

Table e-1. Comparative performance of baseline biomarker concentrations for prediction of change in PSP disease severity.*

Outcome variable	CSF p-tau	CSF NfL	CSF NfL/p-tau	CSF p-tau/Tau	Plasma NfL
	n = 49	n = 50	n = 49	n = 49	n = 141
<i>PSPRS (points)</i>					
Continuous	1.7 (.196)	4.3 (.040)	4.2 (.042)	.121 (.729)	4.1 (.042)
[biomarker] x time interaction	12.0 (.001)^e	10.4 (.001)	16.9 (< .001)^{a,b,e}	6.9 (.009)	16.3 (< .001)^{b,e}
Categorical (above vs. below median) [†]	4.4 (.040)	12.9 (.001)^{a,c,e}	18.1 (< .001)^{a,b,e}	6.1 (.017)	5.7 (.018)
<i>SEADL (points)</i>					
Continuous	4.5 (.038)	.59 (.443)	1.7 (.196)	.437 (.511)	2.8 (.091)
[biomarker] x time interaction	1.0 (.308)	8.2 (.004)^a	8.2 (.004)^a	15.4 (< .001)^{a,b,c,d}	8.0 (.005)
Categorical (high vs. low median) [†]	8.9 (.004)	9.0 (.004)^c	9.5 (.003)	6.7 (.012)	5.6 (.019)
<i>CGI-S (points)</i>					
Continuous	.82 (.367)	.341 (.561)	1.0 (.312)	3.1 (.079)	.016 (.899)
[biomarker] x time interaction	3.5 (.067)	4.0 (.052)	6.4 (.015)	5.6 (.022)	2.4 (.122)
Categorical (high vs. low median) [†]	.12 (.730)	17.3 (< .001)^{a,c,e}	16.2 (< .001)^{a,c,e}	10.1 (.003)^{a,c}	1.6 (.209)
<i>RBANS (points)</i>					
Continuous	2.3 (.125)	.31 (.576)	.86 (.354)	.218 (.642)	.28 (.593)

[biomarker] x time interaction	.166 (.685)	4.1 (.045)	2.3 (.133)	.319 (.574)	14.5 (< .001)^b
Categorical (high vs. low median) [†]	1.9 (.171)	4.2 (.046)	5.8 (< .001)^a	.579 (.450)	6.2 (.013)
<i>Color trails 1 (sec)</i>					
Continuous	6.4 (.012)	2.4 (.118)	4.2 (.041)	4.2 (.042)	5.4 (.021)
[biomarker] x time interaction	.12 (.729)	.13 (.714)	.14 (.703)	1.2 (.274)	1.0 (.316)
Categorical (high vs. low median) [†]	3.2 (.077)	8.2 (.006)^a	12.8 (.001)^{a,b}	1.2 (.268)	11.0 (.001)
<i>Color trails 2 (sec)</i>					
Continuous	7.5 (.007)	4.9 (.028)	7.3 (.008)	8.2 (.005)	3.6 (.056)
[biomarker] x time interaction	.06 (.802)	1.1 (.287)	.91 (.342)	2.1 (.143)	2.0 (.154)
Categorical (high vs. low median) [†]	3.0 (.089)	6.6 (.013)	14.9 (< .001)^{a,b}	2.4 (.127)	10.1 (.002)^b
<i>Letter-number sequencing (points)</i>					
Continuous	.17 (.677)	1.5 (.211)	1.0 (.311)	.003 (.953)	2.3 (.129)
[biomarker] x time interaction	1.0 (.308)	2.6 (.107)	3.2 (.075)	.495 (.484)	3.6 (.056)
Categorical (high vs. low median) [†]	2.7 (.104)	6.7 (.012)	8.2 (.006)^a	.348 (.558)	6.9 (.009)
<i>Phonemic fluency (words/min)</i>					
Continuous	.14 (.702)	.78 (.378)	.55 (.460)	.070 (.792)	2.8 (.094)
[biomarker] x time interaction	.42 (.515)	2.4 (.121)	2.4 (.120)	1.4 (.239)	1.5 (.209)
Categorical (high vs. low median) [†]	.17 (.679)	3.6 (.062)	4.3 (.042)	.361 (.551)	4.3 (.040)

Whole brain volume (mm³)

Continuous	.084 (.774)	.52 (.473)	.20 (.651)	.001 (.978)	.33 (.564)
[biomarker] x time interaction	.17 (.678)	1.2 (.270)	.56 (.457)	.173 (.680)	3.9 (.049)
Categorical (high vs. low median) [†]	.13 (.715)	.80 (.376)	2.1 (.153)	.041 (.841)	2.1 (.144)

Ventricular volume (mm³)

Continuous	4.9 (.031)	.01 (.891)	.689 (.410)	.004 (.952)	4.0 (.047)
[biomarker] x time interaction	.09 (.757)	1.1 (.298)	.60 (.444)	.364 (.550)	2.2 (.135)
Categorical (high vs. low median) [†]	6.6 (.013)	3.1 (.085)	1.0 (.304)	2.2 (.140)	3.6 (.059)

Midbrain volume (mm³)

Continuous	.000 (.998)	5.9 (.019)	4.0 (.052)	1.2 (.264)	4.2 (.040)
[biomarker] x time interaction	.46 (.498)	.85 (.361)	.22 (.636)	.042 (.839)	1.5 (.219)
Categorical (high vs. low median) [†]	.59 (.445)	2.3 (.137)	4.2 (.047)	.482 (.492)	5.4 (.021)

SCP volume (mm³)

Continuous	1.3 (.257)	11.9 (.001)^{a,c,e}	12.5 (.001)^{a,e}	4.9 (.030)	3.8 (.050)
[biomarker] x time interaction	.01 (.920)	1.0 (.311)	.881 (.355)	.137 (.713)	2.3 (.126)
Categorical (high vs. low median) [†]	.000 (.993)	5.7 (.022)^a	7.2 (.011)^a	4.4 (.044)	10.8 (.001)^{b,e}

* Comparison of F values and significance of mixed linear models of fluid biomarkers as predictors of change in clinical, neurocognitive and neuroimaging variables. [†] p-tau > 22 ng/mL vs. ≤ 22 ng/mL, NfL > 4559 ng/mL vs. ≤ 4559 ng/mL, NfL/p-tau >

198.9 vs. ≤ 198.9 , p-tau/Tau > 0.424 vs. ≤ 0.424 and plasma NfL > 37.3 pg/mL vs ≤ 37.3 pg/mL. The F statistic value is presented for models in which fluid biomarkers are entered as continuous predictor values, with a term for biomarker concentration ([]) by time interaction or as categorical values dichotomized by a median split. Because no interactions were observed with categorical values, only comparisons of main (fixed) effects are presented for categorical data. P values for that variable appear in parentheses. Unadjusted data are presented and models that survived false discovery rate adjustment applied across 12 dependent variables for each biomarker appear in bold. a = $> \text{p-tau}$, b = $> \text{CSF NfL}$, c = $> \text{plasma NfL}$, d = $> \text{CSF NfL/p-tau}$, e = $> \text{p-tau/Tau}$.