

Disease-Specific Alterations of Glia-Associated Blood Biomarkers in Hereditary Leukoencephalopathies



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Introduction

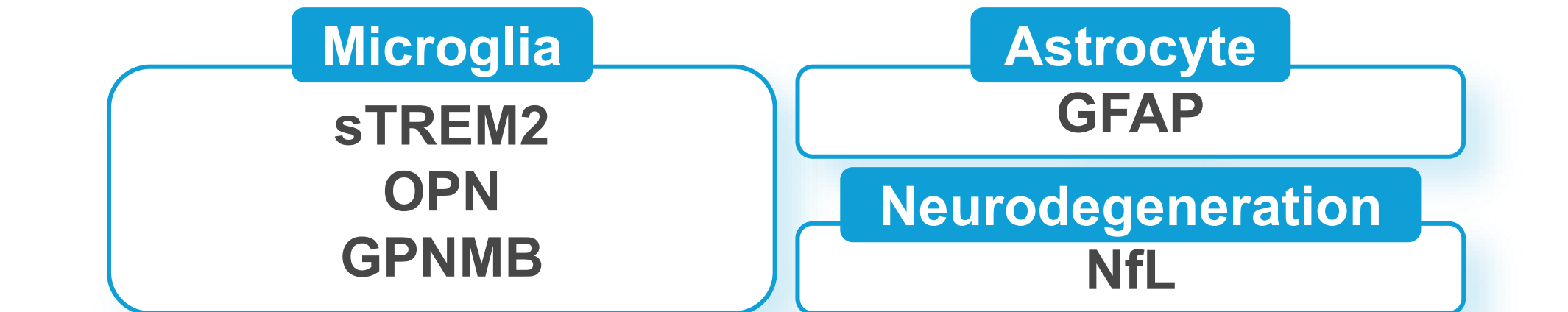
- ALSP
- NIID
- ADLD
- ALSP, NIID, and ADLD are inherited disorders with white matter involvement.
 - Knowledge of their pathophysiology and biomarker profiles remains limited¹⁾²⁾³⁾.
 - We evaluated glial- and neurodegeneration-related plasma biomarkers for their pathophysiological relevance and potential diagnostic utility.

ALSP, adult-onset leukoencephalopathy with spheroids and pigmented glia; NIID, neuronal intranuclear inclusion disease; ADLD, LMNB1-related autosomal dominant leukodystrophy.

Methods

Participants: Patients with ALSP, NIID, ADLD, and healthy controls (HC)

Plasma biomarkers:



Analysis: Age- and sex-adjusted group comparisons, Biomarker correlations (Spearman's ρ), ROC analyses (disease vs HC)

sTREM2, soluble triggering receptor expressed on myeloid cells 2; OPN, osteopontin; GPNMB, glycoprotein non-metastatic melanoma protein B; GFAP, glial fibrillary acidic protein; NfL, neurofilament light chain; ROC, receiver operating characteristic.

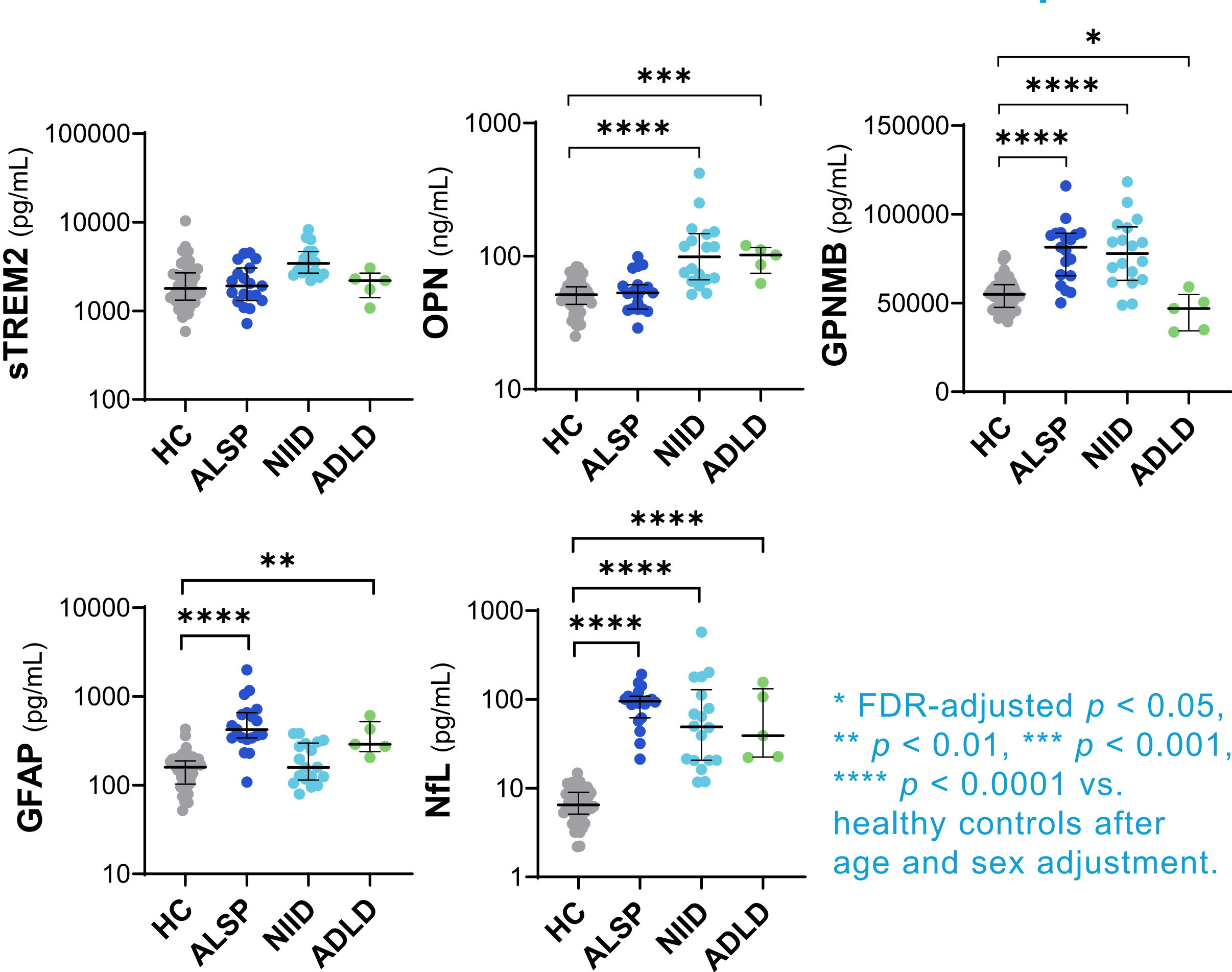
Results

Participant Characteristics

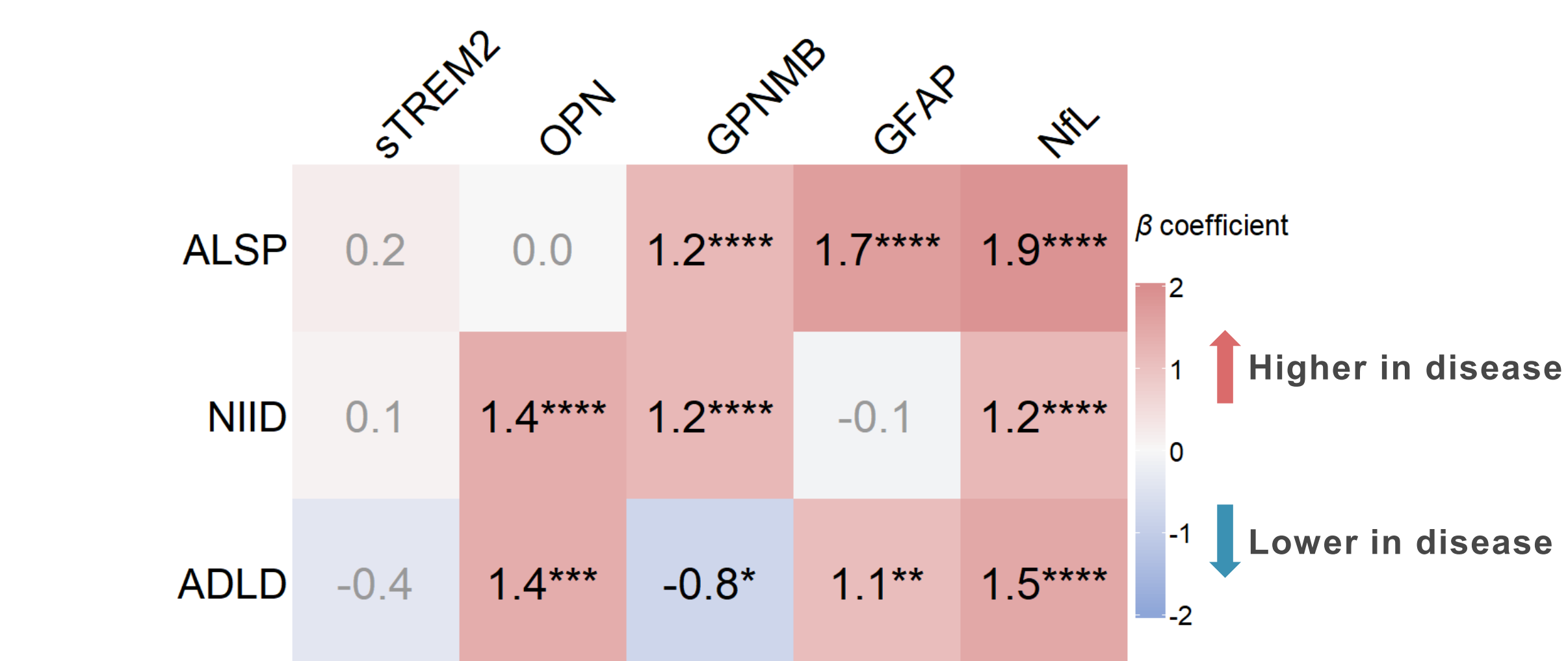
	HC	ALSP	NIID	ADLD	p value
n	48	19	18	5	-
Age, y	52.5 [42-57]	46 [42-51]	71 [66-77]	56 [50-70]	<0.0001 ^a
Female (%)	29 (60)	8 (42)	11 (61)	4 (80)	0.40 ^b
Age at onset, y	-	43 [41-48]	64 [61-70]	44 [43-50]	<0.0001 ^a
Disease duration, y	-	2 [1.0-3.0]	4 [1.3-7.8]	10 [7.0-12.0]	0.0085 ^a

Median [IQR], ^a Kruskal-Wallis test, ^b Fisher's exact test

Plasma Biomarker Levels Across Disease Groups

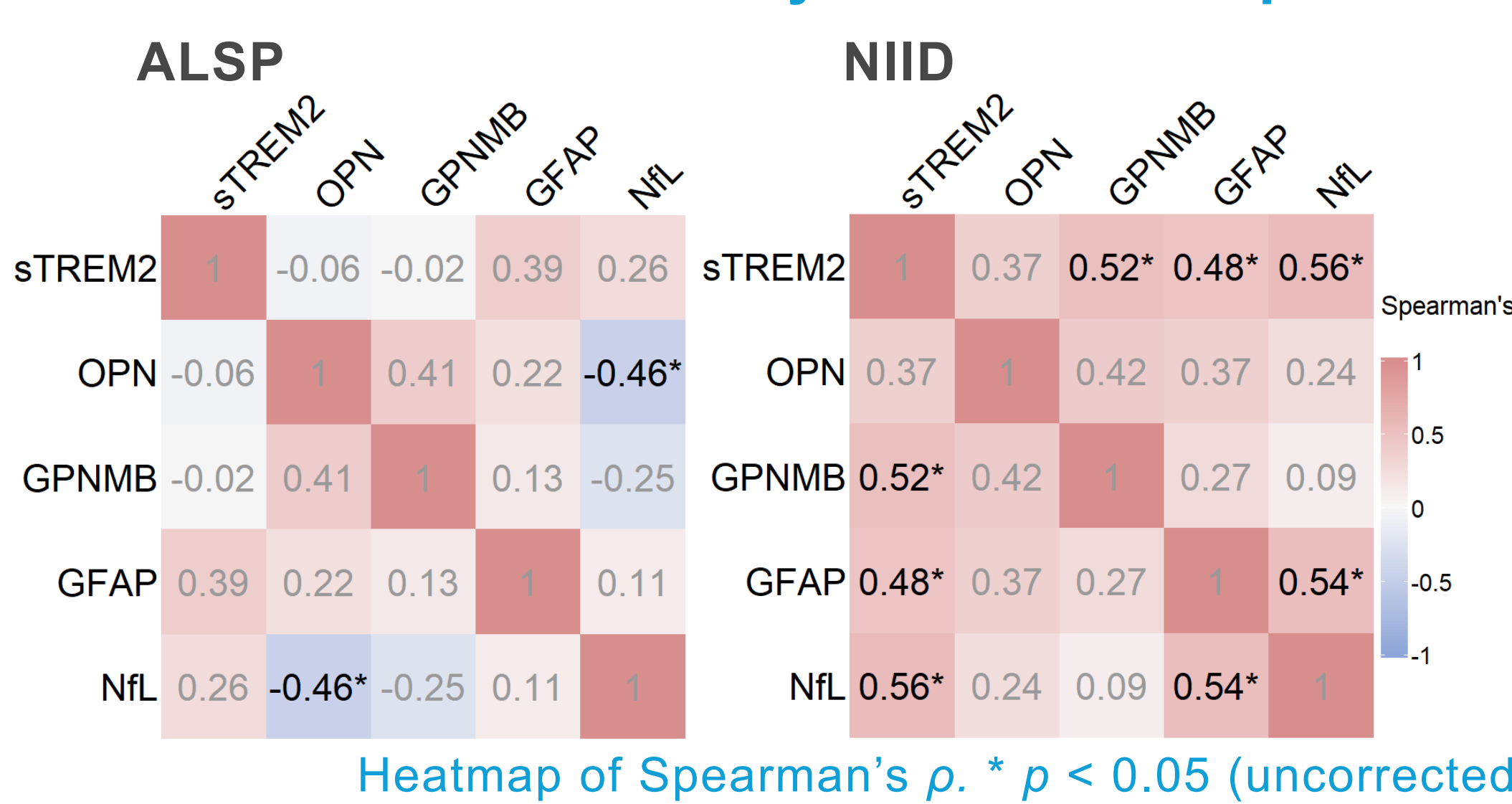


Disease Effects on Plasma Biomarker Levels

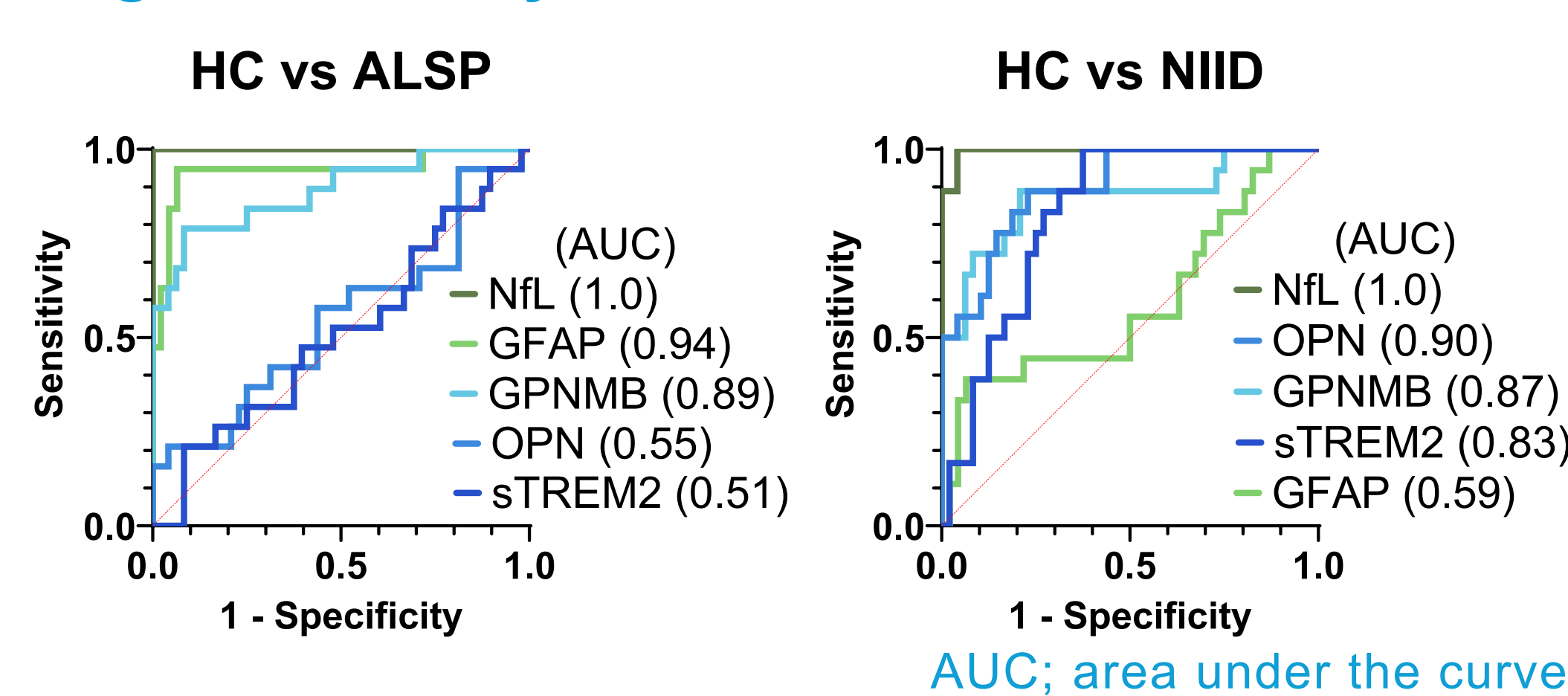


Heatmap of β coefficients from age- and sex- adjusted linear regression models with standardized biomarker levels as outcomes. Positive β values indicate higher biomarker levels relative to healthy controls. * FDR-adjusted $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$.

Biomarker Correlations by Disease Group



Diagnostic Utility of Plasma Biomarkers



Conclusions

- Glia-associated blood biomarkers showed disease-specific alterations in ALSP, NIID, and ADLD. These findings may provide insights into the underlying disease mechanisms.
- NfL showed good discrimination between patients and healthy controls and may be useful as a biomarker of disease presence.

References

- Konno T, et al. Neurology. 2018;91(24):1092-1104.
- Lu X, et al. J Neural Transm (Vienna). 2021;128(3):295-303.
- Neri I, et al. Mol Neurobiol. 2023;60(11):6362-6372.