

Plasma Metabolites Associated With Plasma Amyloid- β 42/40 Ratios In Alzheimer's Disease

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A β 42/A β 40 ratio-associated plasma metabolites provide biologically relevant and clinically promising blood-based biomarkers for classifying brain amyloid pathology across the Alzheimer's disease continuum.

INTRODUCTION

- The plasma amyloid- β (A β)42/A β 40 ratio is an established blood-based biomarker reflecting cerebral amyloid pathology in Alzheimer's disease (AD)^{a, b, c, d}. However, plasma metabolite alterations associated with this ratio across the AD continuum remain poorly characterized.
- This study aimed to identify plasma metabolites associated with the A β 42/A β 40 ratio and evaluate their biomarker potential to improve understanding of the biochemical alterations underlying AD onset and progression.

RESULTS

Table 1: Cohort Characteristics.

	N	Groups by disease status and PET-A β Load			p-value
		CU A β -	CU A β +	AD A β +	
Age (years)	81 (26, 26, 29)	74.46 $\pm$ 4.05	76.04 $\pm$ 4.45	76.28 $\pm$ 7.27	0.432
Female (n (%))	81 (26, 26, 29)	15 (57.70)	14 (53.84)	17 (58.62)	0.932
APOE ϵ 4* status (n (%))	81 (26, 26, 29)	6 (23.08)	14 (53.84)	24 (82.76)	<0.0001
Collection site (n (%))					
Melbourne/Perth	81 (26, 26, 29)	10 (38.5)/16 (61.5)	18 (69.2)/8 (30.8)	14 (48.3)/15 (51.7)	0.076
Body mass index (BMI)	73 (24, 25, 24)	27.05 $\pm$ 3.52	24.70 $\pm$ 3.55	25.64 $\pm$ 4.32	0.103
MMSE	81 (26, 26, 29)	28.85 $\pm$ 1.08	28.81 $\pm$ 1.33	19.59 $\pm$ 5.21	<0.0001
Brain PET-A β Centiloid	75 (26, 26, 23)	-1.24 $\pm$ 5.41	63.02 $\pm$ 29.60	98.74 $\pm$ 28.58	<0.0001
A β 42/A β 40 ratio	81 (26, 26, 29)	0.061 $\pm$ 0.008	0.046 $\pm$ 0.009	0.049 $\pm$ 0.007	<0.0001

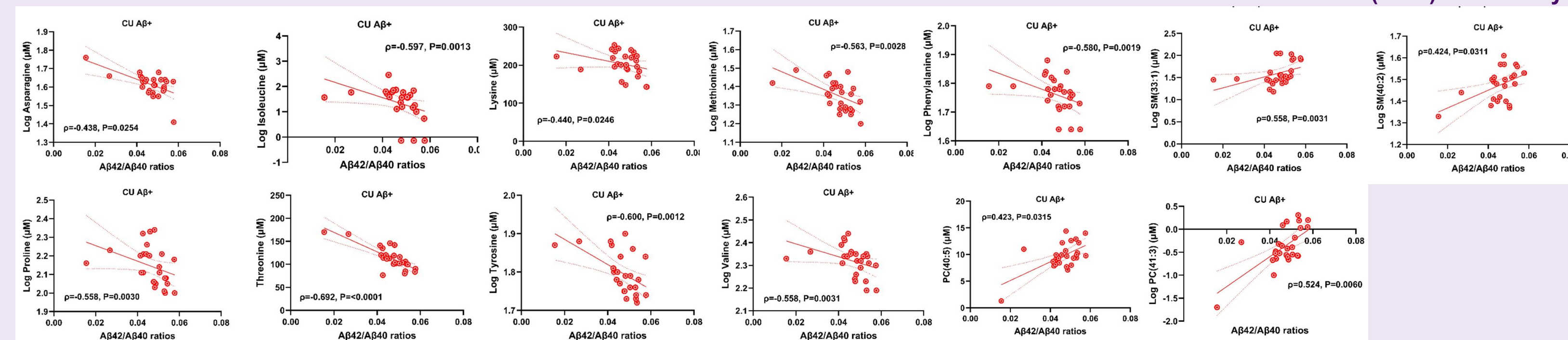


Figure 1: Plasma metabolites correlated with A β 42/A β 40 ratios in CU A β +. No statistically significant correlations were found in CU A β - or AD A β + groups.

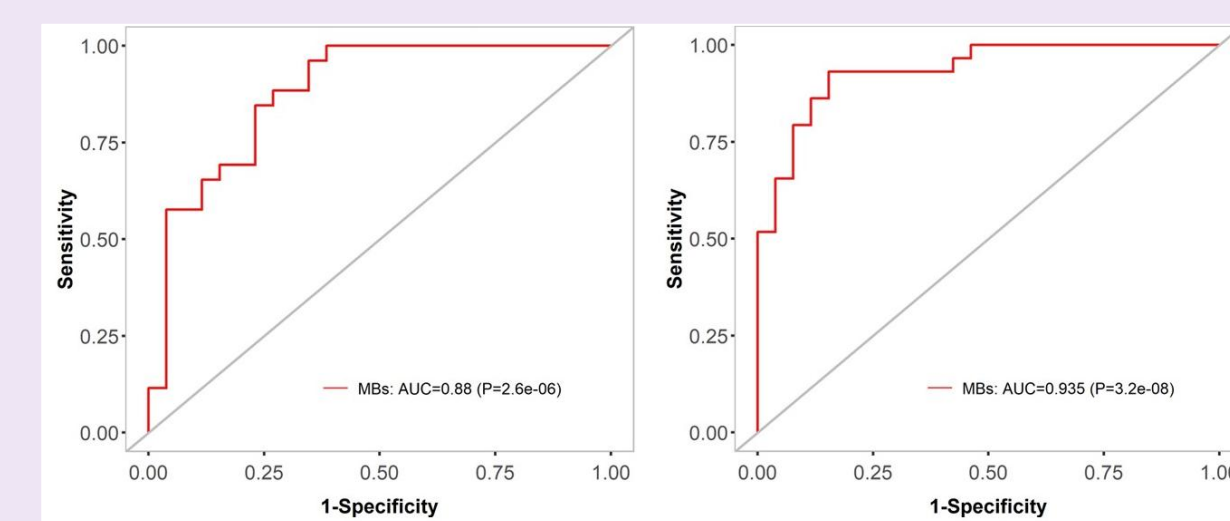


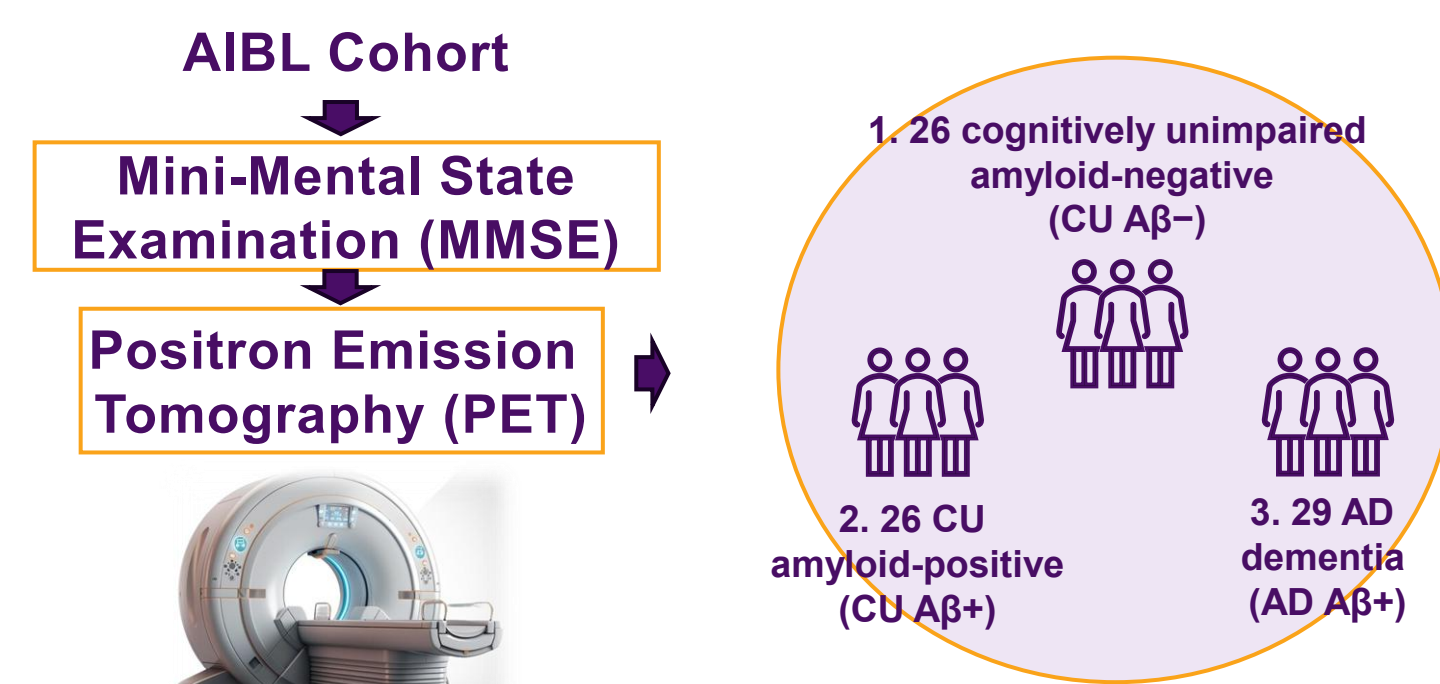
Figure 2: ROC plots of A β 42/A β 40 ratio-associated metabolites (MBs) to classify brain A β status.

CONCLUSION

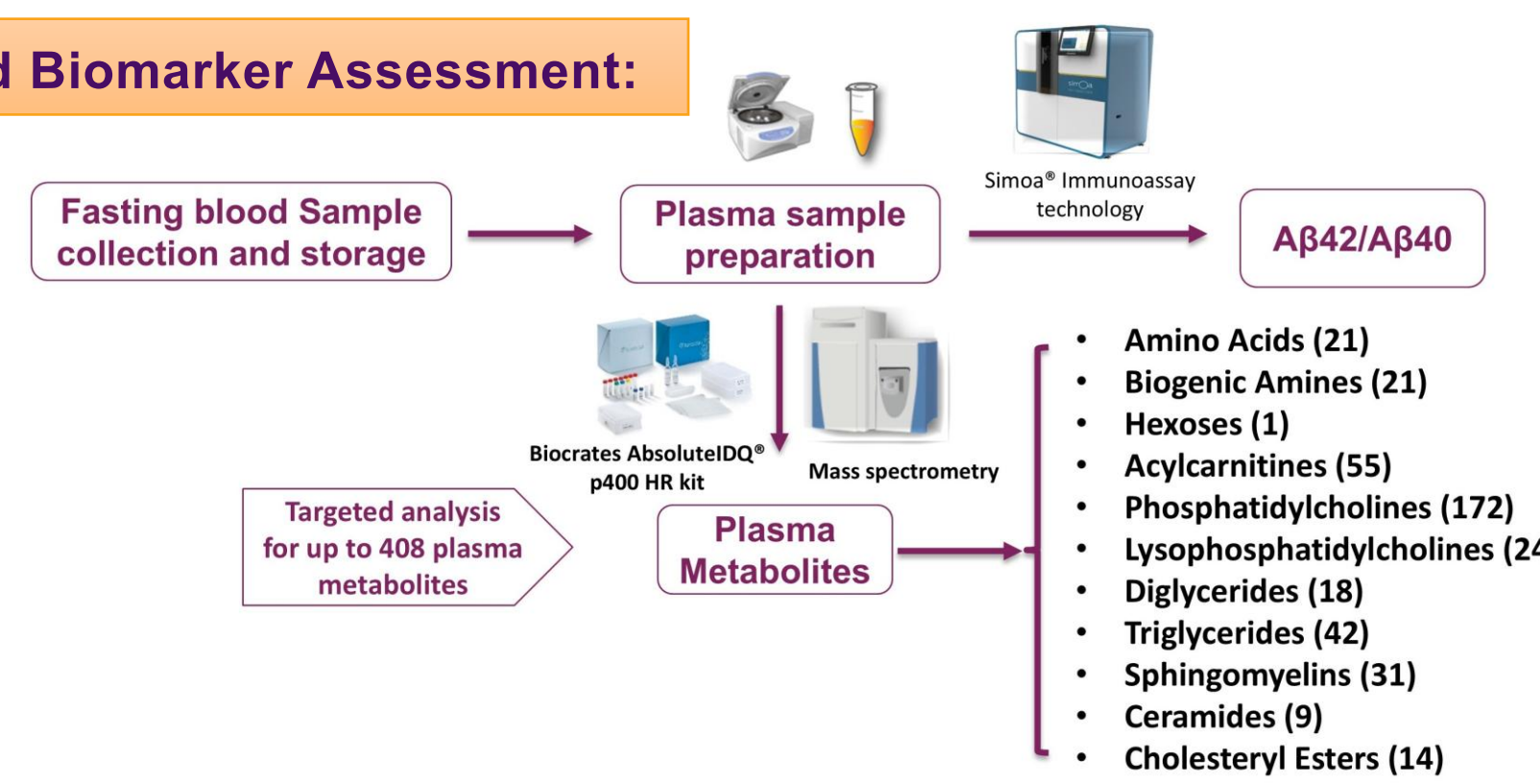
- Lower plasma A β 42/A β 40 ratios were associated with higher amino acid levels and lower lipid levels exclusively in CU A β + individuals, indicating relevant biochemical alterations accompanying initial cerebral amyloid pathology.
- Upon ROC analysis, a panel of A β 42/A β 40 ratio-associated metabolites demonstrated strong discriminatory performance for brain amyloid status, distinguishing CU A β - from CU A β + and AD A β + individuals with AUCs of 88% and 93.5%, respectively.

METHODS

1. Clinical and PET-A β Assessment:



2. Blood Biomarker Assessment:



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