Supplementary material

Table 1 Study subject characteristics

We summarized demographic information at the baseline of the 242 white MCI-AD converters. For continuous variables including age and the length of education, their means and standard deviations were presented. For a binary variable, gender, the percentage of male subjects was shown.

	Mean ± SD or percentage
Age (in years)	74.21 ± 7.16
Education length (in years)	15.82 ± 2.83
Gender (male percentage)	63.22%

Table 2 SNPs showing significant association with accelerated cognitive decline at p-value< 1×10^{-5}

ADAS-cog score trajectory was fitted in the linear mixed-effects models with fixed effects including gender, length of education, age at the baseline, follow-up time trajectory, AD diagnosis trajectory, and each SNP. We included a random intercept and a random slope of the AD diagnosis. An interaction effect of each SNP and the AD diagnosis trajectory was tested and the significant SNPs were shown.

SNP	Chr	Position	P-value	Gene
rs17090219	18	54191033	9.48×10^{-8}	
rs3936289	3	186754957	4.92×10^{-7}	ST6GAL1
rs56378310	13	111189673	1.52×10^{-6}	RAB20
rs192470679	13	33290859	1.55×10^{-6}	PDS5B
rs11121365	1	9357724	1.92×10^{-6}	SPSB1
rs2484	3	197268569	2.83×10^{-6}	BDH1
rs10903488	10	1605998	3.24×10^{-6}	ADARB2
rs6016505	20	39678289	3.72×10^{-6}	TOP1
rs314277	6	105407662	4.51×10^{-6}	LIN28B
rs57905270	2	228486714	4.99×10^{-6}	C2orf83
rs12525341	6	155494724	8.07×10^{-6}	TIAM2

Table 3 Sensitivity analyses results for top meaningful SNPs

We compared estimation and test results for the top meaningful SNPs as varying model specification. Two reduced models were considered: all covariates (1) without the length of education and (2) without the length of education and gender. We also ran a full model on a subsample including subjects whose baseline ages were greater than 60.

		Primary analysis			Reduced model without EDU			Reduced model without EDU and Gender			Full model on a subsample (AGE>60)		
SNP	Gene	Coef	SE	P-value	Coef	SE	P-value	Coef	SE	P-value	Coef	SE	P-value
rs17090219		5.15	0.93	9.48×10^{-8}	5.13	0.93	1.10×10^{-7}	5.13	0.93	1.10×10^{-7}	5.20	0.95	1.53×10^{-7}
rs3936289	ST6GAL1	3.34	0.64	4.92×10^{-7}	3.33	0.64	5.17×10^{-7}	3.34	0.64	4.95×10^{-7}	3.32	0.67	1.35×10^{-6}
rs56378310	RAB20	-2.98	0.6	1.52×10^{-6}	-2.98	0.60	1.53×10^{-6}	-2.98	0.60	1.50×10^{-6}	-2.85	0.61	6.18×10^{-6}
rs192470679	PDS5B	2.89	0.59	1.55×10^{-6}	2.88	0.98	1.69×10^{-6}	2.89	0.59	1.67×10^{-6}	2.74	0.62	1.41×10^{-5}
rs11121365	SPSB1	5.76	1.18	1.92×10^{-6}	5.77	1.18	1.88×10^{-6}	5.73	1.18	2.21×10^{-6}	5.78	1.21	3.25×10^{-6}
rs2484	BDH1	4.53	0.94	2.83×10^{-6}	4.52	0.94	3.01×10^{-6}	4.49	0.94	3.47×10^{-6}	4.72	0.95	1.35×10^{-6}
rs10903488	ADARB2	4.58	0.96	3.24×10^{-6}	4.56	0.96	3.53×10^{-6}	4.56	0.96	3.61×10^{-6}	4.55	0.98	5.78×10^{-6}

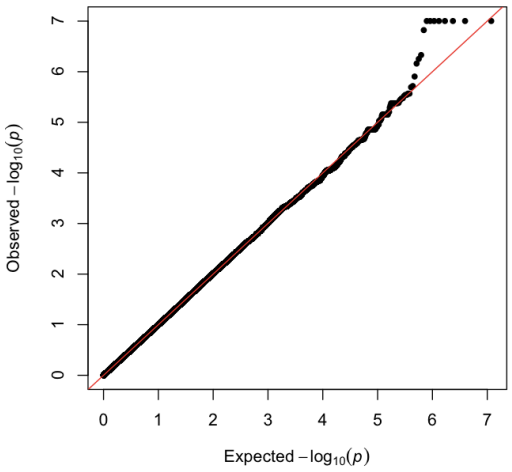

Figure 1 The quantile-quantile (QQ) plot shows the negative logarithm of the observed and the expected p-value for each SNP. There is no evidence of population stratification, as most of the observed p-values do not deviate from the expected line (red line).

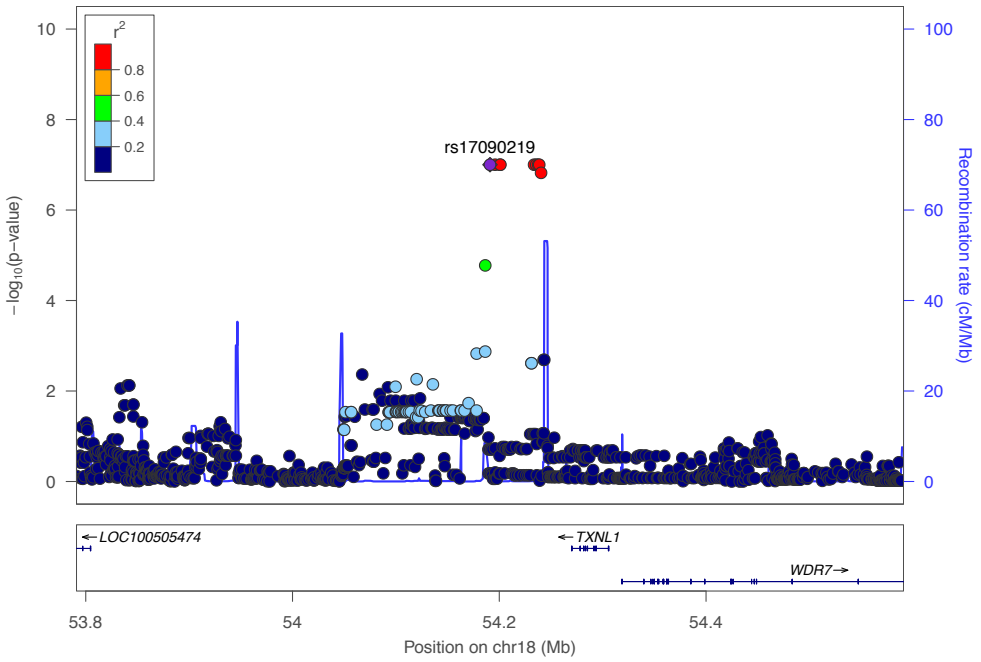

Figure 2 A regional plot for association with cognitive decline

The purple dot is the most significant SNP rs17090219 among SNPs in the region surrounding it within 400kb. Dots are colored according to the range r^2 to show their degree of LD with rs17090219. The blue line shows the estimated recombination rate.

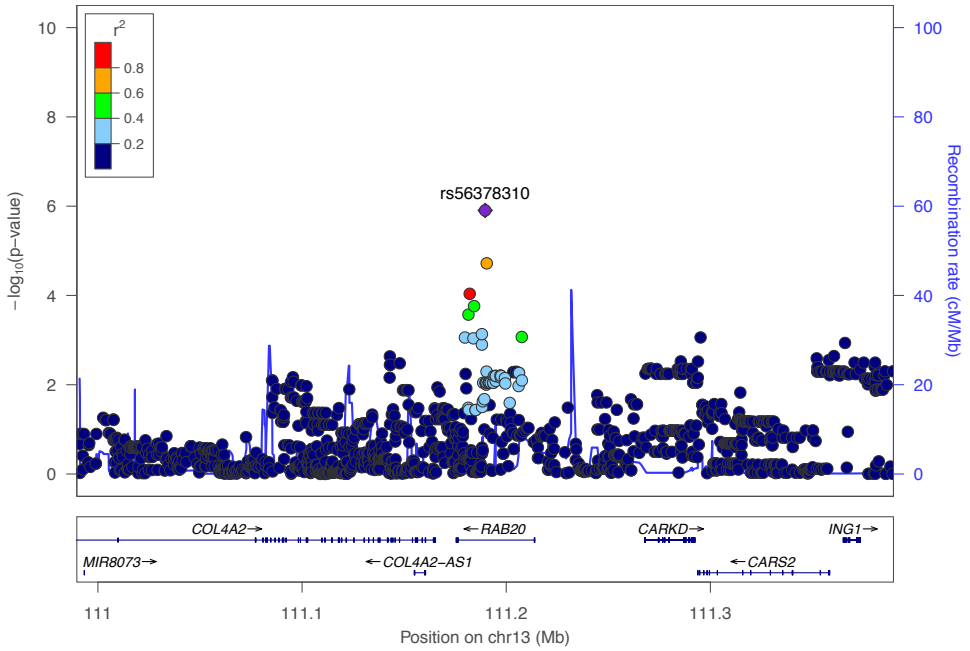

Figure 3 A regional plot for association with cognitive decline

The purple dot is the most significant SNP rs56378310 among SNPs in the region surrounding it within 200kb. Dots are colored according to the range r^2 to show their degree of LD with rs56378310. The blue line shows the estimated recombination rate.

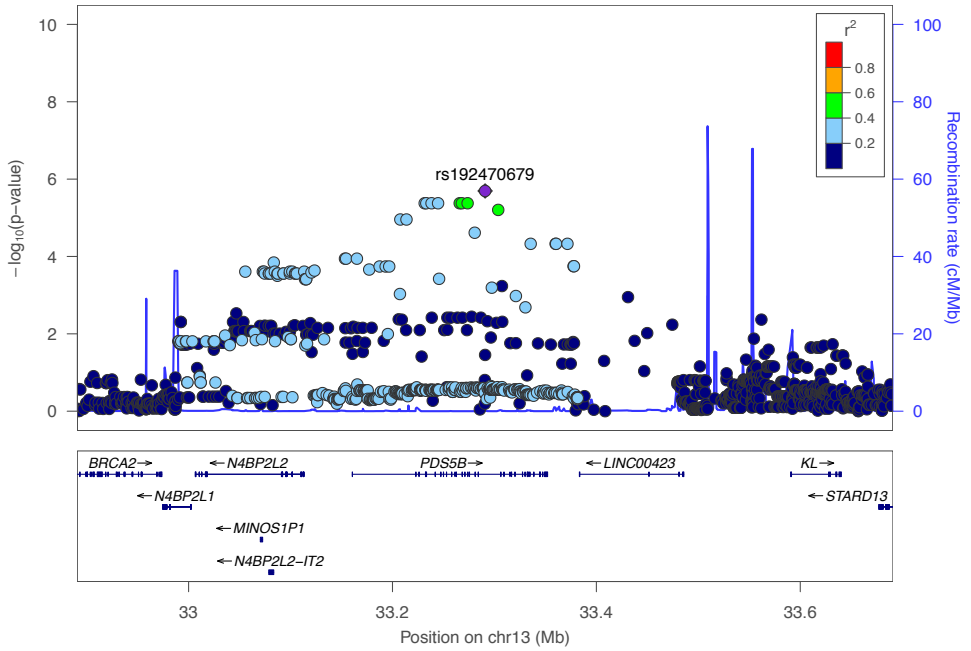

Figure 4 A regional plot for association with cognitive decline

The purple dot is the most significant SNP rs192470679 among SNPs in the region surrounding it within 400kb. Dots are colored according to the range r^2 to show their degree of LD with rs192470679. The blue line shows the estimated recombination rate.

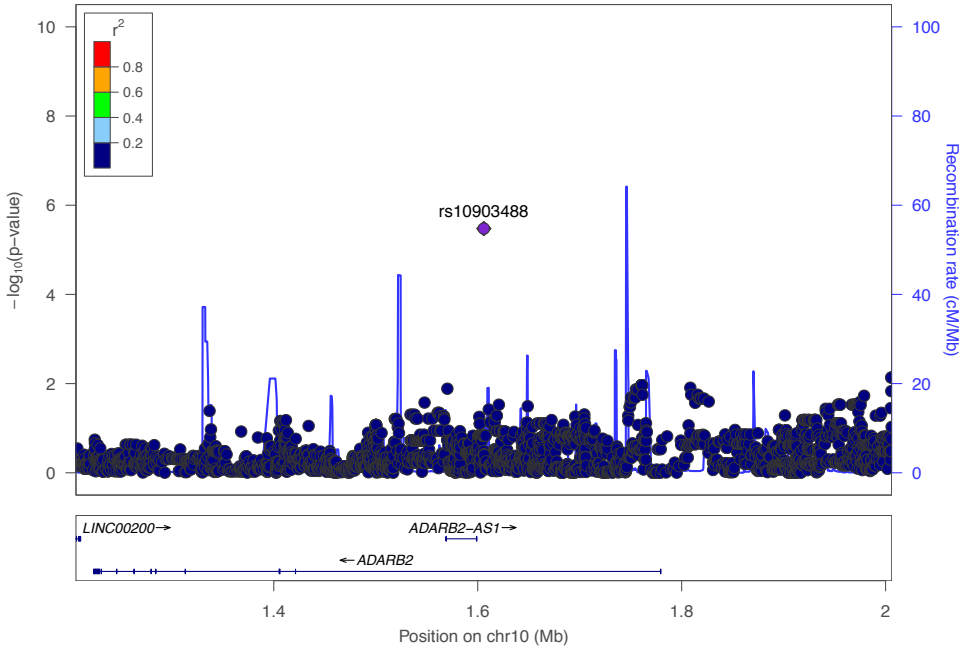

Figure 5 A regional plot for association with cognitive decline

The purple dot is the most significant SNP rs10903488 among SNPs in the region surrounding it within 400kb. Dots are colored according to the range r^2 to show their degree of LD with rs10903488. The blue line shows the estimated recombination rate.

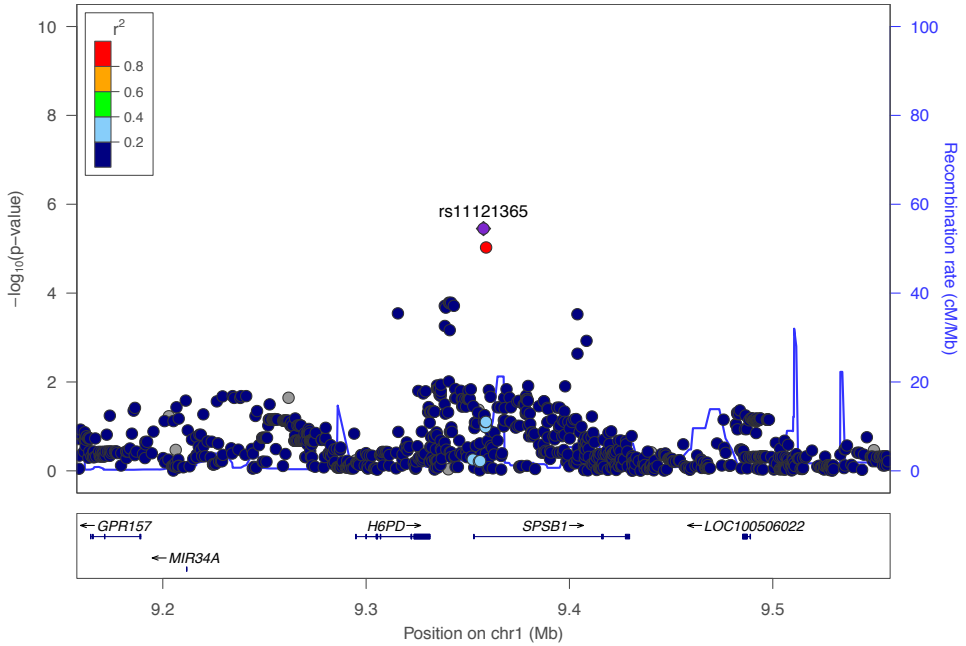

Figure 6 A regional plot for association with cognitive decline

The purple dot is the most significant SNP rs11121365 among SNPs in the region surrounding it within 200kb. Dots are colored according to the range r^2 to show their degree of LD with rs11121365. The blue line shows the estimated recombination rate.