Tau and Amyloid Plasma Biomarkers Are Differentially Associated with Early Neuropsychiatric Symptoms

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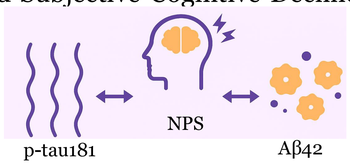
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BACKGROUND

Recent research has suggested that Neuropsychiatric Symptoms (NPS) may be related to AD pathogenesis across the cognitive impairment continuum. However, the role of plasma biomarkers regarding NPS in preclinical stages is not clear.

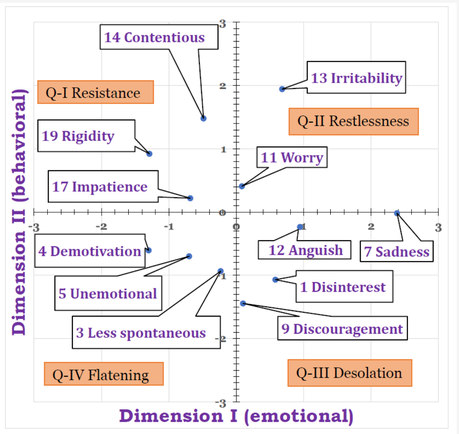
We examined the relationships between NPS and p-tau181 and Aβ42 in a sample of Cognitively Unimpaired (CU) and Subjective Cognitive Decline (SCD) participants.



METHODS

A total of 296 participants aged +50 years from the Compostela Ageing Study (CompAS) recruited from primary care health centers were diagnosed as CU (N=117), and SCD (N=179) according to Jessen et al. (2014), and defined by cognitive complaints exceeding age-adjusted cut-off scores in the Questionnaire d'Autoévaluation de la Mémoire (QAM) (5th percentile, Pereiro et al., 2021). NPS were assessed using the Mild Behavioral Impairment-Checklist (MBI-C) 12-item (proposed by Mallo et al., 2023).

Figure 1. Figure 2. Coordinates for the 12 MBI-C items and quadrants proposed by Mallo et al. (2023).



Legend: Q-I: Quadrant I; Q-II: Quadrant-II; Q-III: Quadrant-III; Q-IV: Quadrant-IV, MBI-C: Mild Behavioral Impairment-Checklist.

Plasma biomarkers, p-tau181 and Aβ42, were obtained. Aβ42 concentrations were measured using the Simoa Human Neurology 3-Plex A Advantage Kit, while plasma levels of p-tau 181 were determined using the ALZpath Simoa® p-tau 217 v2 Assay. Group differences were examined using ANOVA with age, years of schooling, MBI-C 12-item total score and each MBI-C quadrant score as dependent variables, and clinical diagnosis as factor. Linear regression analyses (LRA) were performed with MBI-C 12-item total score and scores in each quadrant, Quadrant-I (Q-I, Resistance), Quadrant-II (Q-II, Restlessness), Quadrant-III (Q-III Desolation), Quadrant-IV (Q-IV Fattening), as dependent variables; p-tau181 and Aβ42 were predictors.

RESULTS

SCD participants were older than the CU group (Table 1). LRA indicated that p-tau181 and Aβ42 were significantly associated with MBI-C 12-item total score, Q-I, Resistance, and Q-II, Restlessness, considering the total sample (Table 2). When analyzed separately, in SCD participants, significant associations were observed only for p-tau181 with the MBI-C 12-item total score and Q-I and Q-II. In CU participants, significant associations were found only for Aβ42 with Q-I and Q-II (Table 3).

Table 1. One-way ANOVA comparing age, education, and MBI-C 12-item total and MBI-C quadrant scores across clinical diagnostic groups CU and SCD. Means and SD (in parentheses).

Variable	CU (N=117)	SCD (N=179)	*F*(1,294)	*p*
Age	63.53 (8.82)	66.48 (8.80)	7.91	**.005**
Years of schooling	14.00 (5.59)	12.96 (5.62)	2.41	.121
MMSE	28.65 (1.50)	28.33 (1.61)	3.08	.080
MBI-C 12 items. Total	2.57 (4.58)	3.59 (4.95)	3.20	.074
Aβ42	10.49(3.91)	9.69(5.32)	1.82	.178
p-tau181	23.86(29.15)	21.99(15,40)	.496	.482

Legend: Q-I: Quadrant I; Q-II: Quadrant-II; Q-III: Quadrant-III; Q-IV: Quadrant-IV, MBI-C: Mild Behavioral Impairment- Checklist; MMSE: Mini Mental State Examination.

Table 2. Linear regression analyses of MBI-C total and quadrant scores with p-tau181 and Aβ42 as predictors with the entire sample (N=296).

	Aβ42					p-tau181				
	B	SE	*β*	*t*	*p*	B	SE	*β*	*t*	*p*
MBI-C 12 items total	-.12	.60	-.12	-2.03	**<.001**	.03	.01	.14	2.44	**.015**
Q-I Resistance	-.03	.01	-.12	-2.14	**.033**	.01	.01	.18	3.09	**.002**
Q-II Restlessness	-.03	.01	-.16	-2.80	**.005**	.01	.01	.17	3.06	**.002**
Q-III Desolation	-.03	.02	-.07	-1.28	.202	.01	.01	.10	1.80	.072
Q-IV Flattening	-.01	.01	-.05	-.96	.333	.01	.01	.02	.40	.68

Legend: Q-I: Quadrant I; Q-II: Quadrant-II; Q-III: Quadrant-III; Q-IV: Quadrant-IV, MBI-C: Mild Behavioral Impairment- Checklist.

Table 3. Linear regression analyses of MBI-C total and quadrant scores with p-tau181 and Aβ42 as predictors with SCD and CU participants.

	Aβ42					p-tau181				
	B	SE	*β*	*t*	*p*	B	SE	*β*	*t*	*p*
SCD (N=179)										
MBI-C 12 items total	-.08	.07	-.09	-1.22	.223	.05	.02	.15	2.06	**.040**
Q-I Resistance	-.01	.01	-.05	.74	.458	.02	.01	.25	3.43	**<.001**
Q-II Restlessness	-.02	.01	-.10	-1.33	.185	.01	.01	.23	3.06	**.003**
Q-III Desolation	-.03	.03	-.07	-1.01	.310	.01	.01	.07	.99	.319
Q-IV Flattening	-.01	.01	-.07	-1.00	.318	.00	.00	.01	.07	.938
CU (N=117)										
MBI-C 12 items total	-.16	.11	-.13	-1.47	.145	.02	.01	.16	1.70	.091
Q-I Resistance	-.08	.03	-.22	-2.40	**.018**	.01	.00	.14	1.52	.131
Q-II Restlessness	-.06	.02	-.25	-2.79	**.006**	.01	.01	.17	1.94	.055
Q-III Desolation	-.01	.04	-.03	-.41	.680	.01	.01	.16	1.73	.086
Q-IV Flattening	-.01	.03	-.01	-.01	.986	.00	.00	.04	.50	.616

Legend: Q-I: Quadrant I; Q-II: Quadrant-II; Q-III: Quadrant-III; Q-IV: Quadrant-IV, MBI-C: Mild Behavioral Impairment- Checklist.

CONCLUSIONS

P-tau181 and Aβ42 were associated with NPS (total score, Q-I and Q-II) across all participants. However, group-specific patterns emerged: p-tau181 was linked to these NPS in SCD, while Aβ42 was associated in CU.

TAKE-HOME MESSAGE

Tau and amyloid may differentially contribute to NPS depending on cognitive status, particularly those related to Resistance and Restlessness domains.

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