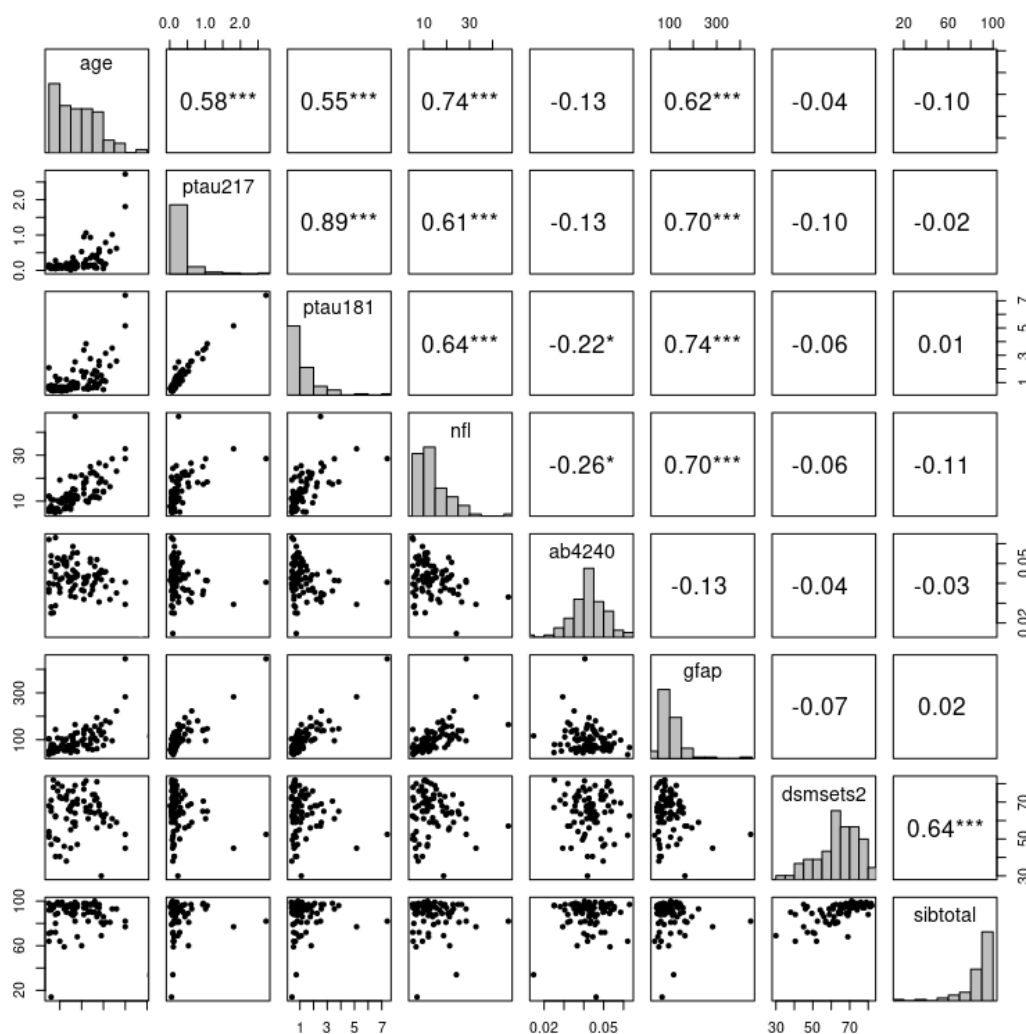


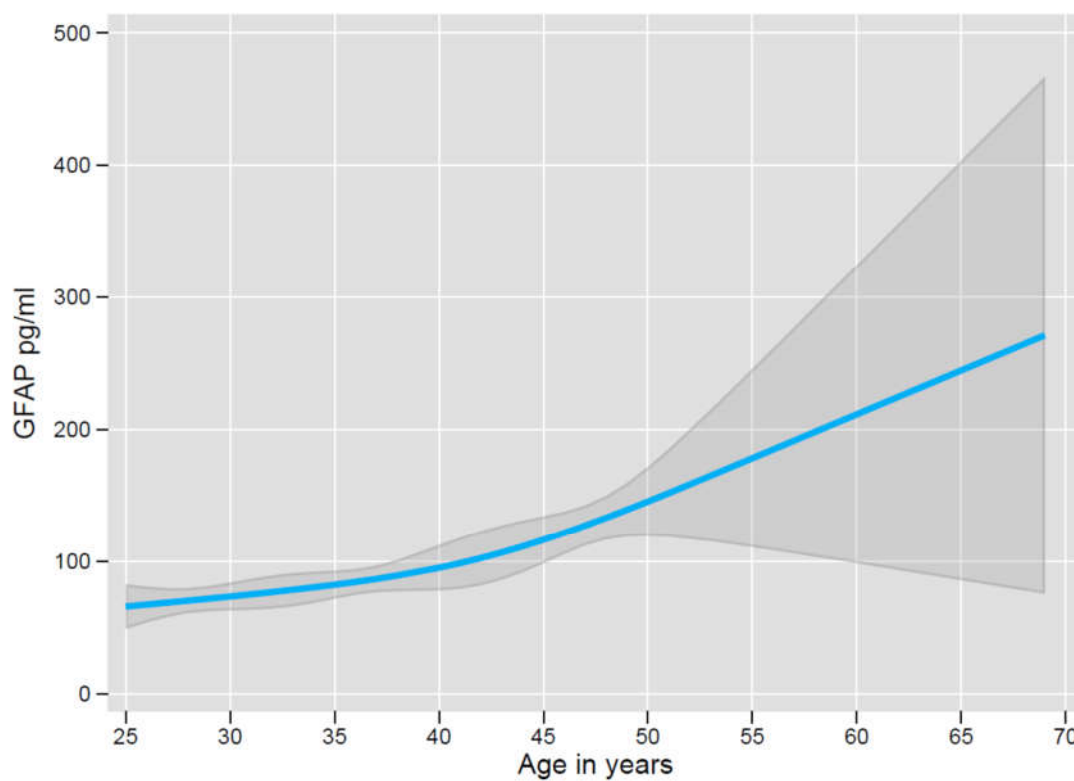
Article

Cross Sectional Exploration of Plasma Biomarkers of Alzheimer's Disease in Down Syndrome: Early Data from the Longitudinal Investigation for Enhancing Down Syndrome Research (LIFE-DSR) Study

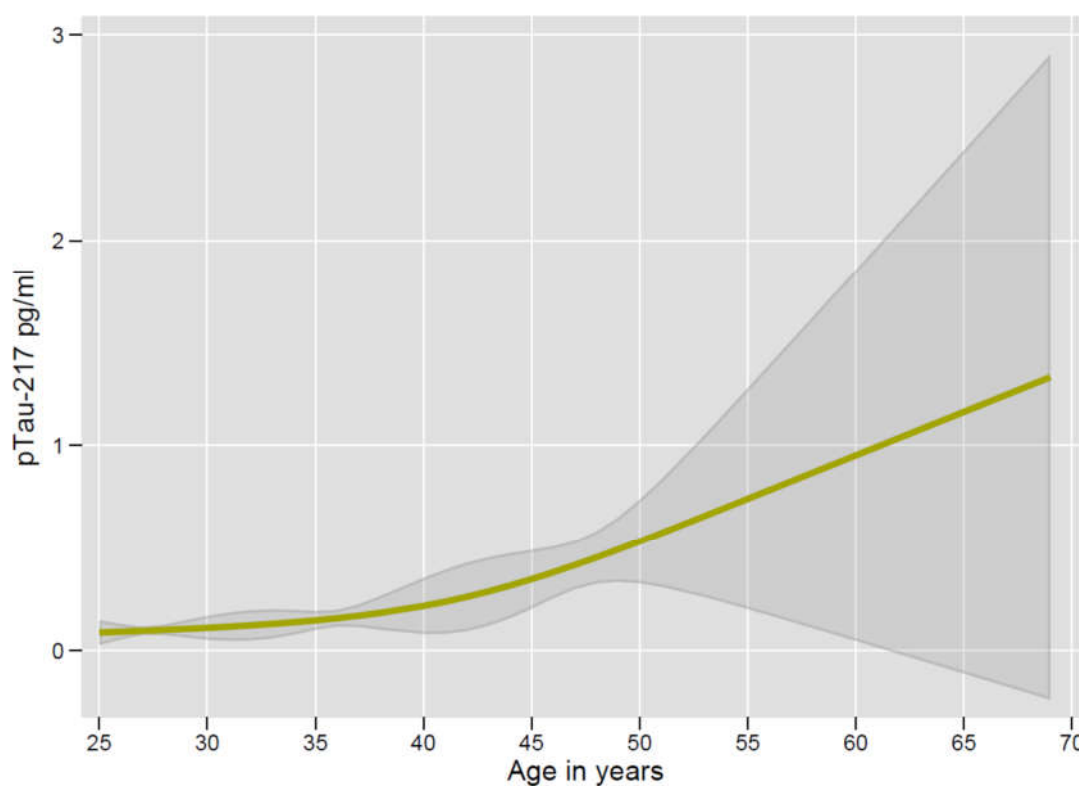
Supplemental Materials



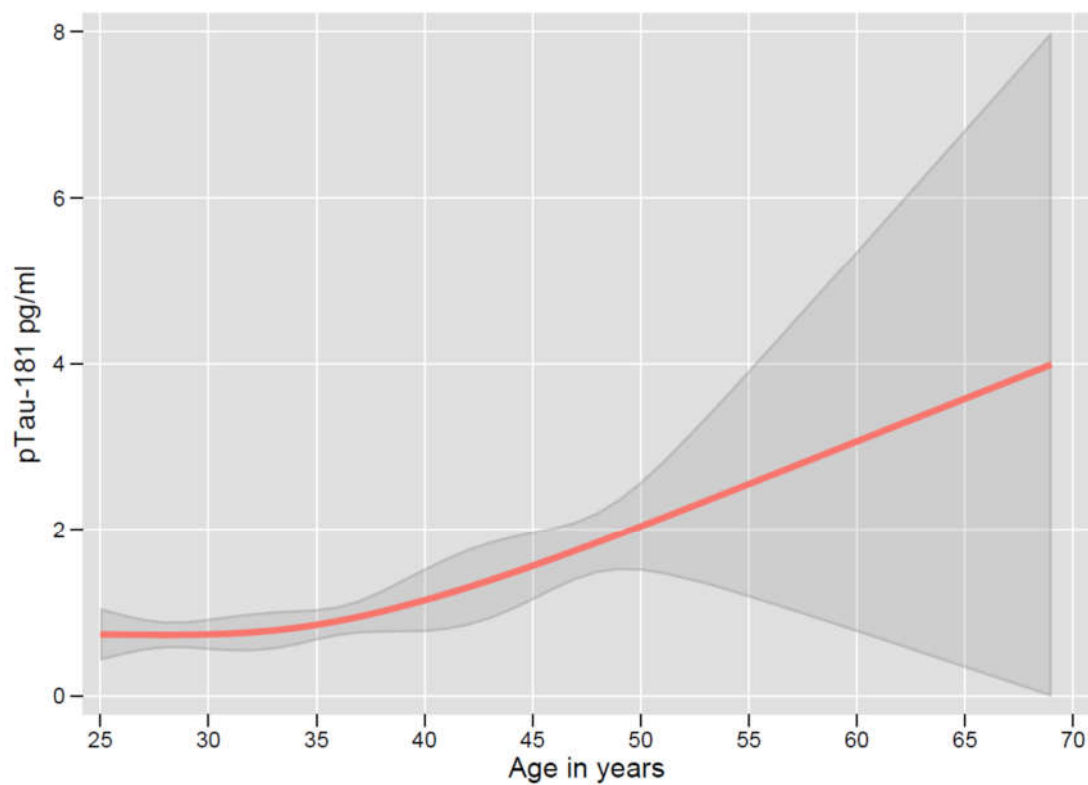
Supplemental Figure 1. Histograms (diagonal), scatterplots (below diagonal), and Spearman correlations (above diagonal) for biomarkers and clinical data. Stars indicate statistical significance at the unadjusted levels of $p \leq 0.05^*$, 0.01^{**} , and 0.001^{***} . A Bonferroni corrected significance level is $p = 0.05/28 = 0.0018$. (Abbreviations: $A\beta_{42/40}$ = amyloid $\beta_{42/40}$ ratio, dsmset2 = Down Syndrome Mental Status Examination method 2 score, GFAP = glial fibrillary acidic protein, NfL = neurofilament light, p = p-value, ptau181 = phosphorylated tau at threonine-181, ptau217 = phosphorylated tau at threonine-217, sibtotal = Severe Impairment Battery total score).



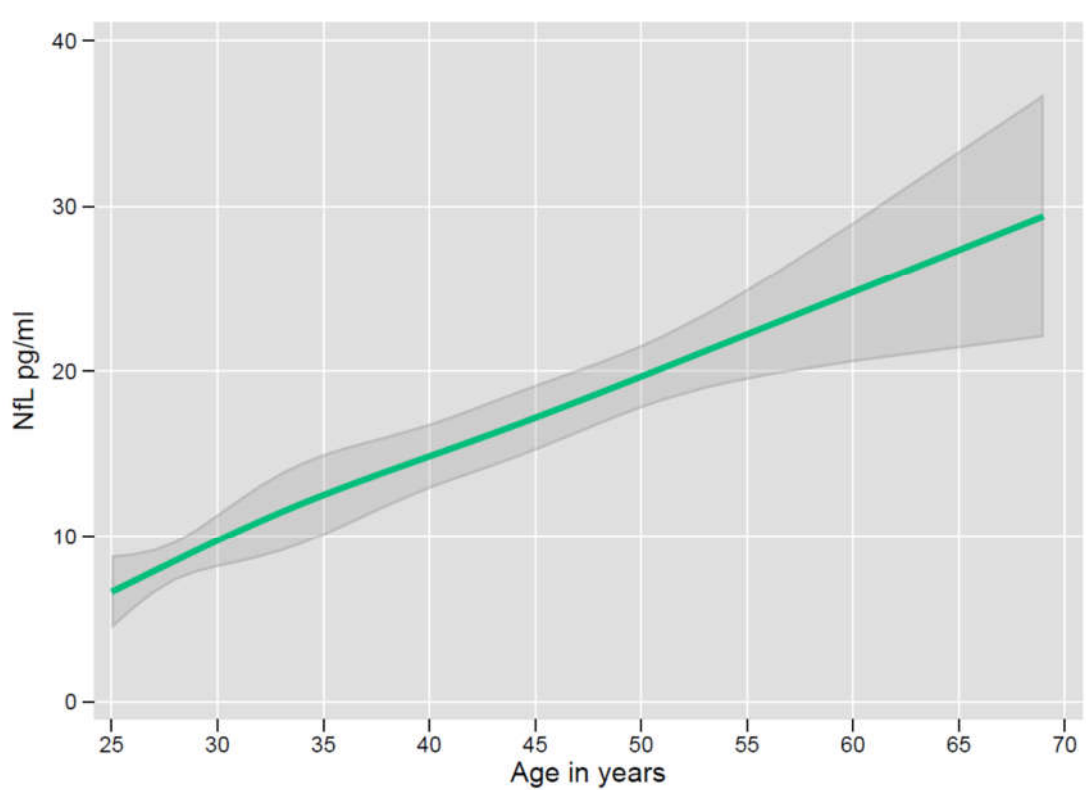
Supplemental Figure 2. Linear regression fit of untransformed GFAP on age, using restricted cubic splines with 4 knots and robust standard errors. $F(3,82) = 14.05$, $p < 0.0001$. (Abbreviations: GFAP = glial fibrillary acidic protein, $F(df1,df2)$ = F statistic (degrees of freedom 1, degrees of freedom 2), p = p-value, pg/mL = picogram/milliliter).



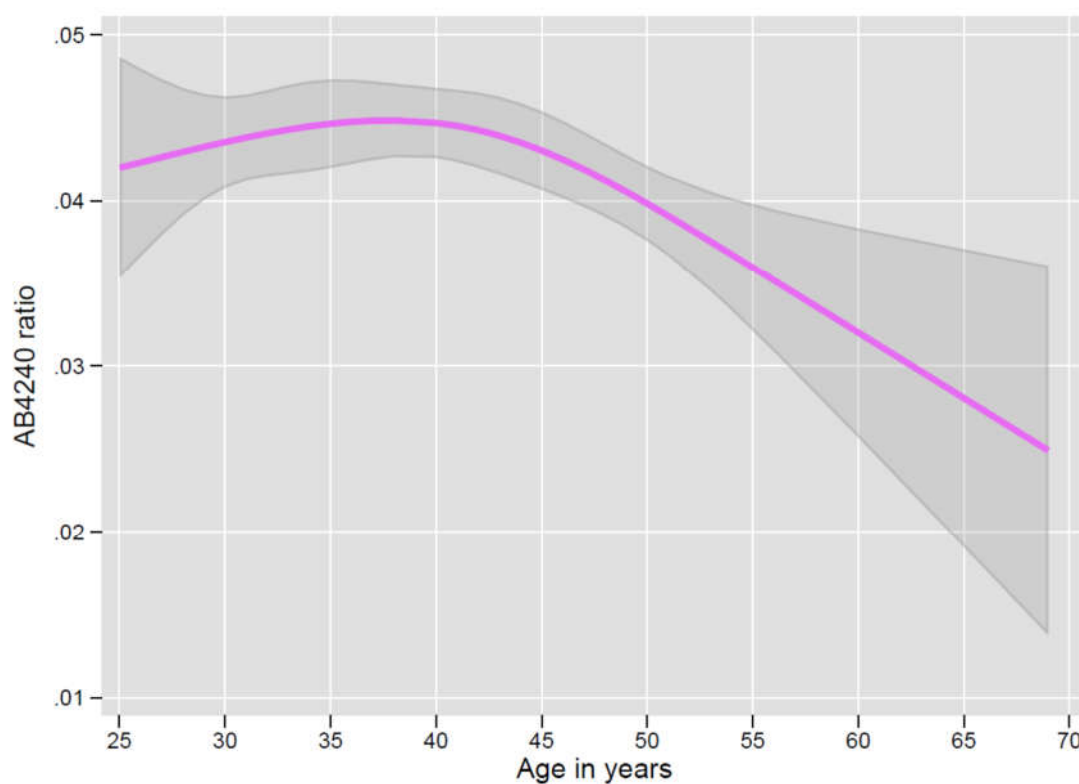
Supplemental Figure 3. Linear regression fit of untransformed p-tau 217 on age, using restricted cubic splines with 4 knots and robust standard errors. $F(3,82) = 9.91$, $p < 0.0001$. (Abbreviations: $F(df1,df2)$ = F statistic (degrees of freedom 1, degrees of freedom 2), p = p-value, p-tau 217 = phosphorylated tau at threonine-217, pg/mL = picogram/milliliter).



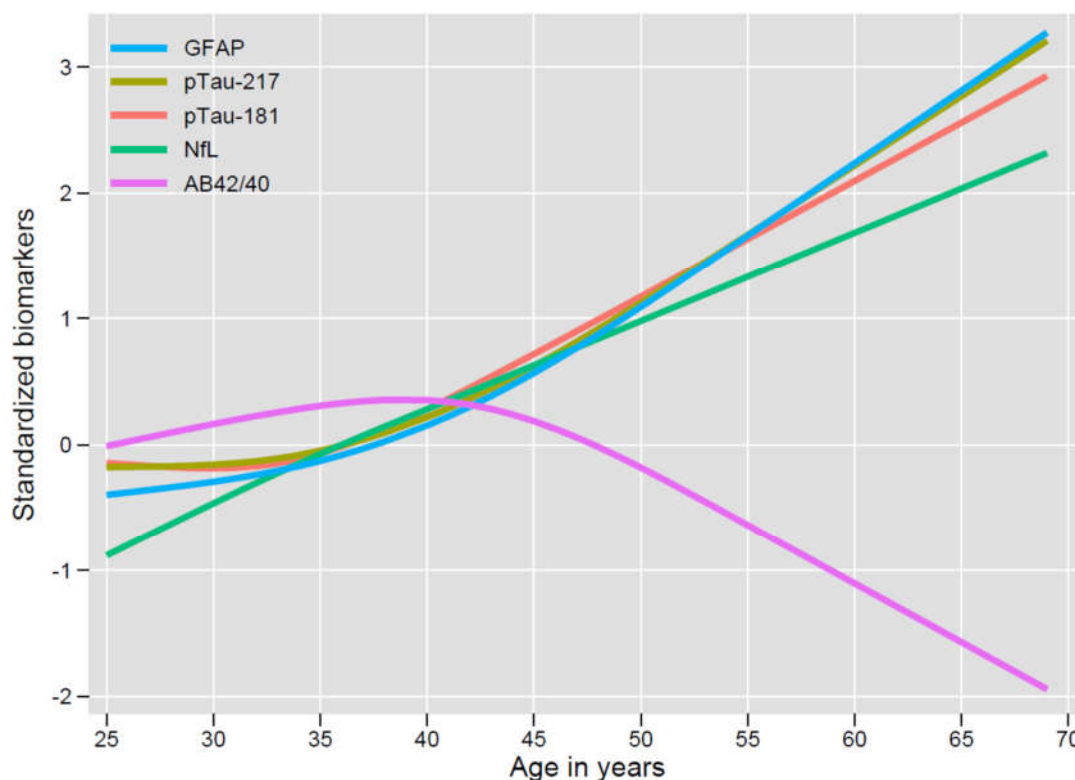
Supplemental Figure 4. Linear regression fit of untransformed p-tau 181 on age, using restricted cubic splines with 4 knots and robust standard errors. $F(3,82) = 10.14$, $p < 0.0001$. (Abbreviations: $F(df1,df2)$ = F statistic (degrees of freedom 1, degrees of freedom 2), p = p-value, p-tau 181 = phosphorylated tau at threonine-181, pg/mL = picogram/milliliter).



Supplemental Figure 5. Linear regression fit of untransformed NfL on age, using restricted cubic splines with 4 knots and robust standard errors. $F(3,82) = 34.57$, $p < 0.0001$. (Abbreviations: $F(df1,df2)$ = F statistic (degrees of freedom 1, degrees of freedom 2), NfL = neurofilament light, p = p-value, pg/mL = picogram/milliliter).



Supplemental Figure 6. Linear regression fit of untransformed $A\beta_{42}/A\beta_{40}$ ratio on age, using restricted cubic splines with 4 knots and robust standard errors. $F(3,82) = 4.71$, $p = 0.0044$; $F(3,81) = 2.41$, $p = 0.0728$ without oldest individual. (Abbreviations: $A\beta_{42/40}$ = amyloid $\beta_{42/40}$, $F(df1,df2)$ = F statistic (degrees of freedom 1, degrees of freedom 2), p = p-value).



Supplemental Figure 7. Shown are the predictions from linear regressions of each biomarker on age, using restricted cubic splines with 4 knots, and adjusted for *APOE ε4* carrier status and sex using additive covariates; *APOE ε4* adjusted to non-carrier and sex adjusted to female. GFAP: $F(3,80) = 11.23$, $p < .0001$; p-tau 217: $F(3,80) = 7.79$, $p = .0001$; p-tau 181: $F(3,80) = 9.25$, $p < .0001$; NfL: $F(3,80) = 36.02$, $p < .0001$; $A\beta_{42}/A\beta_{40}$ ratio: $F(3,80) = 5.01$, $p = .0031$, without oldest individual $F(3,79) = 2.04$, $p = 0.1146$. (Abbreviations: $A\beta_{42}/40$ = amyloid $\beta_{42}/40$ ratio, *APOE ε4* = Apolipoprotein E $\epsilon 4$ allele, GFAP = glial fibrillary acidic protein, $F(df1,df2)$ = F statistic (degrees of freedom 1, degrees of freedom 2), NfL = neurofilament light, p = p-value, p-tau 181 = phosphorylated tau at threonine-181, p-tau 217 = phosphorylated tau at threonine-217).

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