

Supplementary Data

The *CALHM1* P86L Polymorphism is a Genetic Modifier of Age at Onset in Alzheimer's Disease: a Meta-Analysis Study

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Supplementary Table 1
P86L allele and genotype distribution in the different control and AD case populations according to country of origins

Country	n	Allele distribution (frequency)		Genotype distribution (frequency)			
		G	A	GG	AG	AA	
Belgium	Controls	631	901 (0.71)	361 (0.29)	326 (0.52)	249 (0.40)	56 (0.09)
	AD cases	1022	1460 (0.71)	584 (0.29)	524 (0.62)	412 (0.40)	86 (0.08)
Finland	Controls	435	696 (80.0)	174 (20.0)	281 (0.65)	134 (0.31)	20 (0.05)
	AD cases	310	480 (0.77)	140 (0.23)	188 (0.61)	104 (0.34)	18 (0.06)
France	Controls	7386	10979 (0.74)	3793 (0.26)	4059 (0.55)	2861 (0.39)	496 (0.07)
	AD cases	1586	2259 (0.71)	913 (0.29)	820 (0.52)	619 (0.39)	147 (0.09)
Italy	Controls	988	1371 (0.69)	605 (0.31)	489 (0.50)	393 (0.40)	97 (0.10)
	AD cases	979	1421 (0.73)	537 (0.27)	514 (0.52)	393 (0.40)	81 (0.08)
Spain	Controls	1954	2860 (0.73)	1048 (0.27)	1045 (0.54)	770 (0.39)	139 (0.07)
	AD cases	1685	2418 (0.72)	952 (0.28)	875 (0.52)	668 (0.40)	142 (0.08)
Sweden	Controls	256	355 (0.69)	157 (0.31)	121 (0.47)	113 (0.44)	22 (0.09)
	AD cases	296	428 (0.72)	164 (0.28)	153 (0.52)	122 (0.41)	21 (0.07)
UK	Controls	205	320 (0.78)	90 (0.22)	127 (0.62)	66 (0.32)	12 (0.06)
	AD cases	492	673 (0.68)	311 (0.32)	250 (0.51)	173 (0.35)	69 (0.14)
USA	Controls	1419	2034 (0.72)	784 (0.28)	753 (0.53)	548 (0.39)	118 (0.08)
	AD cases	1503	2161 (0.72)	845 (0.28)	777 (0.52)	607 (0.40)	119 (0.08)
Whole	Controls	13274	19516 (0.74)	7012 (0.26)	7201 (0.54)	5134 (0.39)	960 (0.07)
	AD cases	7873	11300 (0.72)	4446 (0.28)	4101 (0.52)	3098 (0.39)	683 (0.09)

Supplementary Table 2
Association of the P86L polymorphism with AAO in the whole AD cases or in the e4 AD cases according to country of origin

Whole AD cases	Belgium		Finland		France		Italy		
	n	age at onset	n	age at onset	n	age at onset	n	age at onset	
PP	450	74.4 ± 8.7	188	72.1 ± 9.5	767	68.0 ± 9.7	426	74.0 ± 9.2	
PL	947	74.0 ± 8.2	103	71.5 ± 7.6	566	68.4 ± 9.9	332	74.1 ± 9.7	
LL	76	75.2 ± 10.0	18	71.4 ± 4.7	135	67.0 ± 9.4	71	71.6 ± 8.6	
p ¹		0.91		0.76		0.38		0.16	
p ²		0.38		0.78		0.27		0.06	
Spain		Sweden		UK		USA			
	n	age at onset	n	age at onset	n	age at onset	n	age at onset	
PP	873	76.3 ± 8.2	153	76.4 ± 8.0	49	65.9 ± 11.6	752	72.8 ± 6.4	
PL	665	76.3 ± 8.5	122	76.5 ± 7.2	49	63.9 ± 9.1	583	73.2 ± 6.3	
LL	143	75.2 ± 7.4	21	74.7 ± 8.6	13	60.5 ± 6.4	111	71.7 ± 6.2	
p ¹		0.04		0.53		0.18		0.07	
p ²		0.01		0.30		0.09		0.04	
e4 AD cases		Belgium		Finland		France		Italy	
	n	age at onset	n	age at onset	n	age at onset	n	age at onset	
PP	244	74.1 ± 8.1	145	71.7 ± 6.4	431	67.7 ± 8.4	176	73.3 ± 8.5	
PL	201	73.4 ± 7.6	72	71.6 ± 6.5	341	67.2 ± 8.9	117	73.0 ± 9.1	
LL	40	71.4 ± 9.7	11	70.3 ± 3.5	79	65.2 ± 8.4	27	72.1 ± 8.0	
p ¹		0.07		0.78		0.11		0.48	
p ²		0.08		0.48		0.04		0.36	
Spain		Sweden		UK		USA			
	n	age at onset	n	age at onset	n	age at onset	n	age at onset	
PP	391	74.5 ± 7.3	95	76.2 ± 7.8	27	68.9 ± 9.1	460	71.6 ± 6.1	
PL	309	75.6 ± 7.8	69	75.0 ± 7.4	27	64.5 ± 6.7	338	72.0 ± 6.2	
LL	75	73.9 ± 6.1	9	75.3 ± 8.5	6	61.3 ± 5.6	69	70.7 ± 6.3	
p ¹		0.04		0.40		0.01		0.26	
p ²		0.03		0.88		0.12		0.19	

¹mixed model adjusted for gender and using centers as a random variable

²mixed model adjusted for gender and using centers as a random variable and recessive model (LL versus PL+PP).

Supplementary Table 3
Main characteristics of the different case-control studies according to country of origins

Belgium (1 center)		Finland (1 center)		France (5 centers)		Italy (10 centers)	
AD cases	Controls	AD cases	Controls	AD cases	Controls	AD cases	Controls
n	1 022	631	310	435	1 586	7386	979
Mean age	78.6 ± 8.1	63.0 ± 15.6	71.9 ± 6.9	69.7 ± 5.1	71.8 ± 9.1	73.3 ± 6.2	75.8 ± 9.0
Mean age at onset	74.3 ± 8.7	—	71.9 ± 6.9	—	68.1 ± 9.8	—	73.8 ± 9.4
% male	34	43	32	40	38	39	32
Spain (4 centers)		Sweden (1 center)		UK (1 center)		USA (3 centers)	
AD cases	controls	AD cases	controls	AD cases	controls	AD cases	controls
n	1 724	1 983	296	256	492	205	1 503
Mean age	78.3 ± 8.1	59.4 ± 16.2	76.3 ± 7.7	74.9 ± 6.2	74.5 ± 7.9	70.4 ± 10.5	77.4 ± 6.4
Mean age at onset	76.3 ± 8.3	—	76.3 ± 7.7	—	64.4 ± 10.1	—	72.9 ± 6.4
% male	32	43	39	35	44	38	34