Chai *et al*. Inflammatory markers are elevated in the neocortex of Alzheimer's Disease but not Lewy Body Dementias

Additional file

Table S1. Multiple comparisons of each inflammatory marker among diagnostic groups, using non-parametric Kruskal-Wallis ANOVA tests.

		IL-1α	IFN-γ	GM-CSF	IL-13	IL-10	IL-1Ra	IL-8	IL-12p70	FGF-2
BA 21	n	75	75	75	75	75	75	72	75	75
	H	12.340	8.994	10.090	14.650	7.349	1.646	1.694	4.154	1.122
	η2	0.132	0.084	0.100	0.164	0.061	-0.019	-0.019	0.016	-0.026
	p-value	**0.006**	**0.029**	**0.018**	**0.002**	0.062	0.649	0.638	0.245	0.772
	q-value	**0.028**	**0.066**	**0.053**	**0.019**	0.111	0.730	0.730	0.368	0.772
BA 9	n	62	69	59	74	46				
	H	12.820	2.564	6.903	6.841	5.087				
	η2	0.169	-0.007	0.071	0.055	0.050	n.a.	n.a.	n.a.	n.a.
	p-value	**0.005**	0.464	0.075	0.077	0.166				
	q-value	**0.025**	0.464	0.129	0.129	0.207				
BA 40	n	87	113	57	112	107				
	H	9.271	9.529	7.431	10.510	14.170				
	η2	0.076	0.060	0.084	0.070	0.108	n.a.	n.a.	n.a.	n.a.
	p-value	**0.026**	**0.023**	0.059	**0.015**	**0.003**				
	q-value	**0.032**	**0.032**	**0.059**	**0.032**	**0.014**				

Abbreviations: BA = Brodmann area, n = number of measurements, H = Kruskal-Wallis H-statistic, η^2 = eta2 squared based on H-statistic: (H - k + 1)/(n - k) where k = 4 diagnostic groups, n.a. = not applicable.

Bold fonts indicate significant differences between diagnostic groups, $p < 0.05$ (Kruskal-Wallis test) and $q < 0.10$ (False Discovery Rate of 10%).

Table S2. Associations between each inflammatory marker in temporal cortex with diagnostic groups.

BA21 marker		Odds Ratio (95% Confidence Interval)		
		PDD	DLB	AD
IL1-α	Model I	2.51 (0.68, 9.22)	2.76 (0.75, 10.22)	**8.36 (2.01, 34.78)**
	Model II	1 (0.09, 11.35)	0.91 (0.06, 12.87)	1.89 (0.12, 30.05)
IFN-γ	Model I	2.32 (0.53, 10.15)	3.09 (0.7, 13.67)	**11.7 (2.17, 63.12)**
	Model II	0.72 (0.06, 8.2)	1.27 (0.08, 19.08)	3.15 (0.17, 58.38)
GM-CSF	Model I	3.17 (0.49, 20.68)	4.55 (0.7, 29.67)	**16.56 (2.22, 123.71)**
	Model II	0.76 (0.03, 17.56)	1.05 (0.03, 32.3)	2.29 (0.06, 83.16)
IL-13	Model I	3.07 (0.42, 22.47)	3.15 (0.42, 23.35)	**38.78 (3.78, 397.88)**
	Model II	0.81 (0.02, 29.83)	0.54 (0.01, 30.66)	4.6 (0.06, 329.71)
IL-10	Model I	4.1 (0.61, 27.41)	2.5 (0.35, 17.7)	**10.2 (1.36, 76.3)**
	Model II	3.02 (0.1, 95.59)	0.86 (0.02, 47.75)	3.47 (0.06, 195.12)
IL-1ra	Model I	0.37 (0.02, 5.91)	0.14 (0.01, 2.41)	0.37 (0.02, 8.66)
	Model II	0.25 (0, 182.88)	0.08 (0, 92.49)	0.18 (0, 300.5)
IL-8	Model I	2.38 (0.41, 13.84)	1.8 (0.29, 10.95)	2.23 (0.3, 16.63)
	Model II	0.67 (0.01, 30.39)	0.2 (0, 12.68)	0.12 (0, 11.18)
IL-12p70	Model I	0.87 (0.11, 7.12)	4.44 (0.61, 32.3)	6.04 (0.73, 49.8)
	Model II	0.9 (0, 924)	1.83 (0, 2328.01)	1.97 (0, 2706.73)
FGF-2	Model I	0.42 (0.02, 7.61)	0.64 (0.04, 11.7)	0.32 (0.01, 8.34)
	Model II	1.67 (0, 926.9)	3.49 (0, 3561.64)	1.12 (0, 1983.26)

Abbreviations: PDD = Parkinson's disease with dementia, DLB = dementia with Lewy Bodies, AD = Alzheimer's disease. Inflammatory markers were log-10 transformed. Model I was adjusted for age and gender, while Model II was adjusted for age, gender and duration of dementia.

Bold fonts indicate significant associations between inflammatory marker and diagnostic group (p<0.05, multiple multinomial regression analysis with bias-reduction using Firth's penalized maximum likelihood method).

Table S3. Multiple comparisons of each inflammatory marker in the presence versus absence of neuropathological features, using non-parametric Mann-Whitney U tests.

		IL-1α	IFN-γ	GM-CSF	IL-13	IL-10	IL-1Ra	IL-8	IL-12p70	FGF-2
NFT	n	72	72	72	72	72	72	70	72	72
	Z	2.482	1.687	1.797	2.983	2.066	1.076	0.392	1.167	0.587
	η2	0.087	0.040	0.045	0.125	0.060	0.016	0.002	0.019	0.005
	p-value	**0.013**	0.092	0.072	**0.003**	**0.039**	0.282	0.695	0.243	0.557
	q-value	**0.059**	0.165	0.163	**0.026**	0.116	0.363	0.695	0.363	0.627
NP	n	69	69	69	69	69	69	67	69	69
	Z	0.505	0.397	0.349	1.300	0.908	0.090	0.289	0.349	0.686
	η2	0.004	0.002	0.002	0.025	0.012	0.000	0.001	0.002	0.007
	p-value	0.613	0.691	0.727	0.194	0.364	0.928	0.772	0.727	0.493
	q-value	0.869	0.869	0.869	0.869	0.869	0.928	0.869	0.869	0.869
LB	n	65	65	65	65	65	65	63	65	65
	Z	-0.510	-0.472	-0.579	-0.015	-0.899	-0.503	-0.095	-0.122	-0.091
	η2	0.004	0.003	0.005	0.000	0.013	0.004	0.000	0.000	0.000
	p-value	0.610	0.637	0.563	0.988	0.369	0.615	0.925	0.903	0.927
	q-value	0.988	0.988	0.988	0.988	0.988	0.988	0.988	0.988	0.988

Abbreviations: NFT = neurofibrillary tangles, NP, neuritic plaques, LB = Lewy bodies, Z = Z-score from Mann-Whitney U test, η^2 = eta2 squared based on Z-statistic: $Z^2/(n - 1)$.

Bold fonts indicate significant differences between diagnostic groups, $p < 0.05$ (Kruskal-Wallis test) and $q < 0.10$ (False Discovery Rate of 10%).

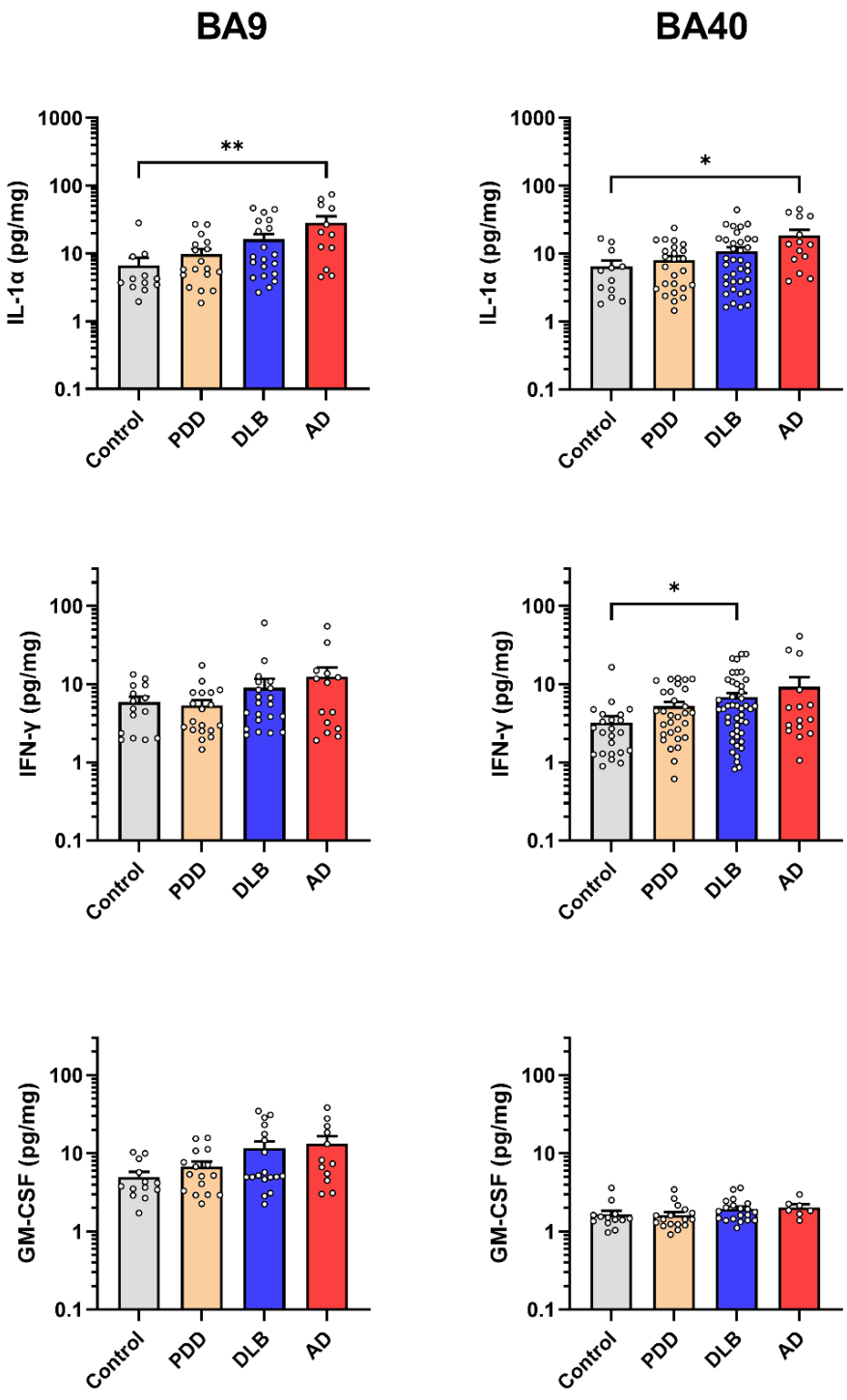
Table S4. Associations between each inflammatory marker in temporal cortex with the presence of Moderate/Severe NFT.

Log-10 transformed marker (BA21)	Presence of Moderate/Severe NFT Odds ratio (95% Confidence Interval), p-value	
	Model I (max n = 21)	Model II (max n = 18)
IL-1α	**3.69 (1.25, 10.9), *p* = 0.018**	3.55 (0.95, 13.22), *p* = 0.059
IFN-γ	**4.04 (1.04, 15.6), *p* = 0.043**	3.18 (0.67, 15.01), *p* = 0.144
GM-CSF	**4.87 (1.07, 22.22), *p* = 0.041**	3.98 (0.65, 24.18), *p* = 0.134
IL-13	**12.73 (1.84, 88.01), *p* = 0.010**	**25.36 (1.94, 332.24), *p* = 0.014**
IL-10	4.68 (0.98, 22.43), *p* = 0.054	4.39 (0.58, 33.35), *p* = 0.153
IL-1Ra	6.72 (0.34, 131.96), *p* = 0.210	17.56 (0.53, 576.42), *p* = 0.108
IL-8	1.03 (0.18, 5.91), *p* = 0.970	0.57 (0.08, 4.07), *p* = 0.577
IL-12p70	4.65 (0.77, 28.25), *p* = 0.095	13.24 (1.22, 143.27), *p* = 0.033
FGF-2	1.13 (0.08, 17.11), *p* = 0.928	16.24 (0.4, 652.76), *p* = 0.139

Abbreviations: NFT = neurofibrillary tangles. Inflammatory markers were log-10 transformed. Model I was adjusted for age, gender and presence of Moderate/Severe neuritic plaque, while Model II was adjusted for age, gender, presence of Moderate/Severe neuritic plaque and duration of dementia.

Bold fonts indicate significant associations between inflammatory marker and diagnostic group ($p<0.05$, multiple binary regression analysis).

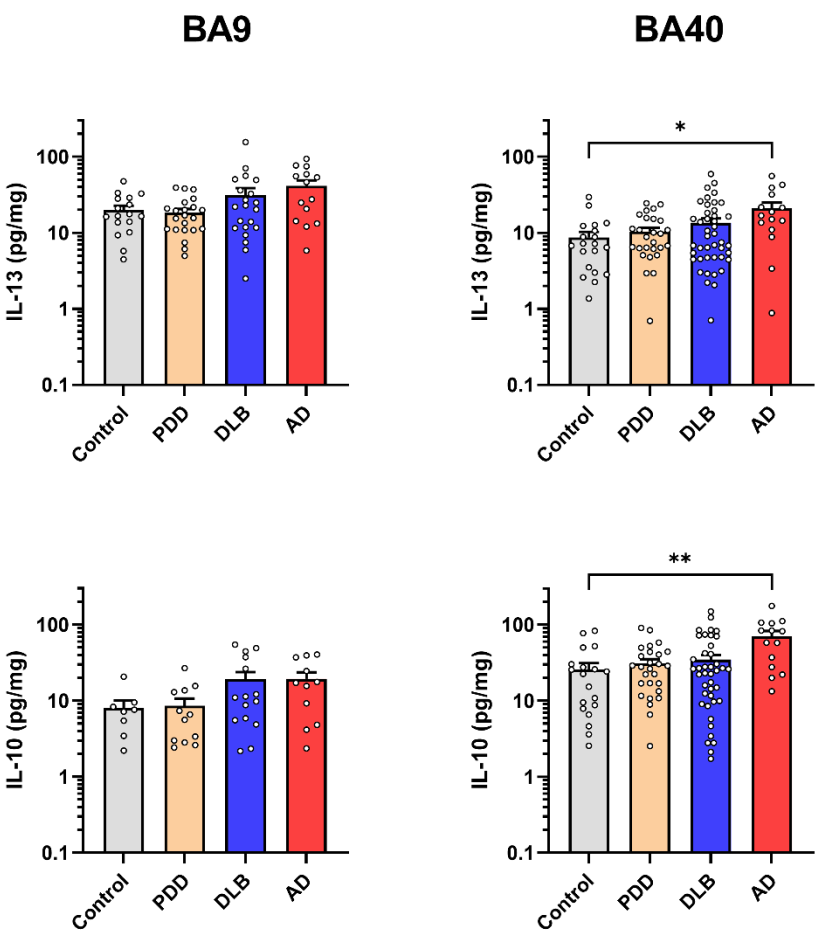
Figure S1. Pro-inflammatory markers in prefrontal and parietal lobes of AD and LBD



Abbreviations: PDD = Parkinson's disease with dementia, DLB = dementia with Lewy Bodies, AD = Alzheimer's disease. Bar graphs of immunoreactivities (in mean ± SEM, with white dots indicating individual measurements) of each inflammatory markers in prefrontal (BA9) and parietal (BA40) lobes of Control, PDD, DLB and AD patients.

*$p < 0.05$ and **$p < 0.01$ indicate significant differences between diagnostic groups (Dunn-Bonferroni *post hoc* tests correction following a significant Kruskal Wallis ANOVA).

Figure S2. Anti-inflammatory markers in frontal and parietal lobes of AD and LBD



Bar graphs of immunoreactivities (in mean ± SEM, with white dots indicating individual measurements) of each inflammatory markers in prefrontal (BA9) and parietal (BA40) lobes of Control, PDD, DLB and AD patients.

*$p < 0.05$ and **$p < 0.01$ indicate significant differences between diagnostic groups (Dunn-Bonferroni *post hoc* tests correction following a significant Kruskal Wallis ANOVA).