



Article

Central and Peripheral Inflammation in Mild Cognitive Impairment in the Context of Alzheimer's Disease

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Supplementary Materials

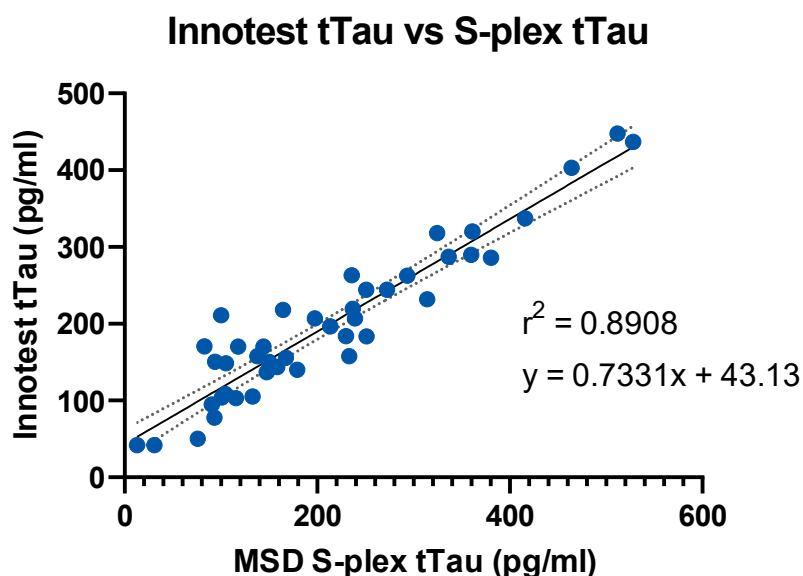


Figure S1. Linear regression between FUJIREBIO INNTOTEST total Tau (tTau) diagnostic test and MESOSCALE DISCOVERY (MSD) S-plex total Tau. Measurements were done with Non-impaired (NIC) CSF samples. Regression curve expression $y = 0.7331x + 43.13$, r-square = 0.8908 and p -value < 0.0001.

(a)

MCI n = 32		CSF biomarkers (r, p)		
		A β 42	tTau	pTau181
CSF biomarkers (r, p)	A β 42	1.0000		
		-		
	tTau	0.2188	1.0000	
		0.2288	-	
	pTau181	0.0710	0.7317	1.0000
		0.7094	<0.0001	-

(b)

NIC n = 45		CSF biomarkers (r, p)		
		A β 42	tTau	pTau181
CSF biomarkers (r, p)	A β 42	1.0000		
		-		
	tTau	-0.0844	1.0000	
		0.5858	-	
	pTau181	-0.0762	0.5213	1.0000
		0.6636	0.0013	-

Table S1. Summary table of Spearman correlation between CSF AD hallmarks. r-value and p-value are displayed for each correlation as r, p respectively. p-values < 0.05 and r-values ≥ 0.50 or ≤ -0.50 are given in bold-italic entries. (a) Mild Cognitive Impairment (MCI) cohort. (b) Non-Impaired control (NIC) cohort.

A β : Amyloid β ; tTau: total Tau; pTau: phosphorylated tau.

(a)

MCI n = 32		Serum biomarkers (r, p)	
		tTau	pTau181
CSF biomarkers (r, p)	A β 42	-0.0301	-0.1123
		0.8703	0.5619
	tTau	0.2636	0.2064
		0.1450	0.2827
	pTau181	0.2169	0.2039
		0.2496	0.3076

(b)

NIC n = 45		Serum biomarkers (r, p)	
		tTau	pTau181
CSF biomarkers (r, p)	A β 42	-0.0189	-0.0346
		0.9102	0.8388
	tTau	0.3805	0.6195
		0.0185	<0.0001
	pTau181	0.3075	0.5625
		0.0817	0.0007

Table S2. Summary table of Spearman correlation between CSF vs serum AD hallmarks. r-value and p-value are displayed for each correlation as r, p respectively. p-values < 0.05 and r-values ≥ 0.50 or ≤ -0.50 are given in bold-italic entries (a) MCI cohort. (b) NIC cohort.

(a)

MCI n = 32		Serum biomarkers (r, p)					
		GFAP	NFL	OPN	TIMP-1	TREM-2	YKL-40
CSF biomarkers (r, p)	GFAP	0.1327	0.1411	0.1338	0.0249	0.0374	0.1679
		0.4691	0.4410	0.4654	0.8923	0.8390	0.3584
	NFL	0.2034	0.3083	0.2372	0.0451	-0.1672	0.1309
		0.2641	0.0860	0.1912	0.8064	0.3605	0.4753
	OPN	0.0975	-0.0777	0.1085	0.1246	0.0704	-0.1012
		0.5955	0.6725	0.5544	0.4967	0.7019	0.5817
	TIMP-1	0.2518	0.3691	0.2617	0.2705	0.1507	0.2911
		0.1644	0.0376	0.1479	0.1343	0.4105	0.1061
	TREM-2	0.0407	0.0363	0.1536	0.0139	0.0191	0.0916
		0.8250	0.8437	0.4013	0.9397	0.9175	0.6179
	YKL-40	0.2837	0.2991	0.3105	0.2093	0.1393	0.2449
		0.1156	0.0963	0.0837	0.2503	0.4470	0.1768

(b)

NIC n = 45		Serum biomarkers (r, p)					
		GFAP	NFL	OPN	TIMP-1	TREM-2	YKL-40
CSF biomarkers (r, p)	GFAP	0.4533	0.1891	0.1205	-0.1148	0.2454	0.2221
		0.0023	0.2247	0.4415	0.4637	0.1127	0.1522
	NFL	-0.1323	0.6498	0.2884	0.1262	-0.0310	0.0046
		0.3921	<0.0001	0.0576	0.4144	0.8416	0.9764
	OPN	0.3290	-0.2163	0.1009	-0.1630	0.1722	0.1801
		0.0273	0.1535	0.5095	0.2848	0.2580	0.2365
	TIMP-1	0.1642	0.2447	0.2868	0.0972	-0.0082	0.1759
		0.2812	0.1053	0.0561	0.5252	0.9575	0.2478
	TREM-2	0.2850	0.1461	0.1132	-0.0584	0.1772	0.0157
		0.0578	0.3382	0.4592	0.7033	0.2442	0.9186
	YKL-40	0.4896	0.0072	0.1665	-0.0568	0.3033	0.3545
		0.0006	0.9623	0.2742	0.7110	0.0428	0.0169

Table S3. Summary table of Spearman correlation between CSF vs serum neuroinflammatory biomarkers. r-value and p-value are displayed for each correlation as r, p respectively. p-values < 0.05 and r-values ≥ 0.50 or ≤ -0.50 are given in bold-italic entries. (a) MCI cohort. (b) NIC cohort.

GFAP: Glial fibrillary acidic protein. NFL: Neurofilament light; OPN: Osteopontin; TIMP-1: Tissue inhibitor of metalloproteinase 1; sTREM-2: soluble Triggering receptor expressed on myeloid cells 2; YKL-40: Chitinase-3-like 1 (CHI3L1).

(a)

MCI n = 32		Serum biomarkers (r, p)					
		CRP	IL-18	IL-6	IL-8	IP-10	MCP-1
CSF biomarkers (r, p)	CRP	0.1889	0.3962	<i>0.5009</i>	0.3452	-0.0734	0.3397
		0.3088	<i>0.0273</i>	<i>0.0041</i>	0.0617	0.6948	0.0616
	IL-18	-0.0844	0.1517	0.2873	0.1262	-0.1139	0.2073
		0.6462	0.4073	0.1108	0.4987	0.5346	0.2549
	IL-6	0.2584	0.1378	0.3530	0.3028	-0.0552	0.2518
		0.1533	0.4519	<i>0.0475</i>	0.0977	0.7642	0.1644
	IL-8	0.1397	0.0356	-0.0561	0.0331	-0.3381	-0.2071
		0.4458	0.8468	0.7602	0.8598	0.0584	0.2554
	IP-10	-0.2782	-0.0918	0.1398	0.2194	-0.0919	-0.0106
		0.1231	0.6172	0.4454	0.2358	0.6171	0.9540
	MCP-1	0.3727	0.4781	<i>0.5248</i>	0.1285	0.1987	0.4202
		<i>0.0357</i>	<i>0.0056</i>	<i>0.0020</i>	0.4910	0.2757	<i>0.0167</i>

(b)

NIC n = 45		Serum biomarkers (r, p)					
		CRP	IL-18	IL-6	IL-8	IP-10	MCP-1
CSF biomarkers (r, p)	CRP	0.3990	0.0848	0.3481	0.4084	0.1329	-0.0042
		<i>0.0098</i>	0.5887	<i>0.0222</i>	<i>0.0065</i>	0.3956	0.9785
	IL-18	-0.1515	<i>0.6151</i>	0.0498	0.1765	0.0922	0.1457
		0.3323	<i><0.0001</i>	0.7453	0.2462	0.5471	0.3395
	IL-6	0.1630	-0.0052	0.1936	0.3506	0.2905	0.2833
		0.2962	0.9731	0.2025	<i>0.0182</i>	0.0529	0.0593
	IL-8	-0.1349	0.0020	-0.0559	0.1851	0.3193	-0.0266
		0.3883	0.9894	0.7152	0.2236	<i>0.0325</i>	0.8622
	IP-10	0.1135	0.1185	0.1948	0.3255	0.3278	0.1262
		0.4687	0.4380	0.1997	<i>0.0291</i>	<i>0.0280</i>	0.4087
	MCP-1	0.1876	0.0061	0.1601	0.3827	0.1591	0.2178
		0.2284	0.9681	0.2935	<i>0.0095</i>	0.2965	0.1507

Table S4. Summary table of Spearman correlation between CSF vs serum inflammatory biomarkers. r-value and p-value are displayed for each correlation as r, p respectively. p-values < 0.05 and r-values ≥ 0.50 or ≤ -0.50 are given in bold-italic entries. (a) MCI cohort. (b) NIC cohort.

CRP: C-reactive protein; IL: Interleukin; IP-10: Interferon gamma-induced protein 10; MCP-1: Monocyte chemoattractant protein 1; TNFα: Tumor necrosis factor α.

(a)

MCI n = 32		Serum biomarkers (r, p)	
		ASC	IL-18
CSF biomarkers (r, p)	ASC	0.1685	0.1327
		0.3566	0.4689
	IL-18	0.0322	0.1517
		0.8611	0.4073

(b)

NIC n = 45		Serum biomarkers (r, p)	
		ASC	IL-18
CSF biomarkers (r, p)	ASC	0.3820	0.1269
		0.0096	0.4062
	IL-18	0.1333	0.5747
		0.3828	<0.0001

Table S5. Summary tables of Spearman correlation between CSF vs serum inflammasome biomarkers. r-value and p-value are displayed for each correlation as r, p respectively. p-values < 0.05 and r-values ≥ 0.50 or ≤ -0.50 are given in bold-italic entries. (a) MCI cohort. (b) NIC cohort. ASC: (apoptosis-associated speck-like protein containing a CARD).

(a)

MCI n = 32		Serum Biomarkers (r, p)							
		ASC	Caspase-1	IL-1 β	IL-1Ra	IL-18	IL-6	CRP	TNF α
Serum biomarkers (r, p)	ASC	1.0000							
		-							
	Caspase-1	0.9663 <0.0001	1.0000 -						
	IL-1 β	0.8079 <0.0001	0.7819 <0.0001	1.0000 -					
	IL-1Ra	0.7735 <0.0001	0.7023 <0.0001	0.6246 <0.0001	1.0000 -				
	IL-18	0.4898 0.0044	0.4223 0.0160	0.4368 0.0124	0.6936 <0.0001	1.0000 -			
	IL-6	0.6605 <0.0001	0.5598 0.0009	0.5111 0.0028	0.7792 <0.0001	0.5485 0.0012	1.0000 -		
	CRP	0.4732 0.0062	0.4172 0.0175	0.4842 0.0050	0.4505 0.0097	0.5074 0.0030	0.6427 <0.0001	1.0000 -	
	TNF α	0.4744 0.0093	0.3399 0.0712	0.4517 0.0139	0.5562 0.0017	0.7395 <0.0001	0.6807 <0.0001	0.6197 0.0003	1.0000 -

(b)

NIC n = 45		Serum Biomarkers (r, p)							
		ASC	Caspase-1	IL-1 β	IL-1Ra	IL-18	IL-6	CRP	TNF α
Serum biomarkers (r, p)	ASC	1.0000							
		-							
	Caspase-1	0.7754 <0.0001	1.0000 -						
	IL-1 β	0.4325 0.0042	0.3501 0.0230	1.0000 -					
	IL-1Ra	0.2048 0.1773	0.2992 0.0459	0.4221 0.0054	1.0000 -				
	IL-18	0.0657 0.6681	0.0561 0.7145	0.1968 0.2117	0.2079 0.1706	1.0000 -			
	IL-6	0.2372 0.1167	0.0916 0.5494	0.6096 <0.0001	0.3963 0.0070	0.0697 0.6491	1.0000 -		
	CRP	0.0671 0.6692	-0.1440 0.3569	0.4625 0.0027	0.2510 0.1045	-0.1313 0.4013	0.8072 <0.0001	1.0000 -	
	TNF α	0.0435 0.8260	0.0104 0.9581	0.0169 0.9360	0.1095 0.5792	0.1196 0.5443	0.4001 0.0349	0.1673 0.4043	1.0000 -

(c)

HC n = 30		Serum Biomarkers (r, p)							
Serum biomarkers (r, p)	ASC	1.0000							
		-							
	Caspase-1	0.4965 0.0053	1.0000 -						
	IL-1 β	0.2582 0.2126	0.3733 0.0661	1.0000 -					
	IL-1Ra	0.2770 0.1384	0.2629 0.1604	0.2135 0.3055	1.0000 -				
	IL-18	0.2148 0.2544	0.1818 0.3363	0.0961 0.6478	0.1237 0.5147	1.0000 -			
	IL-6	-0.2152 0.2535	-0.1715 0.3647	0.4510 0.0236	0.4045 0.0266	0.0336 0.8601	1.0000 -		
	CRP	0.0857 0.6526	-0.3633 0.0484	0.0039 0.9853	0.1916 0.3105	0.2294 0.2226	0.3900 0.0331	1.0000 -	
	TNF α	0.3944 0.0342	0.4382 0.0174	0.4160 0.0386	0.4398 0.0170	0.1996 0.2993	0.3034 0.1095	0.1665 0.3880	1.0000 -

Table S6. Summary tables of Spearman correlation between serum inflammasome and inflammatory biomarkers. r-value and p-value are displayed for each correlation as r, p respectively. p-values < 0.05 and r-values ≥ 0.50 or ≤ -0.50 are given in bold-italic entries. (a) MCI cohort. (b) NIC cohort. (c) Healthy Control (HC) cohort. IL-1Ra: Interleukin-1 receptor antagonist.