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Supplementary Data

Genome-Wide Scan for Copy Number Variation Association with Age at Onset of Alzheimer's Disease

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Supplementary Table 1
Number of events contributing to the association signals detected in the discovery cohort and coverage of the candidate regions in the replication NIA_LOAD Familial dataset

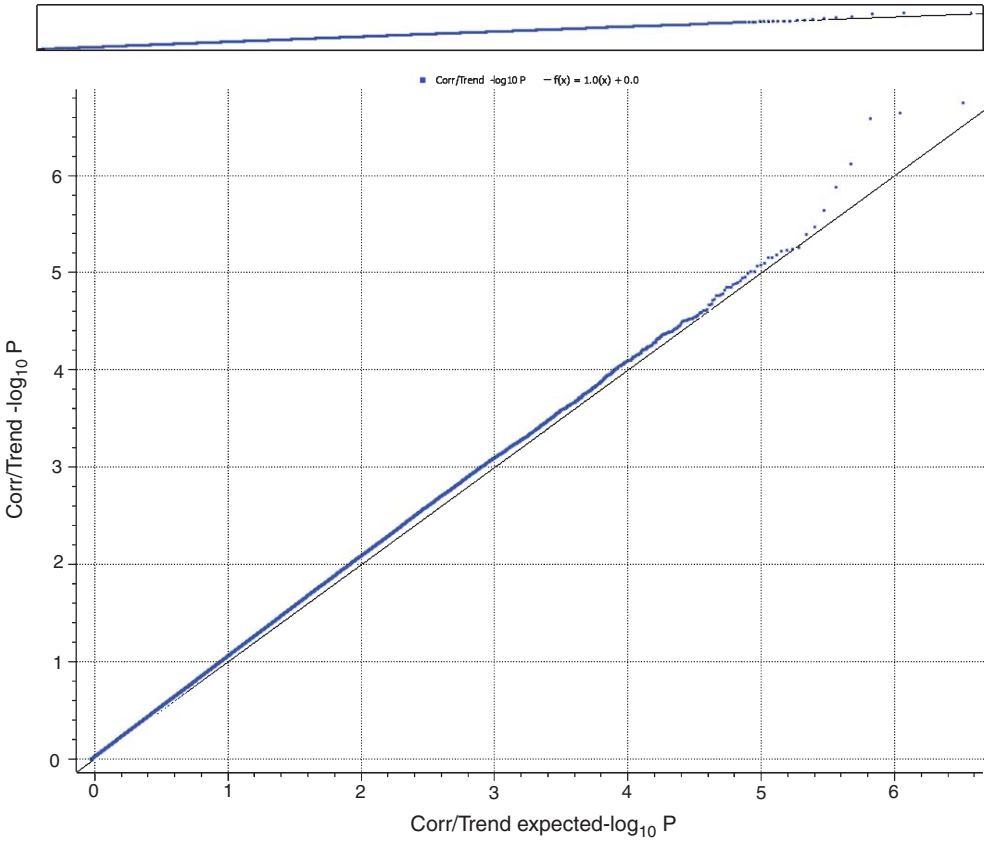
Probe	DGV_CNV	Number_events	Number_probes	Number_probes LOAD	Nearest gene
SNP_A-8600234	No	1	9	2	None
SNP_A-8329031	Yes	2	9	2	CPNE4 intragenic
CN_1082571	Yes	5	3	0	ATP8A1
SNP_A-8584575	No	1	5	2	COL22A1
SNP_A-8327917	Yes	2	14	10	None

Supplementary Table 2
Cox proportional hazard regression in the replication cohort (LOAD) using the normalized probe intensity values as predictors and the age at onset (AAO) as outcome. The lack of adequate coverage for these regions on the Illumina 610 array precluded meaningful segmentation prior to the regression

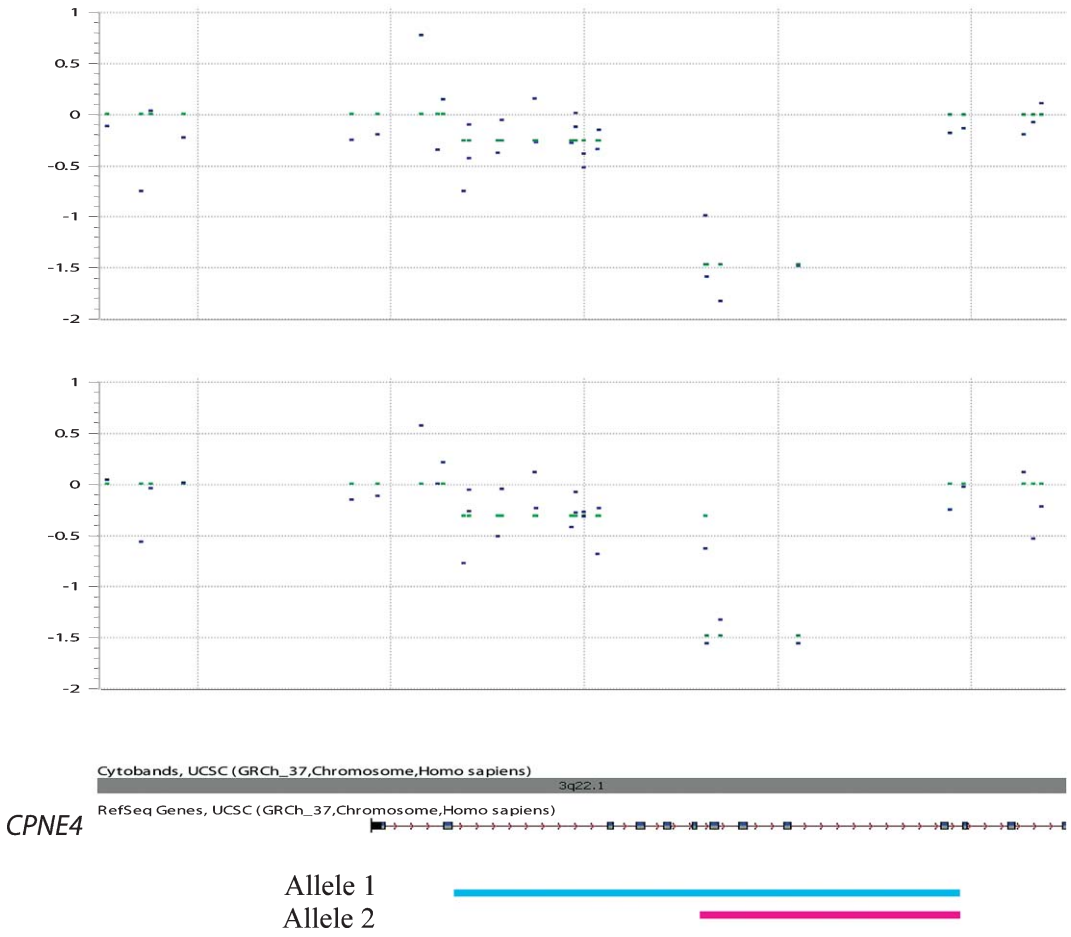
Probe	Chromosome	Position	Chi-square	*p*-value
rs13416465	2	140087319	0.46	0.49
rs12474301	2	140087593	0.15	0.69
rs13085873	3	131985046	0.31	0.57
rs9866280	3	131987887	0.21	0.65
rs11166865	8	139967699	0.29	0.59
rs7009303	8	139971288	0.12	0.73
rs10809648	9	11917701	2.49	0.11
rs1999377	9	11919732	0.6	0.44
rs10960376	9	11929890	0.95	0.33
rs10114153	9	11930627	0.18	0.67
rs10960378	9	11930638	0.69	0.41
rs10117492	9	11934556	0.017	0.89
rs10960384	9	11934943	1.96	0.16
rs12555263	9	11935261	0.26	0.61
rs4273936	9	11936706	0.11	0.74
rs10960385	9	11937390	1.69	0.19

Supplementary Table 3
Events contributing to the association signals detected in the discovery cohort

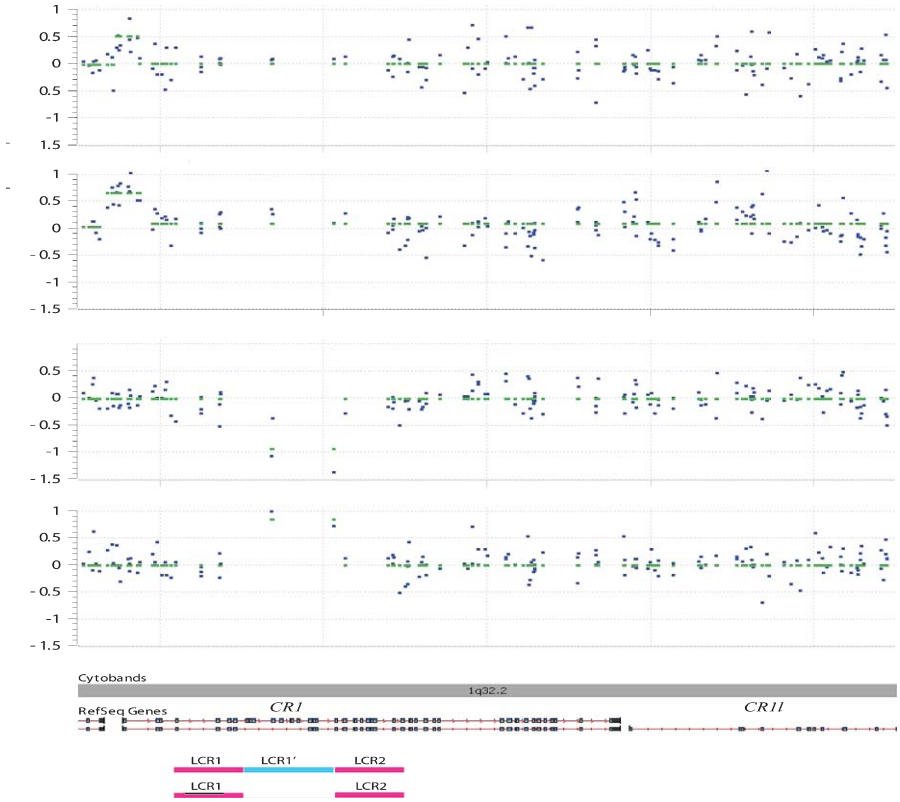
Probe	Chr	Nearest gene	Gain/loss	AAO	Number APOE4
SNP_A-8600234	2	None	gain	50	2
SNP_A-8329031	3	CPNE4 intragenic	loss	45	1
SNP_A-8329031	3	CPNE4 intragenic	loss	52	0
CN_1082571	4	ATP8A1	loss	51	1
CN_1082571	4	ATP8A1	loss	58	2
CN_1082571	4	ATP8A1	loss	58	1
CN_1082571	4	ATP8A1	loss	55	0
CN_1082571	4	ATP8A1	loss	60	1
SNP_A-8584575	8	COL22A1	loss	50	0
SNP_A-8327917	9	None	loss	53	1
SNP_A-8327917	9	None	loss	45	1



Supplementary Figure 1. QQ plot after correcting the logR data of the total cohort for 16 principal components to remove batch effects prior to the copy number variation (CNV) analysis.



Supplementary Figure 2. Sample array data for the detected CNV events. Intragenic deletion of *CPNE4* detected in two samples. The detected deletion is compound heterozygous consisting of a smaller (pink) and a larger event (blue) depicted by the bars. Both events have been reported in the Database of Genomic Variants.



Supplementary Figure 3. CNV events at *CR1*, one of the candidate loci from GWAS analysis and a subsequently confirmed CNV association locus. The pink and blue colored bars on the bottom depict the location of the low copy repeat regions and the site of the deletion is depicted with the blue line between the pink bars. The direction of the association in this study is consistent with the previous report by Brouwers et al. [1].

REFERENCES

[1] Brouwers N, Cauwenberghe CV, Engelborghs S, Lambert JC, Bettens K, Bastard NL, Pasquier F, Montoya AG, Peeters K, Mattheijssens M, Vandenberghe R, Deyn PP, Cruts M, Amouyel P, Sleegers K, Broeckhoven CV (2012) Alzheimer risk associated with a copy number variation in the complement receptor 1 increasing C3b/C4b binding sites. *Mol Psychiatry* **17**, 223-233.