

Supplementary Materials

Reduced retinal thickness and risk of Alzheimer's disease: a bidirectional two-sample Mendelian randomization study

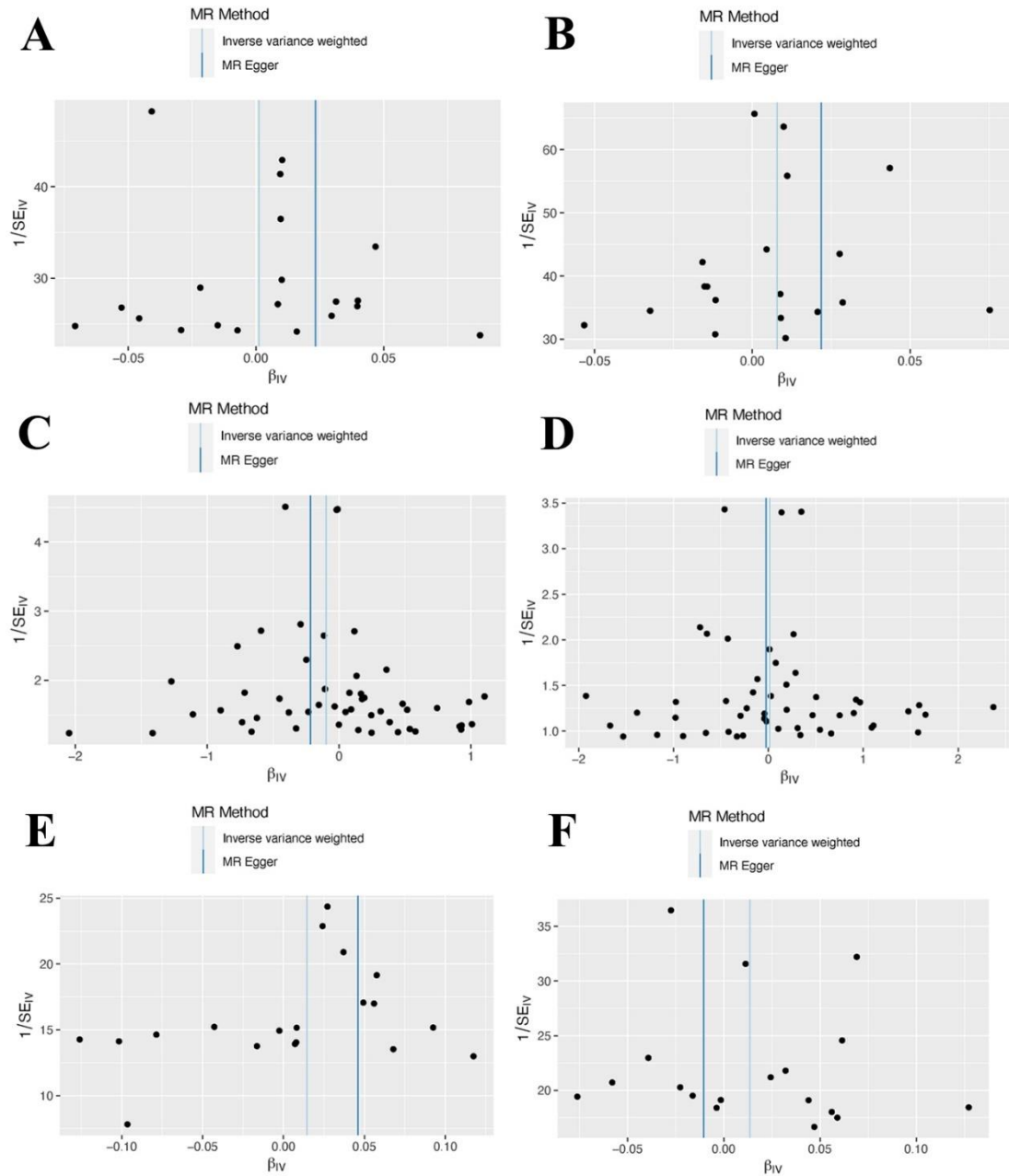
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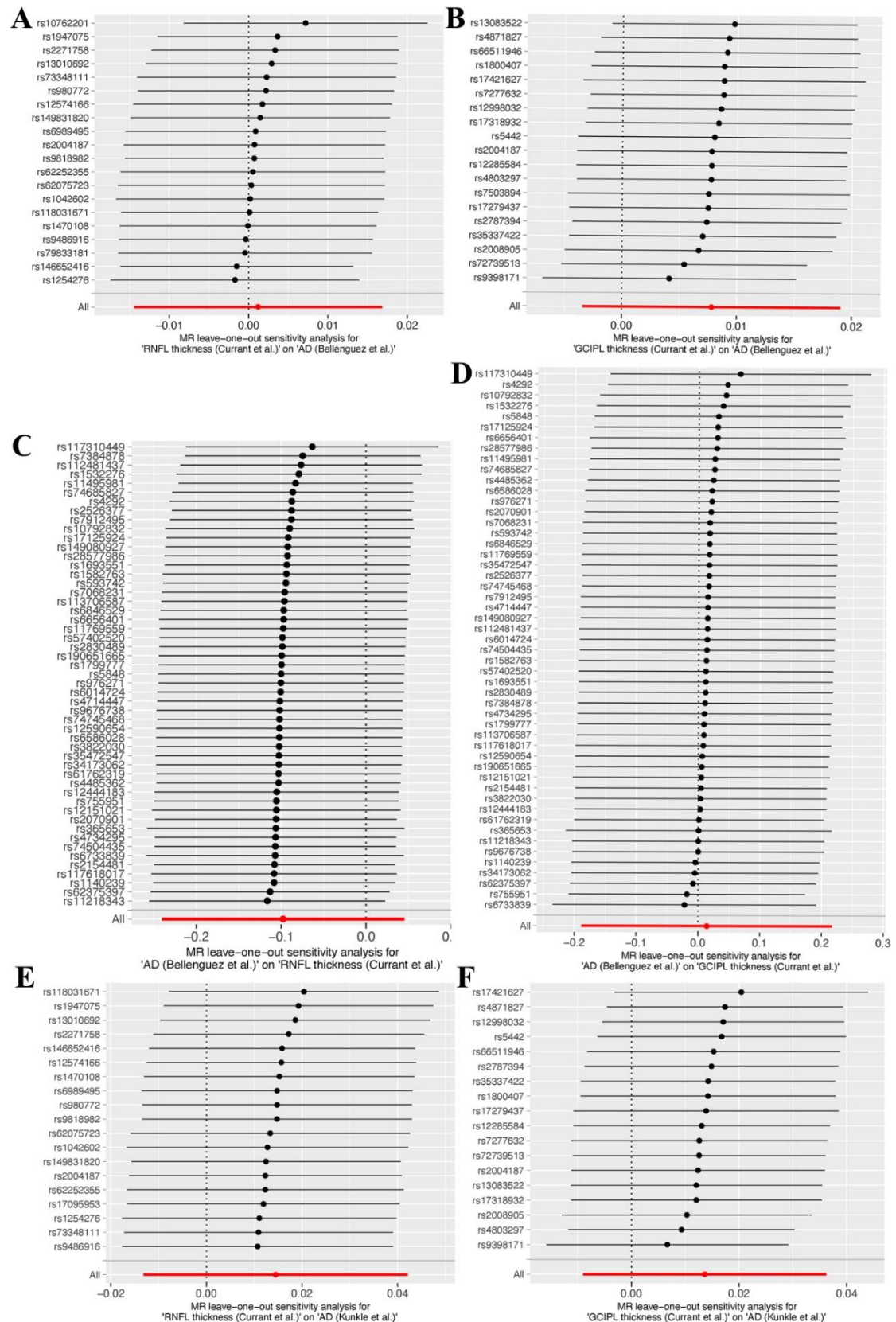
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Section I Figures



Supplementary Figure 1. Funnel plots of Mendelian randomization (MR) analyses for the inner retinal layer, including the retinal nerve fiber layer (RNFL) and the ganglion cell inner plexiform layer (GCIPL), thickness and Alzheimer's disease (AD). (A) RNFL thickness on AD; (B) GCIPL thickness on AD; (C) AD on RNFL thickness; (D) AD on GCIPL thickness; (E) RNFL thickness on AD (validation); (F) GCIPL thickness on AD (validation).



Supplementary Figure 2. Leave-one-out plots of Mendelian randomization (MR) analyses for the inner retinal layer, including the retinal nerve fiber layer (RNFL) and the ganglion cell inner plexiform layer (GCIPL), thickness and Alzheimer's disease

(AD). (A) RNFL thickness on AD; (B) GCIPL thickness on AD; (C) AD on RNFL thickness; (D) AD on GCIPL thickness; (E) RNFL thickness on AD (validation); (F) GCIPL thickness on AD (validation).

Section II Tables

Supplementary Table 1. SNPs used as IVs, their build 20 positions, their associations with RNFL thickness (Currant *et al.*) as exposure and AD (Bellenguez *et al.*) as outcome.

SNP	Ch	Pos	EAO	RNFL thickness (Exposure) ¹				AD (Outcome) ²			
				EA	Beta	SE	P-values	F-statistic	Beta	SE	P-values
				A	F			ic			es
rs980772	2	145442	T	G	0.6	-0.21	0.0383.29E-08	30.545	0.006	0.0084.77E-	
		190			7	16	3		2	7	01
rs130106	2	488006	C	T	0.3	0.225	0.0385.88E-09	33.890	-0.01	0.0082.44E-	
92		67			2	3	7		03	8	01
rs798331	2	156668	C	T	0.0	0.864	0.1431.55E-09	36.495	0.034	0.0312.73E-	
81		02			2	9	2		5	4	01
rs227175	2	172701	G	T	0.5	-0.22	0.0361.51E-09	36.543	0.011	0.0081.57E-	
8		157			9	23	8		7	3	01
rs149831	3	771925	C	T	0.0	-0.41	0.0742.62E-08	30.987	0.003	0.0178.60E-	
820		91			6	55	6		1		01
rs981898	3	458125	A	G	0.1	-0.31	0.0551.19E-08	32.518	-0.00	0.0137.01E-	
2		14			2	89	9		51	2	01
rs622523	3	695720	C	T	0.2	-0.37	0.0451.74E-16	67.958	-0.00	0.0107.22E-	
55		06			0	21	1		36	2	01
rs200418	5	261274	C	A	0.6	0.247	0.0361.97E-11	45.030	0.002	0.0087.67E-	
7		7			0	5	9		5	3	01
rs948691	6	109013	T	C	0.1	-0.27	0.0463.95E-09	34.668	-0.01	0.0102.82E-	
6		930			9	47	7		09	2	01

rs733481	7	503642	C	T	0.0	1.126	0.1826.86E-10	38.083	-0.02	0.0385.29E-	
11		91			1	3	5		45	9	01
rs698949	8	742302	T	G	0.3	0.233	0.0381.24E-09	36.926	0.002	0.0088.12E-	
5		23			3	5	4		6		01
rs118031	9	105210	G	T	0.0	0.931	0.1562.73E-09	35.388	0.027	0.0364.43E-	
671		68			1	8	6		6		01
rs194707	10	497411	T	C	0.6	-0.21	0.0372.89E-08	30.793	0.014	0.0087.79E-	
5		35			4	05	9		9	5	02
rs107622	10	7004011	G	A	0.7	0.458	0.0426.87E-27	115.485	-0.01	0.0094.98E-	
01		1			6	3	6		87	5	02
rs125741	11	692912	T	C	0.1	0.280	0.0503.04E-08	30.695	-0.00	0.0117.11E-	
66		85			5	8	7		42	3	01
rs104260	11	889116	A	C	0.3	-0.36	0.0375.68E-22	92.975	-0.00	0.0086.59E-	
2		96			7	05	4		37	4	01
rs146652	14	299071	G	A	0.0	0.622	0.1134.58E-08	29.904	0.054	0.0263.70E-	
416		03			3	5	8		6	2	02
rs125427	14	608470	T	C	0.3	-0.27	0.0376.08E-14	56.399	-0.01	0.0081.15E-	
6		01			9	77	0		3	3	01
rs147010	15	891537	A	C	0.3	0.236	0.0387.97E-10	37.791	0.007	0.0083.88E-	
8		44			4	0	4		4	6	01
rs620757	17	796113	A	G	0.6	0.368	0.0386.50E-22	92.704	0.003	0.0086.96E-	
23		26			5	4	3		5	9	01

Abbreviations: AD, Alzheimer's Disease; Chr, chromosome; EA, effect allele; EAF, effect allele frequency; IVs, instrumental variables; OA, other allele; Pos, position; RNFL, retinal nerve fiber layer; SNP, single-nucleotide polymorphism

Supplementary Table 2. SNPs used as IVs, their build 19 positions, their associations with GCIPL thickness (Currant et al.) as exposure and AD (Bellenguez et al.) as outcome.

SNP	Ch	Pos	E	O	EAF	GCIPL thickness (Exposure) ¹			AD (Outcome) ²				
						Beta	SE	P-values	F-statistic	Beta	SE	P-values	
rs72739513	1	203080149	A	G	0.0385	0.7164	0.1254	8	1.11E-03	32.6569	0.0537	0.0203	9.16E-0
rs12998032	2	159095496	C	T	0.4436	0.3004	0.0480	0	3.94E-13	139.1665	-0.0033	0.0081	6.71E-0
rs13083522	3	3270368	G	A	0.7769	0.3191	0.0573	8	2.56E-03	31.0300	-0.0179	0.0092	8.64E-0
rs17279437	3	45814094	A	G	0.1068	-0.7765	0.0768	4	5.55E-21	102.1706	-0.0089	0.0131	5.35E-0
rs66511946	4	184932935	G	A	0.4004	-0.3671	0.0493	3	1.03E-15	155.3638	0.0057	0.0081	5.03E-0
rs17318932	5	87688421	T	C	0.0647	-0.5356	0.0963	8	2.66E-03	0.9543	0.0064	0.0171	7.19E-0
rs2004187	5	2612747	C	A	0.5956	0.2769	0.0485	8	1.12E-03	32.6425	0.0025	0.0083	7.67E-0
rs17421627	5	87847586	G	T	0.0743	1.0245	0.0907	9	1.66E-21	27.4987	0.0006	0.0156	9.62E-0
rs9398171	6	108983527	T	C	0.7088	0.5024	0.0523	2	8.30E-29	292.2219	0.0219	0.0088	1.30E-0
rs4871827	8	121061879	A	G	0.3289	-0.2932	0.0505	9	6.62E-03	33.6625	0.0095	0.0085	2.65E-0
rs2787394	9	103007414	T	C	0.4062	-0.2849	0.0485	9	4.35E-03	34.4809	-0.0059	0.0083	4.73E-0
rs12285584	11	88935088	T	C	0.3690	-0.3158	0.0497	0	2.12E-14	140.3848	-0.0028	0.0085	7.40E-0
rs200890	11	1718462	T	C	0.423	-0.361	0.048		6.59E-15	156.238	-0.0100	0.008	2.28E-0

5	3	2	1	2	4	0	3	1			
rs5442	12	6954864	A	G	0.069	-0.707	0.093	4.52E-156.982	-0.003	0.016	8.44E-0
				3	4	7	4	2		1	
rs353374	14	1044072	C	A	0.146	0.404	0.067	1.87E-036.129	0.011	0.011	3.03E-0
22	43			1	8	3	9	6	3	1	
rs180040	15	2823031	T	C	0.081	-0.594	0.086	6.53E-147.201	0.009	0.015	5.64E-0
7	8			3	4	5	2	0	5	1	
rs750389	17	7958347	C	T	0.649	0.553	0.050	3.24E-2121.558	0.005	0.008	5.27E-0
4	3			4	7	2	8	5	7	1	
rs480329	19	4031008	T	C	0.433	-0.265	0.048	3.28E-030.551	-0.002	0.008	7.50E-0
7	4			1	6	1	8	8	8	1	
rs727763	21	4732754	G	A	0.725	0.348	0.053	5.61E-142.983	-0.005	0.009	5.82E-0
2	2			0	8	2	1	0	1	1	

AD: Alzheimer's Disease; Chr: chromosome; EA: effect allele; EAF: effect allele frequency; GCIPL: ganglion cell inner plexiform layer; IV: instrumental variable; OA: other allele; Pos: position; SNP: single-nucleotide polymorphism.

Supplementary Table 3. SNPs used as instruments, their build 51 positions, their associations with AD (Bellenguez *et al.*) as exposure and RNFL thickness (Currant *et al.*) as outcome.

SNP	ChPos	E	O	EAF	AD (Exposure) ²			RNFL thickness (Outcome) ¹			
					Beta	SE	P-value	F-statistic	Beta	SE	P-values
rs20709011	1611850	T	G	0.265	-0.052	0.00	1.20E-0	32.813	-0.048	0.040	2.33E-01
	58				7	92	8		9		
rs66564011	2076920	G	A	0.811	-0.125	0.01	2.84E-3	145.15	0.0145	0.047	7.59E-01
	49			9	3	04	3	6	3		

rs67338392	1278928	T	C	0.389	0.168	0.00	6.48E-9	402.86	-0.00200	0.037	9.58E-01
	10			1	6	84	0	2		7	
rs61762313	1548019	G	A	0.026	0.143	0.02	2.14E-0	31.448	0.0766	0.110	4.87E-01
9	78			3	0	55	8			3	
rs38220304	987343	T	G	0.571	0.051	0.00	5.04E-1	38.350	0.0197	0.036	5.93E-01
				2	4	83	0			8	
rs68465294	1102513	T	C	0.717	-0.067	0.00	1.25E-1	54.695	0.0103	0.040	8.01E-01
	1			4	3	91	3			9	
rs11370655	1796281	A	G	0.110	0.092	0.01	3.38E-1	48.370	-0.0215	0.059	7.19E-01
87	50			3	5	33	2			9	
rs62375395	8629853	T	C	0.210	0.074	0.01	8.58E-1	55.652	0.0734	0.044	9.66E-02
7	1			4	6	00	4			2	
rs976271	6 1146827	A	G	0.361	0.046	0.00	3.23E-0	30.908	0.0115	0.037	7.60E-01
	27			3	7	84	8			6	
rs47144476	4123982	T	C	0.344	0.057	0.00	1.73E-1	45.171	0.0141	0.038	7.15E-01
	2			9	8	86	1			7	
rs35472546	3256037	T	G	0.163	-0.095	0.01	4.26E-1	71.275	-0.0126	0.046	7.85E-01
7	0			4	4	13	7			2	
rs11495987	2817730	T	C	0.209	-0.056	0.01	2.10E-0	31.472	0.1148	0.045	1.14E-02
1	1			4	1	00	8			4	
rs74504437	5494925	G	A	0.093	-0.084	0.01	2.05E-0	35.660	-0.0782	0.062	2.11E-01
5	6			5	2	41	9			5	
rs11769557	1431112	C	T	0.405	-0.069	0.00	4.00E-1	66.855	0.0075	0.037	8.40E-01
9	96			9	5	85	6			1	
rs73848787	9993204	T	C	0.69	0.077	0.00	2.13E-1	75.827	-0.0985	0.039	1.16E-02
	9				5	89	8			1	
rs16935518	1016755	C	T	0.467	0.045	0.00	1.79E-0	32.111	-0.0305	0.036	4.04E-01
	84			2	9	81	8			5	
rs47342958	9600091	G	A	0.460	0.048	0.00	1.98E-0	36.148	0.0445	0.036	2.23E-01

	9		6	7	81	9			5	
rs34173068	1451586	A	G	0.081	0.113	0.01	2.93E-1	48.828	0.0358	0.073 6.25E-01
2	07		4	9	63	2			4	
rs755951	8 2722679	C	A	0.412	0.061	0.00	7.04E-1	55.440	0.0298	0.037 4.24E-01
	0		1	8	83	4			2	
rs15322768	2746615	C	T	0.608	0.100	0.00	2.15E-3	146.03	-0.0594	0.036 1.08E-01
	7		2	3	83	3		1		9
rs17997779	1076660	G	G	0.129	0.070	0.01	9.54E-0	33.133	0.0103	0.055 8.52E-01
	35	C	4	8	23	9				3
rs706823110	6178492	G	T	0.597	0.048	0.00	6.79E-0	33.612	-0.0159	0.037 6.71E-01
	8		4	7	84	9				3
rs791249510	1171871	G	A	0.461	0.057	0.00	2.87E-1	48.659	-0.0514	0.036 1.59E-01
	3		9	2	82	2				5
rs658602810	8225398	T	C	0.803	0.079	0.01	1.33E-1	58.976	0.0151	0.045 7.38E-01
	4		6	1	03	4				3
rs746858211	1213530	G	T	0.018	0.196	0.03	8.63E-1	42.014	-0.2176	0.130 9.46E-02
7	77		6	4	03	1				2
rs112183411	1214355	C	T	0.039	-0.165	0.02	1.01E-1	59.737	-0.1823	0.093 5.15E-02
3	87			4	14	4				6
rs158276311	6002194	A	G	0.371	-0.086	0.00	1.65E-2	104.81	0.0214	0.037 5.68E-01
	8			0	84	4		9		4
rs107928311	8586787	G	A	0.642	0.105	0.00	6.33E-3	158.04	-0.0308	0.037 4.12E-01
2	5		2	6	84	6		1		6
rs747454614	3988767	A	G	0.087	0.082	0.01	1.40E-0	32.137	0.0367	0.065 5.77E-01
8	6		5	2	45	8				7
rs171259214	5339168	G	A	0.089	0.088	0.01	5.82E-1	38.492	-0.0648	0.063 3.06E-01
4	0		2	1	42	0				2
rs285779814	1062002	A	G	0.263	0.069	0.01	13.38E-1	39.543	-0.0315	0.040 4.33E-01
6	32		2	8	1	0				2

rs125906514	9293885	A	G	0.327	-0.069	0.00	2.08E-1	63.449	-0.0115	0.038	7.64E-01
4	5			9	3	87	5				4
rs593742	15 5904577	G	A	0.294	-0.061	0.00	1.04E-1	45.938	0.0232	0.039	5.58E-01
	4			8	0	90	1				7
rs117618015	6356990	T	C	0.143	0.113	0.01	1.75E-2	90.170	0.0406	0.052	4.39E-01
17	2			9	0	19	1				5
rs448536216	8197583	G	T	0.460	-0.046	0.00	2.00E-0	31.118	-0.0268	0.036	4.66E-01
	1			4	3	83	8				7
rs114023916	3002140	T	C	0.378	-0.059	0.00	4.61E-1	47.386	-0.0440	0.037	2.35E-01
	2			9	2	86	2				0
rs124441816	8177320	G	A	0.612	0.059	0.00	2.21E-1	49.501	0.0305	0.037	4.17E-01
3	9			8	1	84	2				5
rs252637717	5641004	G	A	0.444	-0.045	0.00	4.11E-0	30.384	0.0639	0.036	8.02E-02
	1			9	2	82	8				5
rs5848	17 4243024	T	C	0.288	0.064	0.00	1.76E-1	49.305	0.0059	0.040	8.86E-01
	4			6	6	92	2				9
rs574025217	5139807	A	G	0.121	0.090	0.01	6.59E-1	51.589	-0.0030	0.055	9.56E-01
0				7	5	26	3				8
rs4292	17 6155434	T	C	0.617	0.068	0.00	3.47E-1	67.084	-0.0493	0.037	1.92E-01
	1				8	84	6				8
rs149080919	1854253	G	G	0.519	-0.053	0.00	6.14E-0	33.817	0.0333	0.036	3.64E-01
27		C		8	5	92	9				8
rs190651619	4545610	G	T	0.029	-0.159	0.02	8.37E-1	37.775	-0.0078	0.103	9.40E-01
65	3			9	8	60	0				6
rs967673819	4570477	A	G	0.041	0.168	0.02	1.24E-1	54.877	0.0294	0.097	7.63E-01
	1			9	9	28	3				7
rs112481419	4554913	A	G	0.028	0.293	0.02	4.86E-2	111.46	-0.2262	0.117	5.47E-02
37	5			1	5	78	6	2			8
rs121510219	1050874	G	A	0.664	-0.105	0.00	4.09E-3	128.68	-0.0122	0.038	7.54E-01

1		3	5	93	0	8		9			
rs365653	19	4536164	G	A	0.108	-0.256	0.01	1.85E-6	307.45	0.0048	0.057 9.34E-01
	6		2	0	46	8		0		3	
rs117310419	4539351	T	C	0.016	0.770	0.03	3.26E-1	519.11	-0.313	80.170	6.62E-02
49	6		9	1	38	15		2		8	
rs601472420	5499854	G	A	0.089	-0.117	0.01	4.84E-1	65.778	-0.009	20.064	8.87E-01
	4		8	6	45	6				6	
rs283048921	2814819	T	C	0.280	-0.054	0.00	1.72E-0	36.132	0.0001	0.040	9.98E-01
	1		9	7	91	9				3	
rs215448121	2747387	T	C	0.523	0.050	0.00	1.02E-0	37.180	0.0504	0.036	1.69E-01
	5		6	0	82	9				6	

AD: Alzheimer's Disease; Chr: chromosome; EA: effect allele; EAF: effect allele frequency; IV: instrumental variable; OA: other allele; Pos: position; RNFL: retinal nerve fiber layer; SNP: single-nucleotide polymorphism.

Supplementary Table 4. SNPs used as IVs, their build 51 positions, their associations with AD (Bellenguez *et al.*) as exposure and GCIPL thickness (Currant *et al.*) as outcome.

SNP	Ch	Pos	E	O	AD (Exposure) ²				GCIPL thickness (Outcome) ¹			
					EAF	Beta	SE	P-values	F-statistic	Beta	SE	P-value
rs2070901	1	161185058	T	G	0.265	-0.0527	0.0092	1.20E-08	32.813	0.0347	0.0537	5.18E-01
rs6656401	1	207692049	G	A	0.819	-0.1253	0.0104	2.84E-33	145.156	0.0537	0.0622	3.88E-01
rs6733839	2	127892810	T	C	0.389	0.1686	0.0084	6.48E-90	402.862	0.0585	0.0495	2.38E-01
rs617623	3	1548019	G	A	0.02	0.143	0.025	2.14E-31	31.448	0.2256	0.1450	1.20E-0

19	78	63	0	5	08	1
rs382203	4	987343	T	G	0.57 0.051 0.008 5.04E-	38.350 0.0569 0.0484 2.40E-0
0		12	4	3	10	1
rs684652	4	1102513	T	C	0.71 -0.06 0.009 1.25E-	54.695 0.0154 0.0538 7.75E-0
9	1	74	73	1	13	1
rs113706	5	1796281	A	G	0.11 0.092 0.013 3.38E-	48.370 0.0431 0.0787 5.84E-0
587	50	03	5	3	12	1
rs623753	5	8629853	T	C	0.21 0.074 0.01 8.58E-	55.652 0.1185 0.0581 4.13E-0
97	1	04	6		14	2
rs976271	6	1146827	A	G	0.36 0.046 0.008 3.23E-	30.908 -0.042 0.0494 3.95E-0
	27	13	7	4	08	0 1
rs471444	6	4123982	T	C	0.34 0.057 0.008 1.73E-	45.171 -0.002 0.0508 9.60E-0
7	2	49	8	6	11	5 1
rs354725	6	3256037	T	G	0.16 -0.09 0.011 4.26E-	71.275 0.0111 0.0607 8.55E-0
47	0	34	54	3	17	1
rs114959	7	2817730	T	C	0.20 -0.05 0.01 2.10E-	31.472 0.0859 0.0596 1.50E-0
81	1	94	61		08	1
rs745044	7	5494925	G	A	0.09 -0.08 0.014 2.05E-	35.660 -0.008 0.0821 9.15E-0
35	6	35	42	1	09	7 1
rs117695	7	1431112	C	T	0.40 -0.06 0.008 4.00E-	66.855 0.0112 0.0488 8.18E-0
59	96	59	95	5	16	1
rs738487	7	9993204	T	C	0.69 0.077 0.008 2.13E-	75.827 0.0147 0.0513 7.75E-0
8	9		5	9	18	1
rs169355	8	1016755	C	T	0.46 0.045 0.008 1.79E-	32.111 0.0154 0.0480 7.47E-0
1	84	72	9	1	08	1
rs473429	8	9600091	G	A	0.46 0.048 0.008 1.98E-	36.148 0.0265 0.0480 5.81E-0
5	9	06	7	1	09	1
rs341730	8	1451586	A	G	0.08 0.113 0.016 2.93E-	48.828 0.1885 0.0965 5.08E-0
62	07	14	9	3	12	2

rs755951	8	2722679	C	A	0.41	0.061	0.008	7.04E-	55.440	0.1466	0.0489	2.73E-0
		0			21	8	3	14				3
rs153227	8	2746615	C	T	0.60	0.100	0.008	2.15E-	146.031	-0.065	0.0485	1.80E-0
6		7			82	3	3	33		0		1
rs179977	9	1076660	G	G	0.12	0.070	0.012	9.54E-	33.133	0.0468	0.0726	5.19E-0
7		35		C	94	8	3	09				1
rs706823	10	6178492	G	T	0.59	0.048	0.008	6.79E-	33.612	-0.020	0.0491	6.77E-0
1		8			74	7	4	09		4		1
rs791249	10	1171871	G	A	0.46	0.057	0.008	2.87E-	48.659	-0.002	0.0480	9.60E-0
5		3			19	2	2	12		4		1
rs658602	10	8225398	T	C	0.80	0.079	0.010	1.33E-	58.976	-0.035	0.0595	5.52E-0
8		4			36	1	3	14		3		1
rs746858	11	1213530	G	T	0.01	0.196	0.030	8.63E-	42.014	-0.192	0.1711	2.61E-0
27		77			86	4	3	11		3		1
rs112183	11	1214355	C	T	0.03	-0.16	0.021	1.01E-	59.737	-0.152	0.1230	2.14E-0
43		87			9	54	4	14		7		1
rs158276	11	6002194	A	G	0.37	-0.08	0.008	1.65E-	104.819	-0.006	0.0492	8.92E-0
3		8			1	60	4	24		7		1
rs107928	11	8586787	G	A	0.64	0.105	0.008	6.33E-	158.041	-0.076	0.0494	1.23E-0
32		5			22	6	4	36		1		1
rs747454	14	3988767	A	G	0.08	0.082	0.014	1.40E-	32.137	-0.022	0.0864	7.99E-0
68		6			75	2	5	08		0		1
rs171259	14	5339168	G	A	0.08	0.088	0.014	5.82E-	38.492	-0.146	0.0830	7.68E-0
24		0			92	1	2	10		9		2
rs285779	14	1062002	A	G	0.26	0.069	0.011	3.38E-	39.543	-0.068	0.0529	1.98E-0
86		32			32	8	1	10		1		1
rs125906	14	9293885	A	G	0.32	-0.06	0.008	2.08E-	63.449	-0.034	0.0505	4.90E-0
54		5			79	93	7	15		9		1
rs593742	15	5904577	G	A	0.29	-0.06	0.009	1.04E-	45.938	0.0179	0.0522	7.31E-0

	4		48	10		11				1		
rs117618	15	6356990	T	C	0.14	0.113	0.011	1.75E-	90.170	0.0323	0.0689	6.39E-0
017	2				39	0	9	21				1
rs448536	16	8197583	G	T	0.46	-0.04	0.008	2.00E-	31.118	0.0543	0.0483	2.61E-0
2	1				04	63	3	08				1
rs114023	16	3002140	T	C	0.37	-0.05	0.008	4.61E-	47.386	-0.087	0.0486	7.26E-0
9	2				89	92	6	12		3		2
rs124441	16	8177320	G	A	0.61	0.059	0.008	2.21E-	49.501	0.0532	0.0493	2.81E-0
83	9				28	1	4	12				1
rs252637	17	5641004	G	A	0.44	-0.04	0.008	4.11E-	30.384	0.0150	0.0480	7.55E-0
7	1				49	52	2	08				1
rs5848	17	4243024	T	C	0.28	0.064	0.009	1.76E-	49.305	-0.089	0.0537	9.61E-0
	4				86	6	2	12		4		2
rs574025	17	5139807	A	G	0.12	0.090	0.012	6.59E-	51.589	0.0174	0.0733	8.12E-0
20					17	5	6	13				1
rs4292	17	6155434	T	C	0.61	0.068	0.008	3.47E-	67.084	-0.132	0.0496	7.70E-0
	1				7	8	4	16		3		3
rs149080	19	1854253	G	G	0.51	-0.05	0.009	6.14E-	33.817	0.0011	0.0483	9.82E-0
927			C		98	35	2	09				1
rs190651	19	4545610	G	T	0.02	-0.15	0.026	8.37E-	37.775	-0.120	0.1362	3.78E-0
665	3				99	98		10		0		1
rs967673	19	4570477	A	G	0.04	0.168	0.022	1.24E-	54.877	0.1631	0.1284	2.04E-0
8	1				19	9	8	13				1
rs112481	19	4554913	A	G	0.02	0.293	0.027	4.86E-	111.462	0.0034	0.1548	9.82E-0
437	5				81	5	8	26				1
rs121510	19	1050874	G	A	0.66	-0.10	0.009	4.09E-	128.688	-0.027	0.0512	5.85E-0
21					43	55	3	30		9		1
rs365653	19	4536164	G	A	0.10	-0.25	0.014	1.85E-	307.450	-0.035	0.0753	6.38E-0
	6				82	60	6	68		5		1

rs117310	19	4539351	T	C	0.01	0.770	0.033	3.26E-	519.112	-0.355	0.2244	1.13E-0
449		6			69	1	8	115		7		1
rs601472	20	5499854	G	A	0.08	-0.11	0.014	4.84E-	65.778	-0.003	0.0849	9.71E-0
4		4			98	76	5	16		1		1
rs283048	21	2814819	T	C	0.28	-0.05	0.009	1.72E-	36.132	-0.016	0.0529	7.50E-0
9		1			09	47	1	09		9		1
rs215448	21	2747387	T	C	0.52	0.050	0.008	1.02E-	37.180	0.0544	0.0481	2.58E-0
1		5			36	0	2	09				1

AD: Alzheimer's Disease; Chr: chromosome; EA: effect allele; EAF: effect allele frequency; GCIPL: ganglion cell inner plexiform layer; IV: instrumental variable; OA: other allele; Pos: position; SNP: single-nucleotide polymorphism.

Supplementary Table 5. SNPs used as IVs, their build 19 positions, their associations with RNFL thickness (Currant *et al.*) as exposure and AD (Kunkle *et al.*) as outcome.

SNP	Chr	Pos	EA	OA	EAF	RNFL thickness (Exposure) ¹				AD (Outcome) ³		
						Beta	SE	P-values	F-statistic	Beta	SE	P-values
rs980772	2	145442190	T	G	0.66943	-0.21160	0.03833	3.29E-08	30.545	-0.00150	0.01529	2.21E-01
rs13010692	2	48800667	C	T	0.32025	0.2253	0.03875	8.88E-09	33.890	-0.01770	0.01542	5.50E-01
rs2271758	2	172701157	G	T	0.58673	-0.22230	0.03681	5.51E-09	36.543	0.0095	0.01465	1.14E-01
rs1498318203		77192591	C	T	0.062707	-0.41550	0.07462	6.62E-08	30.987	-0.02820	0.03073	5.58E-01
rs9818982	3	45812514	A	G	0.11954	-0.31890	0.05591	1.19E-08	32.518	-0.00250	0.02279	1.12E-01
rs62252355	3	69572006	C	T	0.2004	-0.37210	0.04511	7.4E-16	67.958	-0.01380	0.01784	3.37E-01
rs2004187	5	2612747	C	A	0.59557	0.2475	0.03691	9.97E-11	45.030	0.0122	0.01454	0.03E-01
rs9486916	6	109013930	T	C	0.1947	-0.27470	0.04673	9.95E-09	34.668	-0.02540	0.01811	1.60E-01
rs73348111	7	50364291	C	T	0.0111651	1.1263	0.18256	8.6E-10	38.083	0.1322	0.08671	1.27E-01
rs6989495	8	74230223	T	G	0.32936	0.2335	0.03841	2.4E-09	36.926	0.0019	0.01549	0.00E-01
rs1180316719		10521068	G	T	0.0147310	9.9318	0.15662	7.3E-09	35.388	-0.11730	0.06537	2.25E-02
rs1947075	10	49741135	T	C	0.64483	-0.21050	0.03792	8.89E-08	30.793	0.0214	0.01491	1.50E-01

rs12574166	11	69291285	T	C	0.15388	0.2808	0.05073.04E-08	30.695	-0.00460.02048.23E-01	
rs1042602	11	88911696	A	C	0.37016	-0.36050.03745.68E-22	92.975	-0.00980.01485.07E-01		
rs14665241614	29907103	G	A	0.0314410.6225	0.11384.58E-08	29.904	-0.06000.07964.51E-01			
rs17095953	14	59719393	A	G	0.24079	-0.27880.04351.43E-10	41.144	-0.01560.01643.41E-01		
rs1254276	14	60847001	T	C	0.39037	-0.27770.03706.08E-14	56.399	-0.01600.01452.72E-01		
rs1470108	15	89153744	A	C	0.33727	0.2360	0.03847.97E-10	37.791	-0.00060.01589.69E-01	
rs62075723	17	79611326	A	G	0.64941	0.3684	0.03836.50E-22	29.704	0.0089	0.01615.79E-01

AD: Alzheimer's Disease; Chr: chromosome; EA: effect allele; EAF: effect allele frequency; IV: instrumental variable; OA: other allele; Pos: position; RNFL: retinal nerve fiber layer; SNP: single-nucleotide polymorphism.

Supplementary Table 6. SNPs used as IVs, their build 18 positions, their associations with GCIPL thickness (Currant *et al.*) as exposure and AD (Kunkle *et al.*) as outcome.

SNP	ChrPos	EA	OA	EAF	GCIPL thickness (Exposure) ¹			AD (Outcome) ³			
					Beta	SE	P-values	F-statistic	Beta	SE	P-values
rs727395131	203080149	A	G	0.0385	0.7164	0.1254	1.11E-08	32.656	0.0337	0.0430	4.33E-01
rs129980322	159095496	C	T	0.4436	0.3004	0.0480	3.94E-10	39.166	-0.0174	0.0145	2.29E-01
rs130835223	3270368	G	A	0.7769	0.3191	0.0573	2.56E-08	31.030	0.0179	0.0177	3.12E-01
rs172794373	45814094	A	G	0.1068	-0.7765	0.0768	5.55E-24	102.170	-0.0088	0.0246	7.20E-01
rs665119464	184932935	G	A	0.4004	-0.3671	0.0493	1.03E-13	55.363	0.0083	0.0181	6.47E-01
rs173189325	87688421	T	C	0.0647	-0.5356	0.0963	2.66E-08	30.954	-0.0316	0.0306	3.01E-01
rs2004187	5 2612747	C	A	0.5956	0.2769	0.0485	1.12E-08	32.642	0.0122	0.0145	4.03E-01
rs174216275	87847586	G	T	0.0743	1.0245	0.0907	1.66E-29	127.498	-0.0281	0.0281	3.19E-01
rs9398171	6 108983527	T	C	0.7088	0.5024	0.0523	8.30E-22	29.221	0.0347	0.0156	2.63E-02
rs4871827	8 121061879	A	G	0.3289	-0.2932	0.0505	6.62E-09	33.662	0.0223	0.0151	1.41E-01
rs2787394	9 103007414	T	C	0.4062	-0.2849	0.0485	4.35E-09	34.480	0.0046	0.0146	7.52E-01
rs1228558411	88935088	T	C	0.3690	-0.3158	0.0497	2.12E-10	40.384	-0.0077	0.0149	6.06E-01
rs2008905	11 17184623	T	C	0.4232	-0.3611	0.0482	6.59E-14	56.238	-0.0222	0.0147	1.31E-01

rs5442	12	6954864	A	G	0.0693-0.7074	0.0937	4.52E-14	56.982	0.0277	0.0308	3.69E-01	
rs35337422	14	104407243	C	A	0.1461	0.4048	0.0673	1.87E-09	36.129	-0.0015	0.0220	9.44E-01
rs1800407	15	28230318	T	C	0.0813-0.5944	0.0865	6.53E-12	47.201	0.0009	0.0311	9.77E-01	
rs4803297	19	40310084	T	C	0.4331-0.2656	0.0481	3.28E-08	30.551	-0.0338	0.0144	1.92E-02	
rs7277632	21	47327542	G	A	0.7250	0.3488	0.0532	5.61E-11	42.983	0.0112	0.0160	4.83E-01

AD: Alzheimer's Disease; Chr: chromosome; EA: effect allele; EAF: effect allele

frequency; GCIPL: ganglion cell inner plexiform layer; IV: instrumental variable; OA:

other allele; Pos: position; SNP: single-nucleotide polymorphism.

Supplementary Table 7. MR analysis of inner retinal layer thickness and AD risk using five statistical methods

Outcome	Outcome	IVW		MR-Egger		Weighted median		Weighted mode		Simple mode	
		OR (95%CI)	P-values	OR (95%CI)	P-values	OR (95%CI)	P-values	OR (95%CI)	P-values	OR (95%CI)	P-values
Thickness	AD	1.001	0.883	1.024	0.322	1.010	0.371	1.012	0.516	1.014	
nt et al.) ¹	(Bellenguez	(0.986-1.017)		(0.979-1.071)		(0.989-1.031)		(0.977-1.051)		(0.974-1.056)	
	et al.) ²										
Thickness		1.008	0.172	1.022	0.175	1.009	0.248	1.006	0.560	1.005	
nt et al.) ¹		(0.997-1.019)		(0.992-1.054)		(0.994-1.024)		(0.986-1.027)		(0.979-1.031)	
	RNFL thickness	0.907	0.179	0.805	0.143	0.980	0.861	0.956	0.740	1.094	
guez et al.)(Currant et al.)		(0.786-1.046)		(0.606-1.071)		(0.789-1.219)		(0.734-1.245)		(0.730-1.639)	
	GCIPL thickness	1.014	0.890	0.975	0.904	1.083	0.576	1.132	0.561	1.042	
	(Currant et al.)	(0.828-1.242)		(0.648-1.467)		(0.818-1.434)		(0.747-1.715)		(0.558-1.948)	
Thickness	AD (Kunkle	1.015	0.305	1.047	0.361	1.026	0.179	1.031	0.274	1.027	
nt et al.)	et al.) ³	(0.987-1.043)		(0.951-1.153)		(0.988-1.066)		(0.978-1.086)		(0.965-1.093)	
Thickness		1.014	0.237	0.990	0.737	1.011	0.502	0.991	0.758	1.040	
nt et al.)		(0.991-1.037)		(0.932-1.051)		(0.980-1.042)		(0.935-1.050)		(0.977-1.105)	

AD: Alzheimer's disease; CI: confidence interval; GCIPL: ganglion cell inner

plexiform layer; IVW: inverse-variance weighting; MR: Mendelian randomization;

OR: odds ratio; RNFL: retinal nerve fiber layer.

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