

Cross-platform comparison of brain-derived tau immunoassays in two independent cohorts

Marissa F. Farinas¹, Wasiu G. Balogun¹, Ruyu Shi¹, Michel N. Nafash¹, Xuemei Zeng¹, Sarah E. Svirsky², Ava M. Puccio², Thomas K. Karikari¹

1. Department of Psychiatry, University of Pittsburgh, Pittsburgh, PA, USA, 2. Neurological Surgery, University of Pittsburgh, Pittsburgh, PA, USA



Introduction

- Brain-derived tau (BD-tau) has emerged as a promising biomarker for neurodegenerative disorders (AD, TBI, etc.)
- Limited BD-tau assay availability
- No studies have compared clinical utility

Methods

Simoa

- Single-plex BD-tau
- N4PD (BD-tau, GFAP, NF-light, UCH-L1)
- Pitt in-house BD-tau

NULISA

- CNS Disease Panel 120

Cohort 1

- AD, MCI, non-AD dementia (Pitt ADRC)
- Single-plex & NULISA

Cohort 2

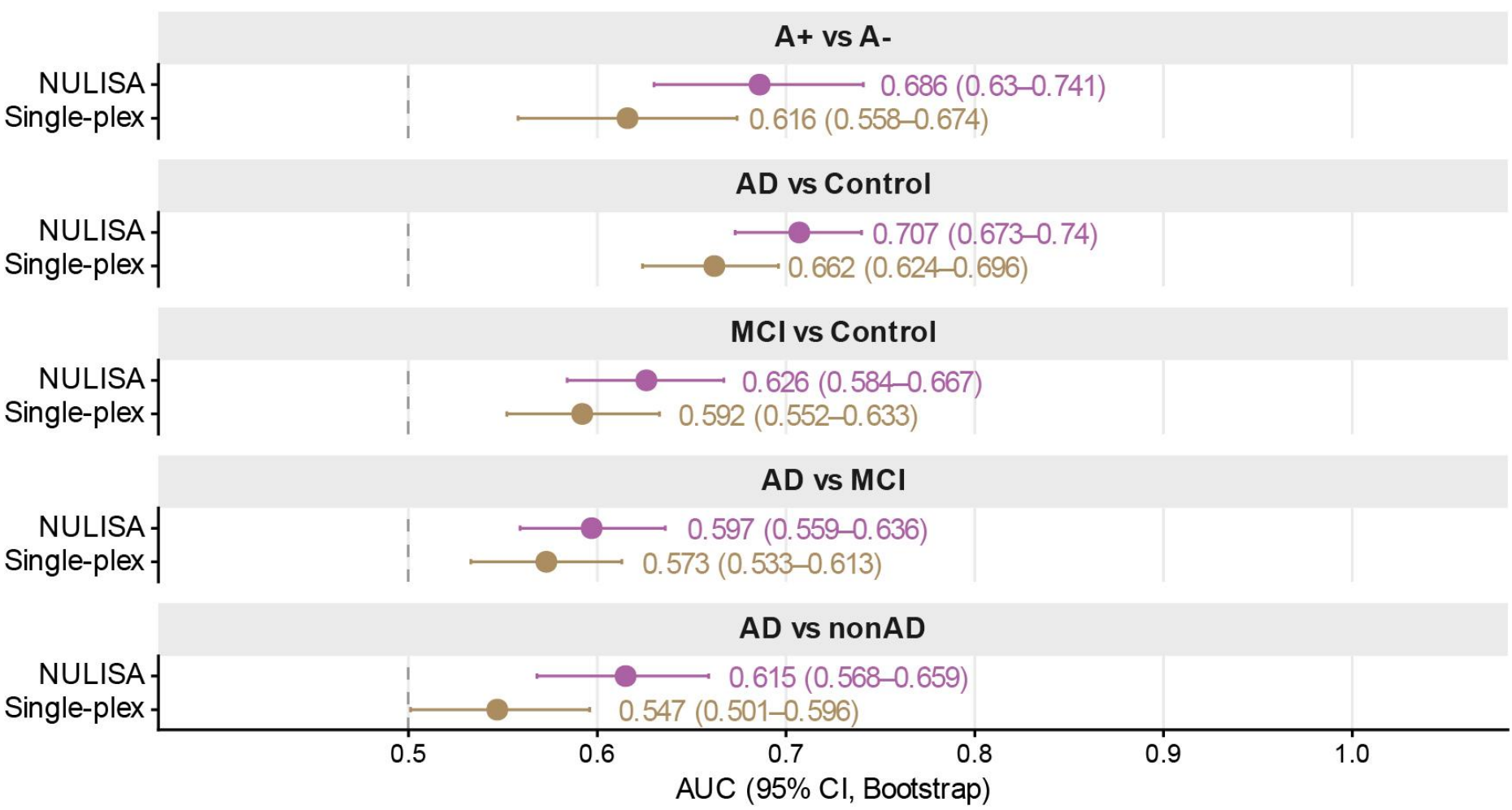
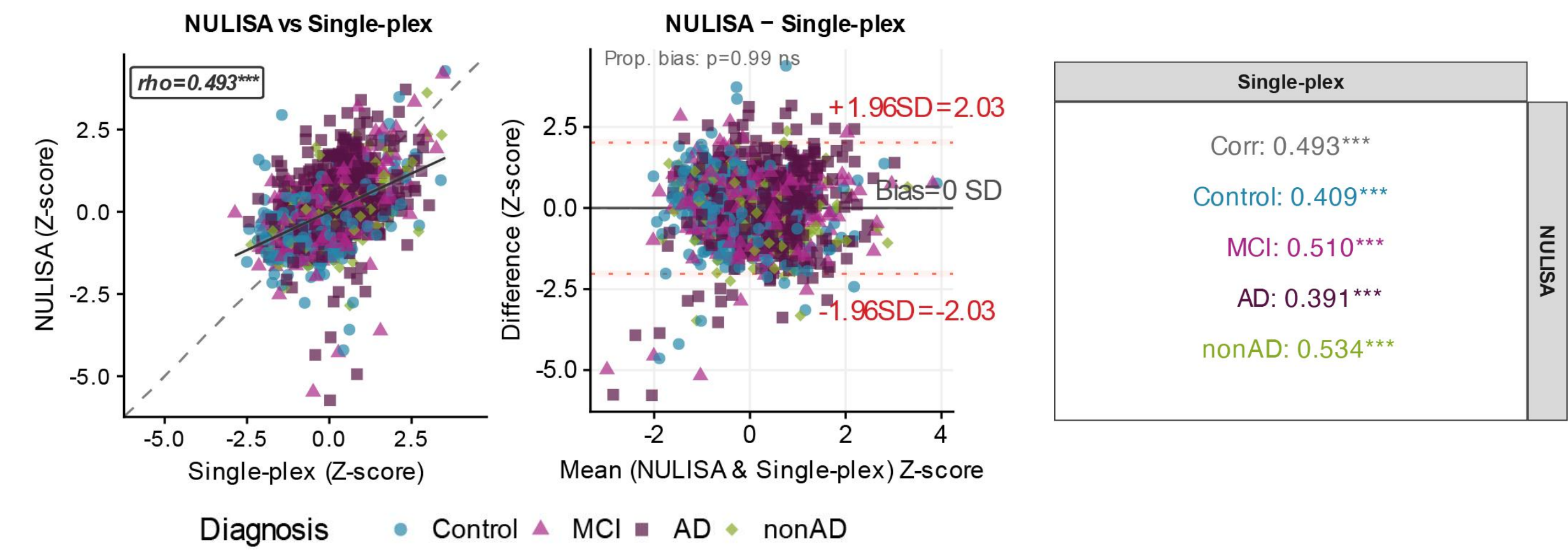
- TBI, SCI
- NULISA, single-plex, N4PD, & Pitt in-house

Participant demographics

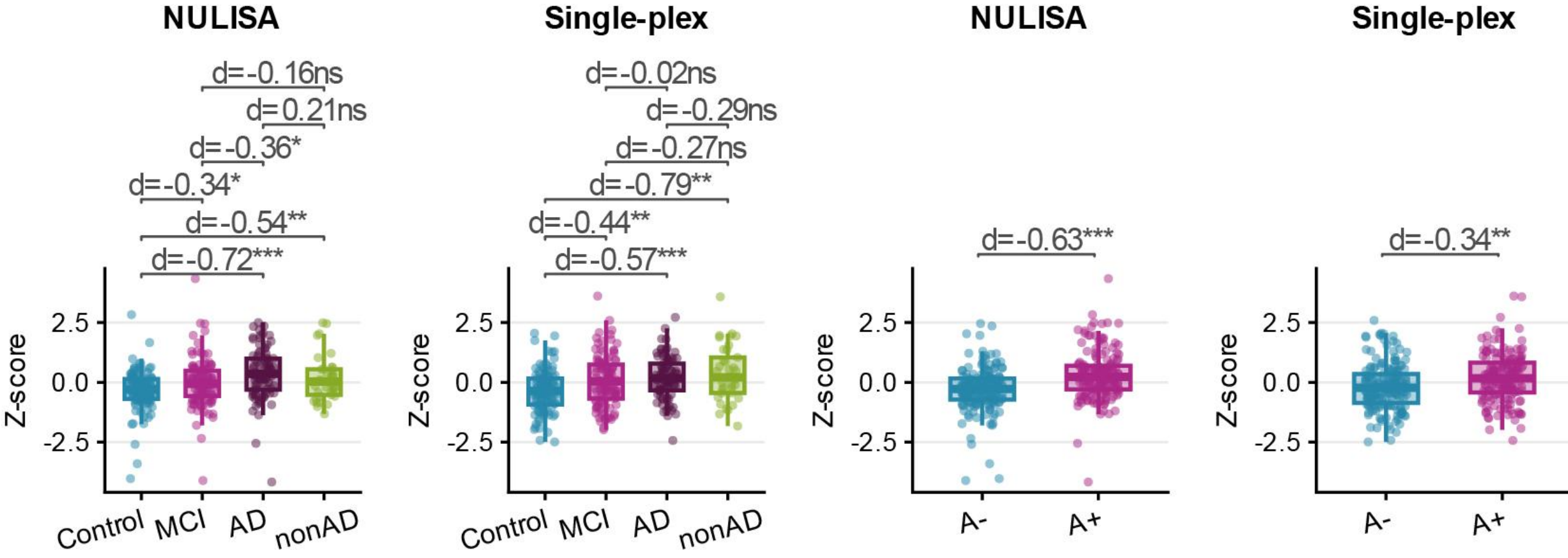
	Cohort 1
Number of participants	1425
Sex	
Female (%)	752 (52.8)
Male (%)	673 (47.2)
Age (years)	70.46 ± 9.81
A status	
A- (%)	175 (51.2)
A+ (%)	167 (48.8)
Clinical status	
AD	481
MCI	323
non-AD	207
Control	414

	Cohort 2
Number of participants	205
Sex	
Female (%)	50 (24.4%)
Male (%)	155 (75.6%)
Age (years)	42.86 ± 19.07
Clinical status	
SCI	40
Severe TBI	143
Control	22

Cohort 1 results



Comparison	Marker1	Marker2	Sig
A+ vs A-	NULISA	Single-plex	*
AD vs Control	NULISA	Single-plex	*
MCI vs Control	NULISA	Single-plex	ns
AD vs MCI	NULISA	Single-plex	ns
AD vs nonAD	NULISA	Single-plex	*



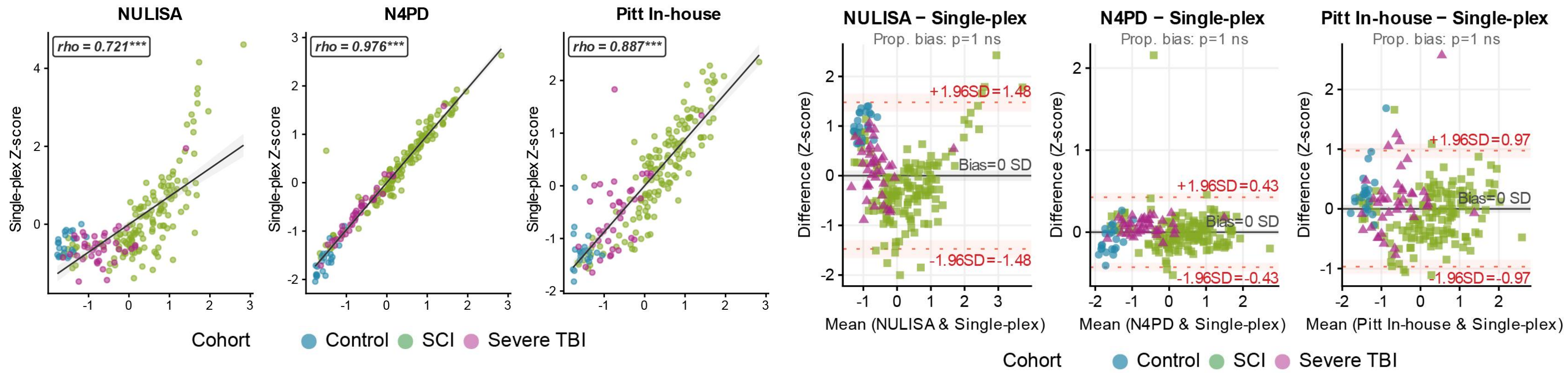
Data processing: NULISA NPQ values are natively log₂-scaled. Values from all other platforms were log₂-transformed prior to analysis and z-scored independently

Correlation analysis and platform agreement: Spearman rho coefficient with overall regression line fitted across full cohort. Pairwise correlation matrix shows within-group correlation coefficients across platforms. Pairwise Bland-Altman analysis performed with bias and 95% limits of agreement reported in SD units

Group distribution: Box-jitter plots of z-scored values with shared y-axis for each biomarker. Effect size reported as Cohen's d computed on raw scale. P values from Welch two-sample t-test with Benjamini-Hochberg correction for multiple comparisons

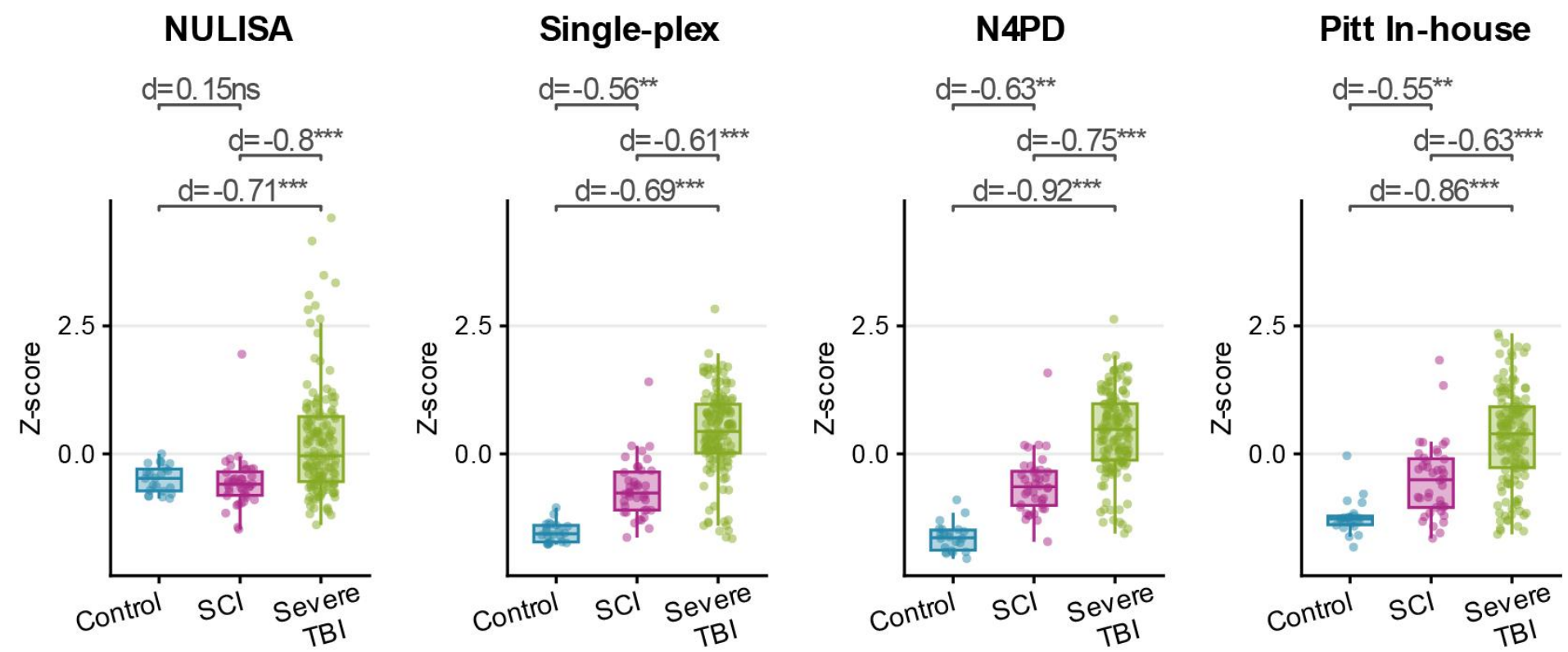
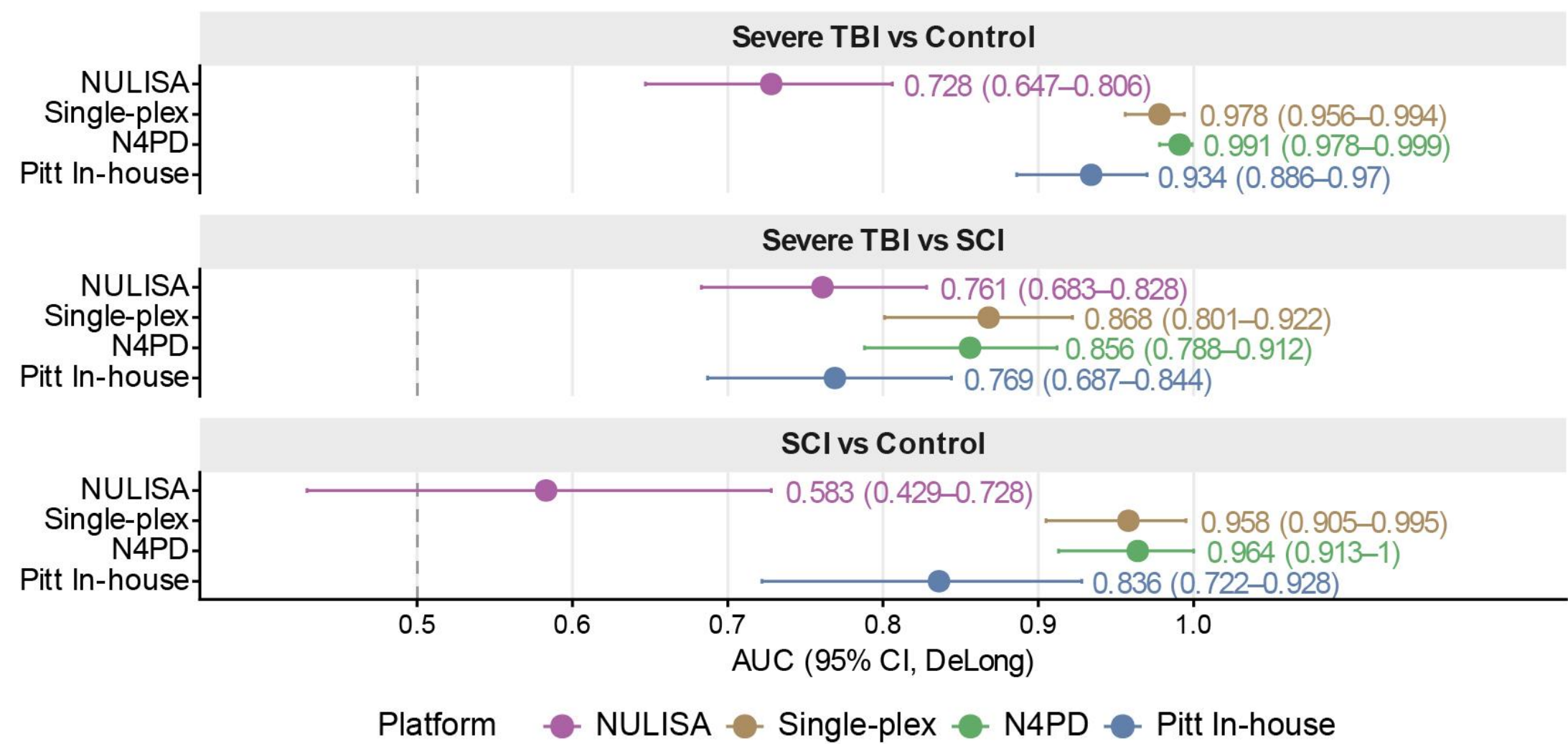
Forest plot: AUC values with 95% confidence intervals for each platform. DeLong test used to assess statistical differences between platforms

Cohort 2 results



Single-plex	N4PD	Pitt In-house	
Corr: 0.721***	Corr: 0.725***	Corr: 0.681***	
Control: 0.411	Control: 0.368	Control: 0.093	
SCI: 0.225	SCI: 0.264	SCI: 0.066	
Severe TBI: 0.784***	Severe TBI: 0.792***	Severe TBI: 0.764***	

Pitt In-house	N4PD	Pitt In-house	
Corr: 0.894***	Corr: 0.976***	Corr: 0.887***	
Control: -0.068	Control: 0.729***	Control: -0.046	
SCI: 0.553***	SCI: 0.988***	SCI: 0.577***	
Severe TBI: 0.884***	Severe TBI: 0.964***	Severe TBI: 0.877***	



Comparison	Marker1	Marker2	Sig
Severe TBI vs Control	NULISA	Single-plex	***
Severe TBI vs Control	NULISA	N4PD	***
Severe TBI vs Control	NULISA	Pitt In-house	***
Severe TBI vs Control	Single-plex	N4PD	ns
Severe TBI vs Control	Single-plex	Pitt In-house	*
Severe TBI vs Control	N4PD	Pitt In-house	**
Severe TBI vs SCI	NULISA	Single-plex	**
Severe TBI vs SCI	NULISA	N4PD	**
Severe TBI vs SCI	NULISA	Pitt In-house	ns
Severe TBI vs SCI	Single-plex	N4PD	ns
Severe TBI vs SCI	Single-plex	Pitt In-house	***
Severe TBI vs SCI	N4PD	Pitt In-house	**
SCI vs Control	NULISA	Single-plex	***
SCI vs Control	NULISA	N4PD	***
SCI vs Control	NULISA	Pitt In-house	**
SCI vs Control	Single-plex	N4PD	ns
SCI vs Control	Single-plex	Pitt In-house	*
SCI vs Control	N4PD	Pitt In-house	*

Conclusions

- Between-platform correlations and agreement**
 - Cohort 2 displayed strong correlations ($\rho > 0.7$), except for Pitt in-house vs. NULISA ($\rho = 0.681$)
 - Cohort 1 had moderate correlations ($\rho = 0.493$)
 - In both cohorts, NULISA vs. single-plex showed larger limits of agreement (greater discrepancy)
- Cohort 1**
 - NULISA was superior to single-plex in distinguishing A+ vs. A-, AD vs. control, and AD vs. non-AD
 - Medium effect sizes observed in both platforms for AD, non-AD, and MCI vs. control
- Cohort 2**
 - N4PD and single-plex were superior to Pitt in-house and NULISA in distinguishing severe TBI vs. control, severe TBI vs. SCI, and SCI vs. control
 - Strong effect sizes observed between severe TBI and controls using N4PD and Pitt in-house and severe TBI vs. SCI using NULISA

Acknowledgements

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