

Prior Traumatic Brain Injury and Alzheimer’s Disease Blood biomarkers



P1-08-3961

Yael Rosen-Lang, Agathe Vrillon, Shlomit Pasternak, Ganna Blazhenets, David Soleimani-Meigooni, Gil D. Ravinovici, Michael W. Weiner, Nathan Hantke, Lisa Silbert, Daniel L. Schwartz, Abigail Livny Ezer, Orit Lesman Segev, Kristine Yaffe, Susan M Landau, Magdalena Korecka, Leslie M. Shaw, Renaud La Joie, and Raquel C. Gardner



AD blood tests may miss >50% of amyloid-PET positives in persons with prior traumatic brain injury

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES																																																												
Traumatic brain injury (TBI) is a risk factor for dementia and is known to impact levels of several Alzheimer’s disease (AD) blood biomarkers. FDA-approved plasma pTau217/ Aβ42 ratio test achieved the required 90% accuracy in detection of brain amyloid in a symptomatic cohort.¹ Objective: To evaluate the accuracy of emerging AD blood biomarkers in veterans with and without TBI history.	This cross-sectional cohort study used data from the ADNI-DOD study.² Participants: 272 older Vietnam veterans, 83% cognitively unimpaired, 17% mild cognitive impairment (MCI). Study groups: by prior history of TBI and loss of consciousness (LOC) duration. Blood test: Fujirebio Lumipulse pTau217/ Aβ42.¹ Gold standard: Amyloid-PET visual read.	In 272 participants, mean age was 70 years (±4.5), 270/272 were male and 30.5% were amyloid-PET positive. TBI exposure was associated with MCI and positive amyloid-PET. <table><tr><td>n (%)</td><td>None N = 93</td><td>TBI with LOC 0-5 min N = 89</td><td>TBI with LOC >5 min N = 90</td><td>p-value</td></tr><tr><td>Mild cognitive impairment</td><td>8 (8.6%)</td><td>15 (17%)</td><td>22 (24%)</td><td>0.016</td></tr><tr><td>Amyloid PET+ (visual read)</td><td>17 (18%)</td><td>24 (27%)</td><td>42 (47%)</td><td><0.001</td></tr><tr><td>Amyloid PET+ (centiloids)</td><td>16 (17%)</td><td>17 (19%)</td><td>34 (38%)</td><td>0.002</td></tr></table> pTau217/Aβ42 AD test had lower accuracy in TBI exposure groups Cohort-optimal cutoff <table><tr><th>TBI group</th><th>Accuracy</th><th>Sen</th><th>Spe</th><th>AUC</th></tr><tr><td>No TBI</td><td>90% (84%-96%)</td><td>53%</td><td>99%</td><td>0.88 (0.80-0.97)</td></tr><tr><td>LOC 0-5min</td><td>78% (69%-87%)*</td><td>38%</td><td>92%</td><td>0.75 (0.63-0.87)</td></tr><tr><td>LOC >5min</td><td>63% (53%-73%)*</td><td>31%</td><td>92%</td><td>0.73 (0.62-0.84)</td></tr></table> Dual cutoff¹ <table><tr><th>TBI group</th><th>Accuracy</th><th>Sen</th><th>Spe</th><th>AUC</th></tr><tr><td>No TBI (n=60)</td><td>88% (81%-95%)</td><td>65%</td><td>93%</td><td>0.92 (0.83–1.0)</td></tr><tr><td>LOC 0-5min (n=54)</td><td>76% (67%-85%)</td><td>46%</td><td>88%</td><td>0.76 (0.62-0.89)</td></tr><tr><td>LOC >5min (n=60)</td><td>64% (54%-74%)*</td><td>40%</td><td>85%</td><td>0.72 (0.59-0.83)</td></tr></table>	n (%)	None N = 93	TBI with LOC 0-5 min N = 89	TBI with LOC >5 min N = 90	p-value	Mild cognitive impairment	8 (8.6%)	15 (17%)	22 (24%)	0.016	Amyloid PET+ (visual read)	17 (18%)	24 (27%)	42 (47%)	<0.001	Amyloid PET+ (centiloids)	16 (17%)	17 (19%)	34 (38%)	0.002	TBI group	Accuracy	Sen	Spe	AUC	No TBI	90% (84%-96%)	53%	99%	0.88 (0.80-0.97)	LOC 0-5min	78% (69%-87%)*	38%	92%	0.75 (0.63-0.87)	LOC >5min	63% (53%-73%)*	31%	92%	0.73 (0.62-0.84)	TBI group	Accuracy	Sen	Spe	AUC	No TBI (n=60)	88% (81%-95%)	65%	93%	0.92 (0.83–1.0)	LOC 0-5min (n=54)	76% (67%-85%)	46%	88%	0.76 (0.62-0.89)	LOC >5min (n=60)	64% (54%-74%)*	40%	85%	0.72 (0.59-0.83)	Prior TBI is a modifier of AD biomarkers’ accuracy in prediction of brain Amyloid-PET positivity. In cognitively unimpaired/mildly impaired persons with TBI history, the test may miss >50% of Aβ-PET+ cases. Caution is advised in interpreting AD blood test results in this context. Aβ= amyloid beta, LOC=loss of consciousness, min=minutes, PET= positron emission tomography, TBI=traumatic brain injury. dashed lines indicate indeterminate zone (values above the upper dashed line are classified as Aβ+, values below the lower dashed line are classified as Aβ-)	¹Barthélemy NR, Salvadó G, Schindler SE, et al. Highly accurate blood test for Alzheimer’s disease is similar or superior to clinical cerebrospinal fluid tests. <i>Nat Med.</i> 2024;30(4):1085-1095. doi:10.1038/s41591-024-02869-z; ²Weiner MW, Harvey D, Landau SM, et al. Traumatic brain injury and post-traumatic stress disorder are not associated with Alzheimer’s disease pathology measured with biomarkers. <i>Alzheimer’s & Dementia.</i> 2023;19(3):884-895. FUNDING: U.S. Department of Defense Congressionally Directed Medical Research Program (DoD CDMRP) Peer-Reviewed Alzheimer’s Research Program (PRARP; W81XWH-21-PRARP-ADRA to RCG). LCS, NH, and DLS were also supported by grant P30AG066518 from the U.S. National Institute of Health (NIH) National Institute of Aging (NIA). AV, DSM, GB and RL were also supported by NIA grant P30AG062422. CONTACT raquel.gardner@gardnerlab.health Rosen-Lang Y, Vrillon A, Pasternak S, et al. Prior Traumatic Brain Injury and Alzheimer Disease Blood Biomarkers. <i>JAMA Neurol.</i> Published online June 29, 2026. doi:10.1001/jamaneurol.2026.2042
n (%)	None N = 93	TBI with LOC 0-5 min N = 89	TBI with LOC >5 min N = 90	p-value																																																												
Mild cognitive impairment	8 (8.6%)	15 (17%)	22 (24%)	0.016																																																												
Amyloid PET+ (visual read)	17 (18%)	24 (27%)	42 (47%)	<0.001																																																												
Amyloid PET+ (centiloids)	16 (17%)	17 (19%)	34 (38%)	0.002																																																												
TBI group	Accuracy	Sen	Spe	AUC																																																												
No TBI	90% (84%-96%)	53%	99%	0.88 (0.80-0.97)																																																												
LOC 0-5min	78% (69%-87%)*	38%	92%	0.75 (0.63-0.87)																																																												
LOC >5min	63% (53%-73%)*	31%	92%	0.73 (0.62-0.84)																																																												
TBI group	Accuracy	Sen	Spe	AUC																																																												
No TBI (n=60)	88% (81%-95%)	65%	93%	0.92 (0.83–1.0)																																																												
LOC 0-5min (n=54)	76% (67%-85%)	46%	88%	0.76 (0.62-0.89)																																																												
LOC >5min (n=60)	64% (54%-74%)*	40%	85%	0.72 (0.59-0.83)																																																												