarker levels, and values to the right indicate abnormal levels. In panels C–D, the two dashed lines represent lower and upper cut-offs; values left of the lower line are classified as normal, values right of the upper line as abnormal, and grey shading marks the intermediate range where status was uncertain. Bar plots display the proportion of each biomarker status (negative, indeterminate, positive) within diagnostic groups. Plasma pTau217 and pTau217/Aβ42 values were log-transformed. CU, cognitively unimpaired; MCI, mild cognitive impairment; DAT, dementia of the Alzheimer’s type.

CONCLUSIONS

Overall, pTau217-based biomarkers demonstrated good performance in admixed South American populations, supporting their implementation in LMICs.

Table 1: Clinical and demographic characteristics of the participants from Cog-Aging-Study-Brazil and GeNED.ar-Argentina.

	Cog-Aging-Study-Brazil				GeNED.ar-Argentina
	CSF only (n = 49)	Plasma only (n = 239)	CSF and plasma (paired ^c , n = 45)	CSF and plasma (unpaired ^d , n = 20)	Plasma only (n = 134)
Age (mean (SD))	72.8 (8.6)	77 (7.1)	75.4 (7.4) ^c /75.5 (7.3) ^d	76 (6) ^c /75.7 (5.2) ^d	72 (6.8)
Sex (female, %)	69.4	71.1	51.1	65	70.1
APOE-ε4 (%)	37.5	28.8	44.4	45	27.9
Education (years, mean (SD))	5.4 (3.9)	6 (5.1)	6.5 (5.2)	4.4 (2.8)	8.7 (4.5)
Clinical diagnosis(%)					
Cognitively Unimpaired (CU)	43.5	34.7	13.3 ^c /15.6 ^d	10 ^c /10 ^d	60.5
Mild Cognitive Impairment (MCI)	21.7	45.6	26.7 ^c /35.6 ^d	70 ^c /70 ^d	26.1
Dementia of the Alzheimer's type (DAT)	34.8	19.7	60 ^c /48.9 ^d	20 ^c /20 ^d	13.4
Body mass index (BMI) (mean, (SD))	26.8 (4.4)	27.1 (4.5)	26.5 (4.9)	27.3 (3.3)	28.9 (5.2)
Smoking (%)	41.2	30.5	27.3	40	16.3
Alcoholism (%)	28.6	40.7	52.3	55	N/A
Hypertension (%)	69.4	74.1	62.2	95	68.1
Estimated glomerular filtration rate (eGFR) (mean, (SD))	70.1 (18.5)	68.6 (16.9)	71.1 (17.7)	65.6 (14)	N/A
Dyslipidemia (%)	50	58	55.6	80	37.5
Diabetes mellitus (%)	27.8	35.1	35.6	35	35.1
Depression (%)	47.2	60.3	44.2	47.4	16.3

^aSamples collected within a 12-month interval; ^bSamples collected more than 12 months apart; ^cAt CSF collection time; ^dAt plasma collection time
SD, standard deviation; CU, cognitively unimpaired; MCI, mild cognitive impairment; DAT, dementia of the Alzheimer’s type; BMI, body mass index; eGFR, estimated glomerular filtration rate; N/A, not available.

Table 2. Predictive performance of plasma pTau217 and pTau217/Aβ42 cut-offs in Cog-Aging-Study-Brazil.

Biomarker	Threshold	Single cut-off (pg/mL)	Lower cut-off (pg/mL)	Upper cut-off (pg/mL)	Indeter-minate (%)	PPV (95% CI)	NPV (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
pTau217	-	≥ 0.63	-	-	-	0.85 (0.68-0.94)	0.75 (0.51-0.90)	0.85 (0.68-0.94)	0.75 (0.51-0.90)
	0.80	-	≤ 0.52	≥ 0.76	7.0	0.88 (0.70-0.96)	0.80 (0.55-0.93)	0.88 (0.70-0.96)	0.80 (0.55-0.93)
	0.85	-	≤ 0.50	≥ 0.79	11.6	0.88 (0.69-0.96)	0.86 (0.60-0.96)	0.91 (0.73-0.98)	0.80 (0.55-0.93)
	0.90	-	≤ 0.47	≥ 0.84	18.6	0.86 (0.67-0.95)	0.85 (0.58-0.96)	0.90 (0.71-0.97)	0.79 (0.52-0.92)
pTau217/Aβ42	-	≥ 0.12	-	-	-	0.88 (0.69-0.96)	0.71 (0.47-0.87)	0.81 (0.62-0.91)	0.80 (0.55-0.93)
	0.80	-	≤ 0.09	≥ 0.16	14.6	0.90 (0.71-0.97)	0.71 (0.45-0.88)	0.83 (0.63-0.93)	0.83 (0.55-0.95)
	0.85	-	≤ 0.08	≥ 0.17	22.0	0.89 (0.69-0.97)	0.77 (0.50-0.92)	0.85 (0.64-0.95)	0.83 (0.55-0.95)
	0.90	-	≤ 0.07	≥ 0.19	34.1	0.88 (0.66-0.97)	1 (0.72-1)	1 (0.80-1)	0.83 (0.55-0.95)

PPV, positive predictive value; NPV, negative predictive value, CI, confidence interval.

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