Supplementary information

CHRNA7 Polymorphisms and Dementia Risk: Interactions with Apolipoprotein ε4 and Cigarette Smoking

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Supplementary Table S1. Association between *CHRNA7* haplotypes and LOAD by *APOE* ε4 status.

Haplo-type Block	Haplotype (frequency among controls)		Dominant model				
			0 copies		1 or 2 copies		
			Case/ Control	AOR	Case/ Control	AOR (95% CI)	$P_{interaction}$
1	Hap1: TC	All	57/69	1.00	197/366	**0.51 (0.30-0.86)**	0.50
	(59%)	*APOE*ε4 (-)	35/58	1.00	119/310	**0.44 (0.24-0.82)**	
		*APOE*ε4 (+)	22/10	1.00	77/55	0.76 (0.28-2.07)	
1	Hap2: GC	All	121/209	1.00	133/226	1.47 (0.96-2.23)	0.33
	(30%)	*APOE*ε4 (-)	70/173	1.00	84/195	1.27 (0.77-2.08)	
		*APOE*ε4 (+)	49/36	1.00	50/29	1.88 (0.83-4.26)	
1	Hap3: GG	All	185/350	1.00	69/85	1.52 (0.92-2.51)	0.67
	(11%)	*APOE*ε4 (-)	114/296	1.00	40/72	1.50 (0.83-2.72)	
		*APOE*ε4 (+)	71/52	1.00	28/13	1.68 (0.64-4.47)	
3	Hap1: ATCT	All	137/206	1.00	117/229	0.70 (0.45-1.09)	0.28
	(31%)	*APOE*ε4 (-)	88/171	1.00	66/197	0.62 (0.37-1.04)	
		*APOE*ε4 (+)	48/34	1.00	51/31	1.19 (0.51-2.80)	
3	Hap2: TTTT	All	135/233	1.00	119/202	0.97 (0.63-1.50)	0.96
	(27%)	*APOE*ε4 (-)	87/202	1.00	67/166	0.96 (0.58-1.60)	
		*APOE*ε4 (+)	47/31	1.00	52/34	0.96 (0.42-2.23)	
3	Hap3: ACCC	All	146/274	1.00	108/161	1.22 (0.78-1.90)	0.17
	(20%)	*APOE*ε4 (-)	83/228	1.00	71/140	1.43 (0.86-2.39)	
		*APOE*ε4 (+)	62/44	1.00	37/21	0.75 (0.30-1.86)	
3	Hap4: TTTC	All	227/372	1.00	27/63	0.54 (0.28-1.05)	0.88
	(7%)	*APOE*ε4 (-)	139/318	1.00	15/50	0.57 (0.25-1.29)	
		*APOE*ε4 (+)	87/52	1.00	12/13	0.47 (0.16-1.44)	
3	Hap5: TCCC	All	219/382	1.00	35/53	1.40 (0.74-2.67)	0.86
	(6%)	*APOE*ε4 (-)	130/326	1.00	24/42	1.42 (0.67-2.98)	
		*APOE*ε4 (+)	87/55	1.00	12/10	1.17 (0.31-4.46)	

Numbers in bold indicate significant findings (P <0.05). The effects of *CHRNA7* haplotypes in block4 on LOAD risk are shown in Table 3 because the results remained significant after correction for multiple tests. Block2 included only one htSNP and was excluded from the haplotype analysis. Abbreviations: LOAD, late-onset Alzheimer's disease; AOR, adjusted odds ratio; CI, confidence interval; *APOE*, apolipoprotein E. Block 2 included only one haplotype-tagging single nucleotide polymorphism and thus was not included in the haplotype analysis. All models were adjusted for age, sex, *APOE* ε4, and education years and conditional on 5-year age strata.

Supplementary Table S2. Association between *CHRNA7* haplotypes and VaD by *APOE* ε4 status.

Haplo-type Block	Haplotype (frequency among controls)		Dominant model				
			0 copies		1 or 2 copies		
			Case/ Control	AOR	Case/ Control	AOR (95% CI)	$P_{interaction}$
1	Hap1: TC	All	18/60	1.00	97/365	1.05 (0.49-2.26)	0.21
	(59%)	*APOE*ε4 (-)	17/50	1.00	72/310	0.86 (0.37-2.00)	
		*APOE*ε4(+)	1/10	1.00	25/55	4.18 (0.40-44.0)	
1	Hap2: GC	All	60/208	1.00	55/225	0.88 (0.51-1.52)	0.50
	(30%)	*APOE*ε4 (-)	44/172	1.00	45/196	0.77 (0.41-1.43)	
		*APOE*ε4(+)	16/36	1.00	10/29	1.05 (0.29-3.83)	
1	Hap3: GG	All	92/349	1.00	23/84	1.19 (0.60-2.35)	0.39
	(11%)	*APOE*ε4 (-)	69/297	1.00	20/71	1.07 (0.50-2.28)	
		*APOE*ε4(+)	23/52	1.00	3/13	2.10 (0.38-11.7)	
3	Hap1: ATCT	All	63/205	1.00	52/228	0.86 (0.49-1.50)	0.94
	(31%)	*APOE*ε4 (-)	49/171	1.00	40/197	0.87 (0.46-1.65)	
		*APOE*ε4(+)	14/34	1.00	12/31	0.93 (0.28-3.03)	
3	Hap2: TTTT	All	63/234	1.00	52/199	0.97 (0.56-1.71)	0.89
	(27%)	*APOE*ε4 (-)	49/202	1.00	40/166	0.97 (0.51.1.85)	
		*APOE*ε4(+)	14/32	1.00	12/33	1.11 (0.30-4.05)	
3	Hap3: ACCC	All	66/274	1.00	49/159	1.34 (0.76-2.38)	0.72
	(20%)	*APOE*ε4 (-)	51/230	1.00	38/138	1.40 (0.73-2.69)	
		*APOE*ε4(+)	15/44	1.00	11/21	1.36 (0.36-5.06)	
3	Hap4: TTTC	All	103/373	1.00	12/60	**0.33 (0.12-0.88)**	0.42
	(7%)	*APOE*ε4 (-)	80/321	1.00	9/47	0.40 (0.13-1.20)	
		*APOE*ε4(+)	23/52	1.00	3/13	0.17 (0.02-1.48)	
3	Hap5: TCCC	All	95/381	1.00	20/52	1.63 (0.73-3.61)	0.61
	(6%)	*APOE*ε4 (-)	73/326	1.00	16/42	1.86 (0.76-4.59)	
		*APOE*ε4(+)	22/55	1.00	4/10	1.01 (0.13-7.91)	
4	Hap1: AC	All	6/33	1.00	109/400	1.30 (0.42-3.97)	0.86
	(76%)	*APOE*ε4 (-)	6/27	1.00	83/341	1.13 (0.35-3.66)	
		*APOE*ε4(+)	0/6	1.00	26/59	NA	
4	Hap2: AT	All	89/321	1.00	26/112	1.07 (0.57-2.00)	0.76
	(15%)	*APOE*ε4 (-)	67/273	1.00	22/95	1.15 (0.57-2.30)	
		*APOE*ε4(+)	22/48	1.00	4/17	0.82 (0.18-3.79)	
3	Hap3: GT	All	91/356	1.00	24/77	0.89 (0.43-1.85)	0.74
	(9%)	*APOE*ε4 (-)	70/303	1.00	19/65	0.88 (0.39-1.99)	
		*APOE*ε4(+)	21/53	1.00	5/12	1.09 (0.23-5.14)	

Block2 included only one htSNP and was excluded from the haplotype analysis. Abbreviations: VaD, vascular dementia; AOR, adjusted odds ratio; CI, confidence interval; *APOE*, apolipoprotein E; NA, not applicable. All models were adjusted for age, sex, *APOE* ε4, and education years and conditional on 5-year age strata.