

Brain *APOE* expression quantitative trait loci-based association study identified one susceptibility locus for Alzheimer's disease by interacting with *APOE* ϵ 4

Aiqian Zhang¹, Qingnan Zhao², Dabao Xu^{1,*}, Shan Jiang^{3,*}

¹Department of Gynecology, Third Xiangya Hospital of Central South University, Changsha, Hunan, China

²Department of Pediatrics, The University of Texas MD Anderson Cancer center, Houston, Texas, USA

³Department of Psychiatry, Washington University School of Medicine, St. Louis, MO, USA

***Corresponding authors:**

1- Dabao Xu, MD

Email: dabaoxu@yahoo.com

Department of Gynecology, Third Xiangya Hospital of Central South University, 138 Tongzipo Rd, Changsha, Hunan 410013, China.

2- Shan Jiang, PhD

Email: shannjiang@hotmail.com

Department of Psychiatry, Washington University School of Medicine, St. Louis, MO, USA.

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Table S1. Complete list of the 34 proxy brain eQTLs for *APOE*

SNP	Chr.	Position*	Position relative to <i>APOE</i>	LD with rs429358 (R ²)†	LD with rs7412 (R ²)†	P-value for eQTL	Normalized effect size	Brain tissue	Source	P-value for AD association‡	P-value for AD association in <i>APOE</i> ε4 carriers§	P-value for AD association in <i>APOE</i> ε4 non- carriers§
rs55848260	chr 19	45080369	Upstream 328670 bases	0.003	0.001	5.20E-04	Not available	Cerebellar cortex	BRAINEAC	3.13E-01	5.34E-02	7.29E-01
rs74439218	chr 19	45196254	Upstream 212785 bases	0.004	0.001	4.40E-04	Not available	Cerebellar cortex	BRAINEAC	9.32E-01	5.96E-01	7.44E-01
rs34342452	chr 19	46000901	Downstream 588251 bases	0.002	0	4.80E-04	Not available	Cerebellar cortex	BRAINEAC	4.17E-01	5.60E-01	5.49E-01
rs2722667	chr 19	44912270	Upstream 496769 bases	0.002	0.002	6.50E-04	Not available	Cerebellar cortex	BRAINEAC	5.58E-01	6.56E-01	6.71E-01
rs35864669	chr 19	45591771	Downstream 179121 bases	0	0.001	1.20E-04	Not available	Hippocampus	BRAINEAC	2.44E-01	9.27E-02	9.71E-01
rs28715089	chr 19	46151134	Downstream 738484 bases	0.001	0	2.60E-04	Not available	Hippocampus	BRAINEAC	7.67E-01	4.51E-01	7.27E-01
rs404982	chr 19	44960218	Upstream 448821 bases	0.003	0.001	5.30E-04	Not available	Hippocampus	BRAINEAC	9.12E-01	5.77E-01	7.95E-01
rs59135122	chr 19	45120905	Upstream 288134 bases	0	0	1.20E-04	Not available	Medulla	BRAINEAC	5.70E-01	6.28E-01	7.86E-01
rs1967311	chr 19	45819307	Downstream 406657 bases	0.004	0	5.90E-04	Not available	Medulla	BRAINEAC	6.41E-01	4.73E-01	1.97E-01
rs7252108	chr 19	44619542	Upstream 789497 bases	0	0.001	4.00E-04	Not available	Occipital cortex	BRAINEAC	1.26E-01	5.37E-01	1.70E-01

rs12975617	chr 19	46208023	Downstream 795373 bases	0.001	0.001	7.30E-05	Not available	Occipital cortex	BRAINEAC	9.33E-02	1.58E-02	7.39E-01
rs12972749	chr 19	44898017	Upstream 511022 bases	0.003	0.001	5.90E-04	Not available	Occipital cortex	BRAINEAC	4.26E-01	3.72E-01	7.77E-01
rs12462616	chr 19	46310512	Downstream 897862 bases	0.001	0	2.40E-04	Not available	Occipital cortex	BRAINEAC	2.00E-01	9.04E-02	7.16E-01
rs846881	chr 19	45078553	Upstream 330486 bases	0.003	0	2.70E-04	Not available	Putamen	BRAINEAC	5.55E-01	2.54E-01	8.46E-01
rs112401916	chr 19	45645553	Downstream 232903 bases	0.003	0	1.30E-04	Not available	Putamen	BRAINEAC	4.06E-03	4.20E-02	2.71E-02
rs117560401	chr 19	45125369	Upstream 283670 bases	0	0.001	1.40E-04	Not available	Putamen	BRAINEAC	6.05E-01	9.93E-01	5.89E-01
rs438811	chr 19	45416741	Downstream 4091 bases	0.404	0.202	3.10E-04	Not available	Substantia nigra	BRAINEAC	2.37E-01	1.12E-04	2.78E-02
rs73035960	chr 19	44514195	Upstream 894844 bases	0	0	9.40E-05	Not available	Substantia nigra	BRAINEAC	9.65E-01	9.13E-01	8.76E-01
rs2972557	chr 19	45360573	Upstream 48466 bases	0.001	0	9.70E-04	Not available	Temporal cortex	BRAINEAC	6.05E-01	6.59E-01	8.03E-01
rs2103262	chr 19	45029894	Upstream 379145 bases	0.004	0.001	3.60E-04	Not available	Temporal cortex	BRAINEAC	7.29E-01	6.73E-01	3.34E-01
rs3916855	chr 19	45860202	Downstream 447552 bases	0	0	5.80E-04	Not available	Thalamus	BRAINEAC	2.64E-01	7.21E-01	1.10E-01
rs62109650	chr 19	46052898	Downstream 640248 bases	0	0	4.70E-04	Not available	Intralobular white matter	BRAINEAC	1.09E-01	2.01E-03	6.80E-01
rs74253343	chr 19	45670248	Downstream 257598 bases	0.002	0	1.70E-04	Not available	Intralobular white matter	BRAINEAC	5.63E-01	3.57E-01	9.94E-01

rs2030404	chr 19	44043448	Upstream 1365591 bases	0.001	0	9.59E-04	Not available	Cerebellum	BRAINEAC	2.44E-02	1.19E-03	7.87E-01
rs2682592	chr 19	43940597	Upstream 1468442 bases	0	0.002	6.46E-04	Not available	Cerebellum	BRAINEAC	9.88E-01	3.82E-01	5.07E-01
rs17206386	chr 19	36931957	Upstream 8477082 bases	0	0	6.62E-04	Not available	Cerebellum	BRAINEAC	2.92E-01	3.07E-01	5.18E-01
rs2972448	chr 19	38168913	Upstream 7240126 bases	0.001	0	3.97E-04	Not available	Cerebellum	BRAINEAC	6.51E-01	6.83E-01	8.87E-01
rs4803551	chr 19	38399461	Upstream 7009578 bases	0	0.001	4.47E-04	Not available	Cerebellum	BRAINEAC	5.65E-01	7.89E-01	6.01E-01
rs4802074	chr 19	40848081	Upstream 4560958 bases	0	0	7.77E-04	Not available	Cerebellum	BRAINEAC	4.28E-02	4.60E-01	6.09E-02
rs4490099	chr 19	40731491	Upstream 4677548 bases	0	0	9.66E-04	Not available	Cerebellum	BRAINEAC	2.25E-02	8.36E-01	6.81E-03
rs1628394	chr 19	38535008	Upstream 6874031 bases	0.003	0	9.54E-04	Not available	Cerebellum	BRAINEAC	2.45E-03	1.63E-01	6.32E-03
rs2909088	chr 19	38176548	Upstream 7232491 bases	0.001	0	3.97E-04	Not available	Cerebellum	BRAINEAC	6.90E-01	6.98E-01	9.29E-01
rs147910350	chr 19	46146762	Downstream 734112 bases	0	0	2.90E-06	-2	Frontal cortex (BA9) and Nucleus accumbens (basal ganglia)	BRAINEAC	6.39E-01	9.71E-01	5.97E-01
rs35899189	chr 19	45025134	Upstream 383905 bases	0.005	0.001	6.60E-06	-0.25	Brain - Nucleus accumbens (basal ganglia)	BRAINEAC	8.81E-01	8.41E-01	8.07E-01

*Build 37, assembly hg19.

†Information of linkage disequilibrium with the two *APOE* genotype determinant SNPs was retrieved from LDlink:

<https://analysistools.nci.nih.gov/LDlink/>

‡Adjusted for age, gender and *APOE* ε4 status

§Adjusted for age and gender

Table S2. *APOE* eQTL *P*-values of rs438811 for the ten different brain regions

Brain region	P-value
Cerebellar cortex	5.90E-01
Frontal cortex	3.30E-01
Hippocampus	8.30E-02
Medulla	6.70E-01
Occipital cortex	6.80E-01
Putamen	6.20E-01
Substantia nigra	3.10E-04
Temporal cortex	9.30E-01
Thalamus	2.20E-01
Intralobular white matter	4.60E-01
average all	3.60E-01

Table S3. -491A/T was associated with AD

			Adjusted for age and gender		Adjusted for age, gender and <i>APOE</i> ε4 status	
SNP	Minor allele	MAF*	OR (95% CI)	<i>P</i> -value	OR (95% CI)	<i>P</i> -value
-491A/T	T	0.127	0.631 (0.576-0.692)	7.30×10^{-23}	0.801 (0.726-0.885)	1.17×10^{-5}

*Weighed-average minor allele frequency.

Table S4. -491A/T was associated with AD independent of APOE ε4 status

	<i>APOE</i> ε4 carriers*		<i>APOE</i> ε4 non-carriers*		SNP × <i>APOE</i> ε4 status interaction*	
SNP	OR (95% CI)	<i>P</i> -value	OR (95% CI)	<i>P</i> -value	OR (95% CI)	<i>P</i> -value
- 491A/T	0.785 (0.663-0.931)	5.14×10^{-3}	0.815 (0.721-0.921)	1.05×10^{-3}	1.639 (0.008-328.080)	0.855

*Adjusted for age and gender.

Table S5. Detailed information of the 14 high-throughput genotyping cohorts from NIA Genetics of Alzheimer's Disease Data Storage Site (NIAGADS)

Abbreviated cohort name*	NIAGADS cohort accession number	Weblink for description
NIA-LOAD	NG00020	https://www.niagads.org/datasets/ng00020
ADC1	NG00022	https://www.niagads.org/datasets/ng00022
ADC2	NG00023	https://www.niagads.org/datasets/ng00023
ADC3	NG00024	https://www.niagads.org/datasets/ng00024
UPITT	NG00026	https://www.niagads.org/datasets/ng00026
TGEN II	NG00028	https://www.niagads.org/datasets/ng00028
ROSMAP	NG00029	https://www.niagads.org/datasets/ng00029
WashU1	NG00030	https://www.niagads.org/datasets/ng00030
MIRAGE	NG00031	https://www.niagads.org/datasets/ng00031
ACT	NG00034	https://www.niagads.org/datasets/ng00034
UMVUMSSM	NG00042	https://www.niagads.org/datasets/ng00042
MAYO	NG00043	https://www.niagads.org/datasets/ng00043

*Cohort full names: NIA-LOAD, National Institute on Aging Genetics Initiative for Late-Onset Alzheimer's Disease; ADC1, Alzheimer's Disease Center Dataset 1; ADC2, Alzheimer's Disease Center Dataset 2; ADC3, Alzheimer's Disease Center Dataset 3; UPITT, University of Pittsburgh;

TGEN II, Translational Genomics Research Institute II; ROSMAP, Religious Orders Study and Memory and Aging Project; WashU1, Washington University Dataset 1; MIRAGE, Multi Institutional Research on Alzheimer Genetics Epidemiology; ACT, Adult Changes in Thought; UMVUMSSM, University of Miami (UM), Vanderbilt University (VU) and Mount Sinai School of Medicine (MSSM); ADNI, Alzheimer's Disease Neuroimaging Initiative.

