

Concordance Of Cerebrospinal Fluid And Plasma Protein Abundance Differs Across Age, Sex, And Diagnosis Strata

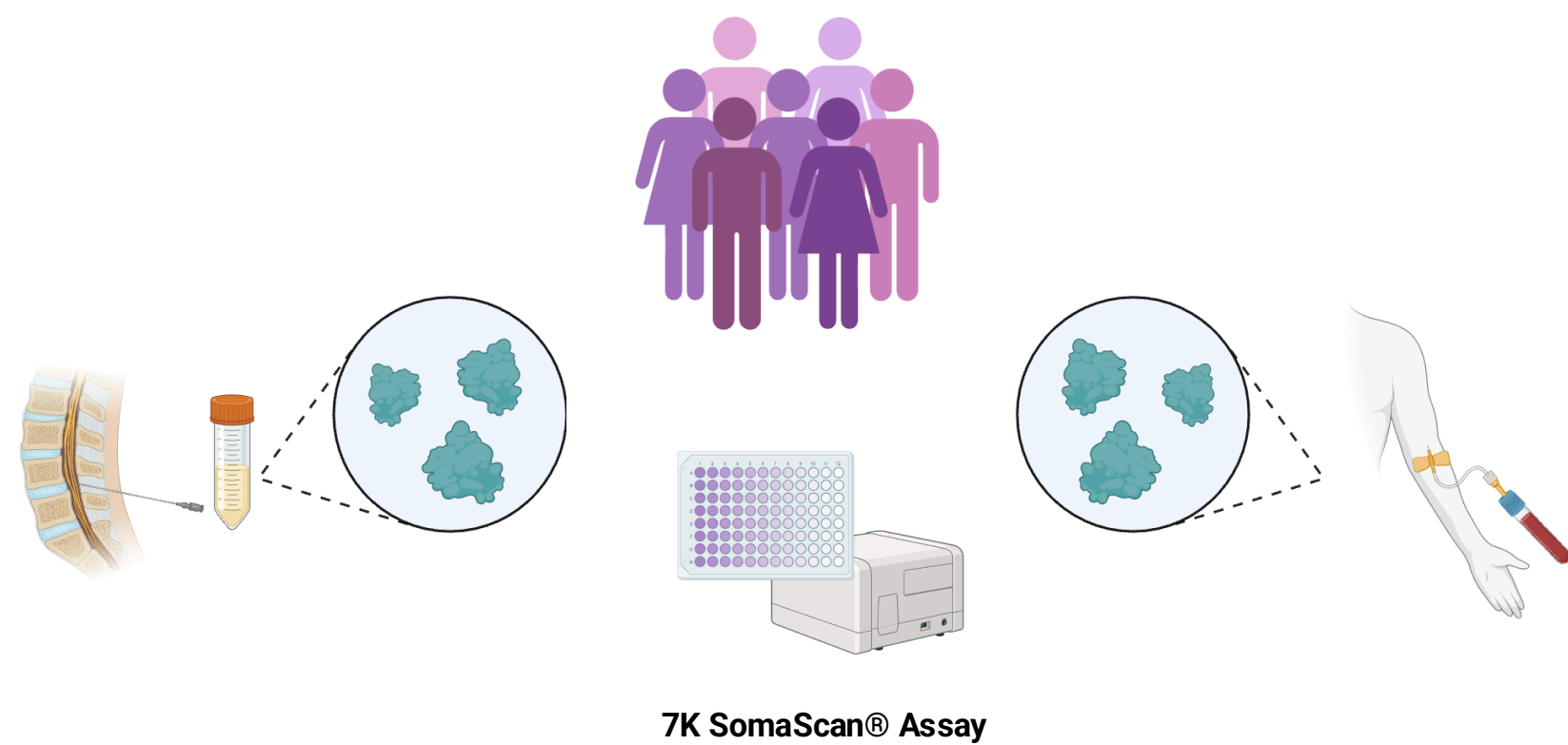
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Introduction

- Protein quantification is challenging in cerebrospinal fluid (CSF) due to low protein abundance and a limited understanding CSF protein dynamics and regulatory factors.
- Protein levels in CSF and plasma do not correspond 1:1, with protein-specific differences in how they cross the blood-brain barrier
- There are several factors that may determine the correspondence between CSF and plasma protein levels, including advanced age, disease state, and protein hydrophobicity
- In this study, we characterized the concordance of ~7000 CSF and plasma proteins using the 7K SomaScan® platform

Methods

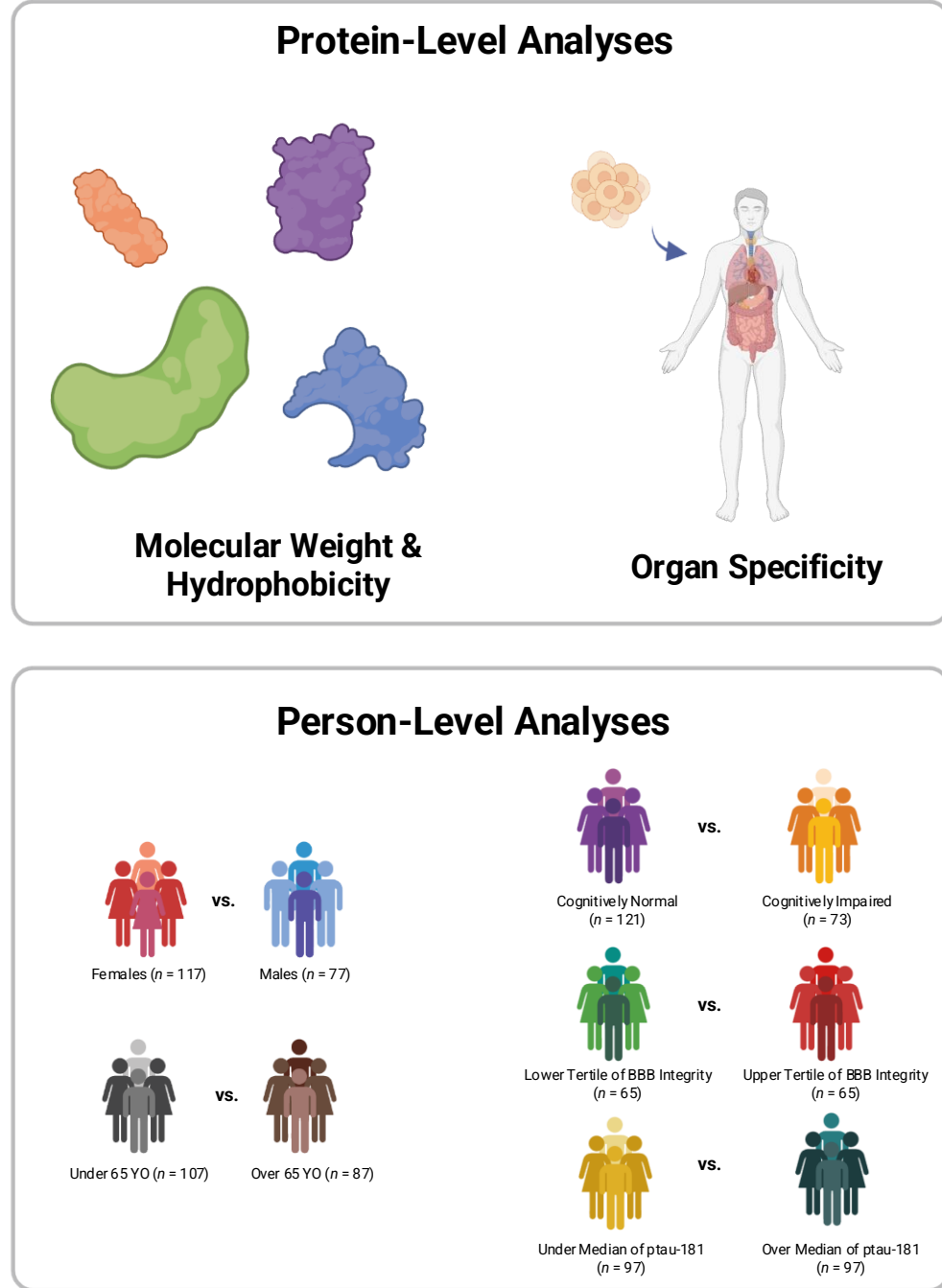


This study included 194 adults from whom CSF and plasma were collected and measured concurrently in a Johns Hopkins Neurology Clinical cohort.

Age, M (SD)	55.25 (21.24)
% Female	60.3
% Impaired (MCI or Dementia)	37.6

A series of spearman correlations were conducted in R (R 4.3.2). We conducted protein-level analyses in the entire sample ($n = 194$) looking at the effects of molecular weight, hydrophobicity, and organ specificity on CSF-plasma concordance.

We subsequently conducted person-level analyses across different participant strata, including age, sex, diagnosis, measures of AD-relevant neuropathology, and measures of blood-brain barrier integrity.



Results

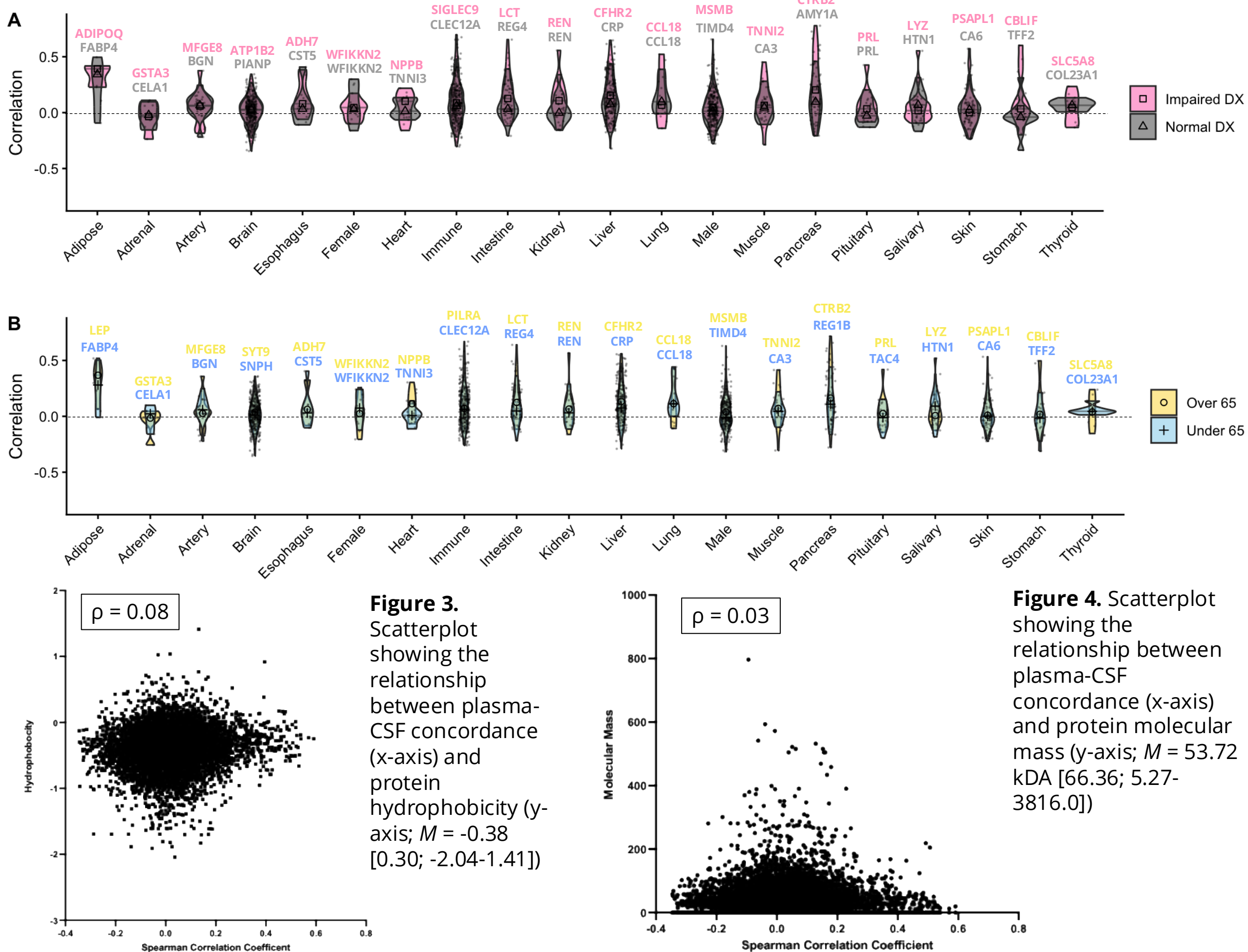
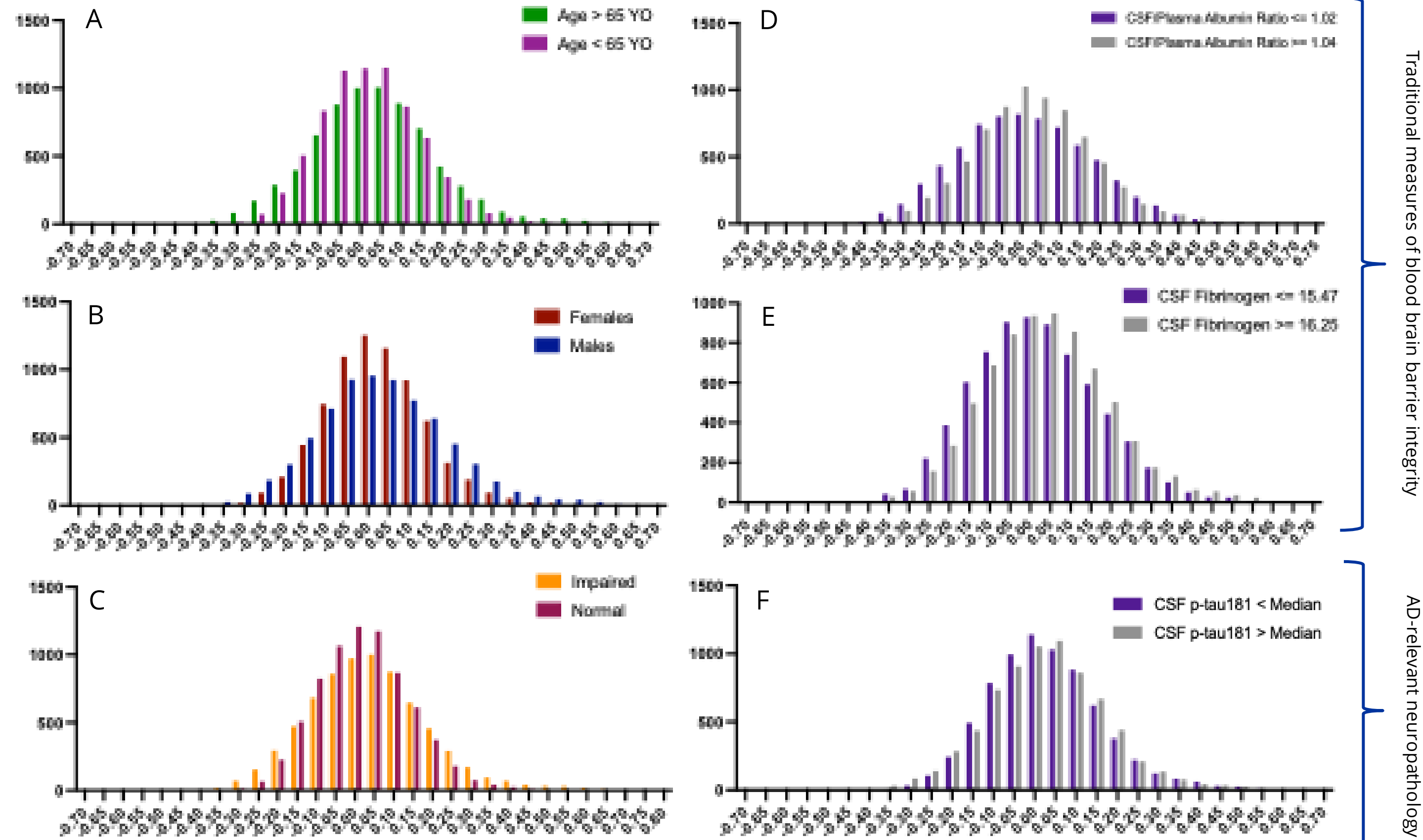


Figure 2 (A-B). Violin plots showing the distribution of spearman correlation coefficients representing plasma-CSF concordance (y-axis) across protein organ-types (x-axis) comparing diagnostic groups (A) and age groups (B). Individual proteins belonging to each organ system are overlaid as jittered points. The violin shape reflects the density and spread of spearman correlation coefficient values within each organ group. The strongest correlation among the dementia diagnosis group, the normal diagnosis group, the age over 65 group, and the age under 65 group is indicated by text annotation on the plot.

Conclusion

- Protein molecular weight and hydrophobicity were not meaningfully related to CSF-plasma concordance
- The correlation distribution differed across demographic participant strata, with the over 65, impaired diagnosis, and male distributions being generally wider
- The distribution of correlation coefficients was also wider in strata characterized by elevated blood-brain barrier disintegration measures and greater AD-relevant neuropathology
- Plasma-CSF concordance was variable across protein organ systems, with some of the strongest associations seen in the pancreas for over 65s and impaired strata

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