

Supplementary Material

The Causal Associations Between Adipokines and Alzheimer's Disease: A Two-Sample Mendelian Randomization Study

Supplementary Table 1. Characteristics of the selected SNPs associated with adiponectin and resistin.

Variables	SNP	Chr	Position	Sample size	EA	OA	Beta	SE	EAF	<i>p</i>	R ²	F
adiponectin	rs2062632	3	186461181	29,028	C	T	-0.055	0.006	0.686	2.52E-19	0.001	37.391
	rs17366568	3	186570453	24,865	A	G	-0.154	0.009	0.908	1.00E-200	0.004	98.720
	rs1108842	3	52720080	29,338	C	A	0.030	0.004	0.458	3.66E-11	0.0004	13.051
	rs6810075	3	186548565	29,140	C	T	-0.066	0.005	0.633	1.00E-200	0.002	59.795
	rs7615090	3	186591003	21,869	G	T	-0.058	0.008	0.883	2.81E-11	0.001	15.254
	rs2980879	8	126481475	24,084	T	A	0.030	0.005	0.375	1.08E-08	0.0004	10.063
	rs7955516	12	20498036	29,178	C	A	0.026	0.005	0.442	2.43E-08	0.0003	10.069
	rs601339	12	123174743	29,325	G	A	0.039	0.006	0.150	3.87E-11	0.0004	11.382
	rs7964945	12	124437668	29,252	A	T	0.037	0.006	0.808	2.61E-08	0.0004	12.331
	rs8042532	15	74255230	7,850	G	T	-0.340	0.055	0.992	2.86E-09	0.002	15.000
	rs12051272	16	82663288	15,593	T	G	-0.277	0.018	0.009	1.00E-200	0.001	21.513
	rs2927324	16	81512821	29,184	T	C	0.032	0.005	0.475	1.29E-11	0.0005	14.461
	rs731839	19	33899065	29,166	A	G	0.037	0.005	0.672	2.20E-13	0.001	17.246
resistin	rs17073300	6	144349648	3,301	G	A	-0.233	0.040	0.107	7.41E-09	0.010	34.572
	rs149110519	6	144385777	3,301	T	C	0.417	0.064	0.040	9.33E-11	0.013	44.230
	rs60666652	17	38148272	3,301	C	T	0.142	0.026	0.372	4.90E-08	0.009	31.349
	rs34124816	19	7733676	3,301	C	A	-0.608	0.065	0.038	4.37E-21	0.027	90.849

EA, effect allele; EAF, effect allele frequency; OA, other allele; SE, standard error; SNP, single-nucleotide polymorphism

Supplementary Table 2. Characteristics of the selected SNPs associated with AD.

SNP	Chr	Position	Sample size	EA	OA	SE	Beta	EAF	<i>p</i>	R2	F
rs679515	1	207750568	63,926	C	T	-0.151	0.018	0.172	1.55E-16	0.006	415.785
rs6733839	2	127892810	63,926	T	C	0.169	0.015	0.407	4.02E-28	0.014	896.825
rs114812713	6	41034000	63,926	C	G	0.298	0.043	0.019	4.47E-12	0.003	211.220
rs34665982	6	32560306	63,926	C	T	-0.097	0.017	0.301	5.80E-09	0.004	252.620
rs9381563	6	47432637	63,926	T	C	-0.082	0.015	0.644	2.93E-08	0.003	198.105
rs11767557	7	143109139	63,926	C	T	-0.103	0.018	0.803	1.56E-08	0.003	214.198
rs867230	8	27468503	63,926	A	C	0.133	0.016	0.607	3.49E-17	0.008	546.801
rs73223431	8	27219987	63,926	T	C	0.094	0.015	0.367	8.34E-10	0.004	261.118
rs11257242	10	11721119	63,926	G	C	0.084	0.015	0.367	4.64E-08	0.003	210.831
rs1582763	11	60021948	63,926	A	G	-0.123	0.015	0.351	1.19E-16	0.007	445.182
rs3851179	11	85868640	63,926	C	T	0.120	0.015	0.361	5.81E-16	0.007	425.934
rs3740688	11	47380340	63,926	T	G	0.094	0.014	0.553	9.70E-11	0.004	277.456
rs12590654	14	92938855	63,926	A	G	-0.091	0.016	0.337	8.73E-09	0.004	235.164
rs72654445	19	45417200	63,926	A	G	-0.543	0.081	0.010	2.27E-11	0.006	389.606
rs7412	19	45412079	63,926	T	C	-0.467	0.031	0.072	6.40E-53	0.029	1923.980
rs1081105	19	45412955	63,926	C	A	0.942	0.044	0.974	1.51E-103	0.045	3019.937
rs12151021	19	1050874	63,926	G	A	-0.107	0.017	0.319	2.56E-10	0.005	320.277
rs111278137	19	45215081	63,926	A	G	-0.474	0.071	0.021	3.20E-11	0.009	597.580
rs147711004	19	45337918	63,926	A	G	1.135	0.037	0.028	1.00E-200	0.070	4824.058
rs139136389	19	45427136	63,926	T	C	-0.494	0.085	0.020	6.43E-09	0.009	607.758
rs150685845	19	45675180	63,926	G	A	0.556	0.065	0.988	6.62E-18	0.008	491.785

AD, Alzheimer's disease; EA, effect allele; EAF, effect allele frequency; OA, other allele; SE, standard error; SNP, single-nucleotide polymorphism.

Supplementary Table 3. Causation analysis of the effects of adiponectin on AD without rs17366568.

MR method	No. of SNPs	Beta	SE	OR	95% CI	p
MR Egger	10	-0.082	0.127	0.921	0.719-1.181	0.536
Weighted median	10	-0.053	0.111	0.948	0.763-1.178	0.630
Inverse variance weighted	10	-0.109	0.087	0.897	0.756-1.063	0.209
Simple mode	10	-0.087	0.164	0.917	0.665-1.264	0.608
Weighted mode	10	-0.069	0.113	0.934	0.748-1.165	0.558

AD, Alzheimer's disease; CI, confidence interval; MR, Mendelian randomization; OR, odds, ratio; SE, standard error; SNP, single-nucleotide polymorphism.

Supplementary Table 4. Causation analysis of the effects of AD on adiponectin and resistin.

Outcome	Exposure	MR method	No. of SNPs	Beta	SE	OR	95% CI	<i>p</i>
adiponectin	AD	MR Egger	5	0.042	0.144	1.043	0.786-1.383	0.790
		Weighted median	5	0.005	0.027	1.005	0.953-1.060	0.847
		Inverse variance weighted	5	-0.019	0.024	0.981	0.935-1.029	0.440
		Simple mode	5	0.016	0.042	1.016	0.936-1.103	0.725
		Weighted mode	5	0.012	0.035	1.012	0.945-1.084	0.742
resistin	AD	MR Egger	18	-0.004	0.052	0.996	0.900-1.103	0.941
		Weighted median	18	-0.004	0.046	0.996	0.910-1.089	0.922
		Inverse variance weighted	18	-0.011	0.037	0.989	0.920-1.062	0.758
		Simple mode	18	-0.004	0.073	0.996	0.864-1.149	0.958
		Weighted mode	18	-0.008	0.046	0.992	0.907-1.085	0.868

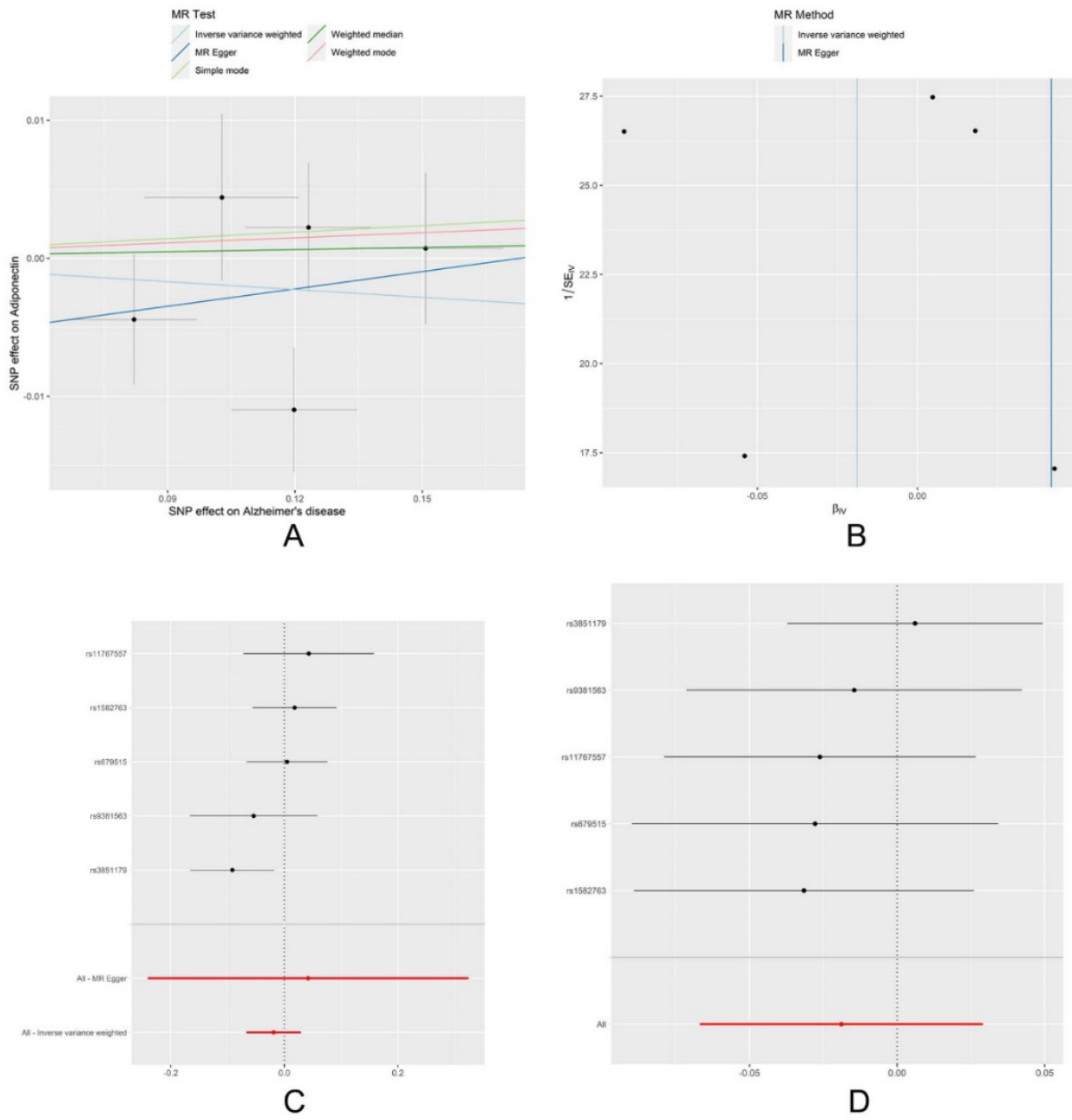
AD, Alzheimer's disease; CI, confidence interval; MR, Mendelian randomization; OR, odds, ratio; SE, standard error; SNP, single-nucleotide polymorphism.

Supplementary Table 5. Results of the Cochrane’s Q test, MR-Egger intercept test and MRPRESSO Global test of the reverse causation analysis in the MR study.

	Cochrane's Q test		MR-Egger intercept test		MR-PRESSO Global test
	Q-value	<i>P</i> -Q test	intercept	<i>P</i> -intercept	<i>P</i> -global
AD versus adiponectin	6.592	0.159	-0.007	0.697	0.205
AD versus resistin	20.252	0.262	-0.002	0.836	0.321

AD, Alzheimer’s disease; MR, Mendelian randomization. * $p < 0.05$.

Supplementary Figure 1. Scatter plot (A), funnel plot (B), forest plot (C) and leave-one-out sensitivity analysis (D) of the associations of AD and adiponectin. AD, Alzheimer's disease.



Supplementary Figure 2. Scatter plot (A), funnel plot (B), forest plot (C) and leave-one-out sensitivity analysis (D) of the associations of AD and resistin. AD, Alzheimer's disease

