# Supplementary Material

**Identifying Suitable Targets for Alzheimer's Disease and Other Eight Common Neurological Disorders Using the Human Plasma Proteome: A Mendelian Randomization Study**

**Supplementary Table 1.** Reverse causal relationships of plasma proteins with neurological diseases performed by MR.

| Exposure | nSNPs | Method | β (se) | p | Q pval | Intercept pval | Global pval |
|---|---|---|---|---|---|---|---|
| Myeloid cell surface antigen CD33 versus AD | 18 | IVW | -0.023 (0.034) | 0.499 | 0.843 | | |
| | | MR Egger | -0.040 (0.046) | 0.392 | | 0.580 | |
| | | MR-PRESSO | -0.015 (0.028) | 0.585 | | | 0.707 |
| | | Weighted median | -0.066 (0.047) | 0.158 | | | |
| | | Weighted mode | -0.079 (0.050) | 0.136 | | | |
| Cyclin-dependent kinase 8 versus ischemic stroke | 9 | IVW | 0.044 (0.129) | 0.736 | 0.635 | | |
| | | MR Egger | -0.128 (0.934) | 0.895 | | 0.858 | |
| | | MR-PRESSO | 0.044 (0.386) | 0.710 | | | 0.649 |
| | | Weighted median | 0.175 (0.171) | 0.307 | | | |
| | | Weighted mode | 0.237 (0.233) | 0.339 | | | |
| Neuralized E3 ubiquitin-protein ligase 1 versus migraine | 23 | IVW | -0.071 (0.057) | 0.207 | 1 | | |
| | | MR Egger | 0.794 (0.743) | 0.297 | | 0.255 | |
| | | MR-PRESSO | -0.073 (0.020) | 0.001 | | | 1 |
| | | Weighted median | -0.075 (0.069) | 0.281 | | | |
| | | Weighted mode | -0.078 (0.127) | 0.546 | | | |
| Prolactin versus epilepsy | 3 | IVW | 0.361 (0.407) | 0.375 | 0.177 | | |
| | | MR Egger | 0.790 (2.145) | 0.775 | | 0.870 | |
| | | MR-PRESSO | 0.066 (0.016) | 0.001 | | | 0.312 |
| | | Weighted median | 0.109 (0.397) | 0.784 | | | |
| | | Weighted mode | -0.181 (0.600) | 0.791 | | | |
| Fc receptor-like protein 4 versus multiple sclerosis | 64 | IVW | -0.019 (0.040) | 0.623 | 3.61E-26 | | |
| | | MR Egger | 0.024 (0.061) | 0.688 | | 0.344 | |
| | | MR-PRESSO Outlier-corrected | 0.004 (0.018) | 0.834 | | | <0.001 |
| | | Weighted median | 0.008 (0.031) | 0.796 | | | |
| | | Weighted mode | 0.016 (0.030) | 0.610 | | | |

AD, Alzheimer's disease; IVW, inverse-variance weighted; MR-PRESSO, Pleiotropy Residual Sum and Outlier; nSNPs, number of single nucleotide polymorphisms; Q_pval, *p*-value of the Cochran Q statistic; SE, Standard Error.

**Supplementary Table 2.** Power calculation for two-sample MR analysis of plasma proteins on neurological diseases.

| Outcome | Sample size | Proportion of cases | OR | $R^2$ | Power |
|---|---|---|---|---|---|
| Myeloid cell surface antigen CD33 versus AD | 63,926 | 0.34 | 1.079 | 0.534 | 100% |
| Cyclin-dependent kinase 8 versus ischemic stroke | 440,328 | 0.08 | 0.927 | 0.247 | 100% |
| Neuralized E3 ubiquitin-protein ligase 1 versus migraine | 873,341 | 0.12 | 0.914 | 0.180 | 100% |
| Prolactin versus epilepsy | 44,889 | 0.34 | 1.068 | 0.227 | 89% |
| Fc receptor-like protein 4 versus multiple sclerosis | 115,803 | 0.41 | 0.929 | 0.530 | 100% |

AD, Alzheimer's disease; MR, Mendelian randomization; OR, odds ratio; Type-I error rate ($\alpha$) was set as 0.05.

**Supplementary Table 3.** Characteristics of selected SNPs for Myeloid cell surface antigen CD33.

| SNP | Chr | Pos. | Effect allele | Other allele | EAF | Beta | SE | $p$ | $R^2$ | F statistic |
|---|---|---|---|---|---|---|---|---|---|---|
| rs181273405 | 1 | 113847592 | G | T | 0.012 | -0.601 | 0.120 | 5.37E-07 | 0.0084 | 27.917 |
| rs1918695 | 2 | 84902208 | G | C | 0.724 | -0.126 | 0.028 | 7.08E-06 | 0.0063 | 21.019 |
| rs344888 | 2 | 140083467 | T | C | 0.340 | 0.129 | 0.026 | 6.31E-07 | 0.0075 | 24.848 |
| rs17486095 | 4 | 21609494 | G | C | 0.059 | 0.246 | 0.054 | 4.47E-06 | 0.0067 | 22.205 |
| rs78044881 | 7 | 130915645 | T | C | 0.008 | 0.683 | 0.149 | 4.57E-06 | 0.0073 | 24.140 |
| rs9298071 | 8 | 63928350 | C | A | 0.094 | -0.191 | 0.043 | 9.55E-06 | 0.0062 | 20.572 |
| rs138967676 | 8 | 88826102 | A | G | 0.011 | 0.612 | 0.126 | 1.23E-06 | 0.0082 | 27.217 |
| rs113227419 | 8 | 383102 | G | C | 0.067 | -0.252 | 0.054 | 3.39E-06 | 0.0080 | 26.557 |
| rs72803897 | 10 | 57108985 | A | G | 0.088 | 0.227 | 0.045 | 3.63E-07 | 0.0082 | 27.321 |
| rs147372994 | 10 | 96654088 | G | T | 0.061 | 0.226 | 0.051 | 9.33E-06 | 0.0059 | 19.609 |
| rs11594486 | 10 | 17729832 | C | A | 0.065 | -0.245 | 0.050 | 1.02E-06 | 0.0073 | 24.244 |
| rs78361338 | 12 | 114306019 | G | A | 0.019 | -0.436 | 0.092 | 2.24E-06 | 0.0070 | 23.387 |
| rs11054265 | 12 | 11504539 | G | A | 0.108 | -0.177 | 0.040 | 9.55E-06 | 0.0060 | 20.066 |
| rs1107478 | 16 | 9795190 | A | G | 0.540 | 0.133 | 0.026 | 1.91E-07 | 0.0088 | 29.250 |
| rs75685588 | 17 | 50963397 | A | T | 0.034 | -0.329 | 0.073 | 7.24E-06 | 0.0070 | 23.305 |
| rs62114140 | 19 | 51575009 | T | C | 0.100 | -0.249 | 0.042 | 4.68E-09 | 0.0111 | 37.129 |
| rs62114169 | 19 | 51873306 | T | C | 0.141 | 0.200 | 0.039 | 2.63E-07 | 0.0097 | 32.169 |
| rs3865444 | 19 | 51727962 | A | C | 0.329 | -0.942 | 0.021 | 1.00E-200 | 0.3916 | 2123.365 |
| rs77314901 | 20 | 22900228 | G | A | 0.023 | -0.380 | 0.085 | 7.76E-06 | 0.0064 | 21.276 |
| rs7510521 | 21 | 22466510 | C | T | 0.236 | 0.134 | 0.030 | 5.62E-06 | 0.0065 | 21.419 |

Chr, chromosome; EAF, Effect allele frequency; Pos, position; SE, standard error; SNP, single-nucleotide polymorphism. The threshold was set at $p < 1 \times 10^{-5}$.

**Supplementary Table 4.** Characteristics of selected SNPs for cyclin-dependent kinase 8.

| SNP | Chr | Pos. | Effect allele | Other allele | EAF | Beta | SE | $p$ | $R^2$ | F statistic |
|---|---|---|---|---|---|---|---|---|---|---|
| rs2937268 | 1 | 66553607 | T | C | 0.053 | 0.268 | 0.060 | 7.41E-06 | 0.0072 | 23.996 |
| rs115838075 | 1 | 147041838 | T | A | 0.016 | 0.466 | 0.100 | 3.16E-06 | 0.0069 | 23.031 |
| rs114627775 | 1 | 103308746 | G | A | 0.047 | 0.265 | 0.058 | 4.37E-06 | 0.0063 | 20.910 |
| rs1689804 | 1 | 182121598 | A | G | 0.491 | -0.111 | 0.025 | 6.31E-06 | 0.0062 | 20.443 |
| rs147849632 | 1 | 245059378 | G | C | 0.021 | -0.452 | 0.101 | 8.32E-06 | 0.0085 | 28.449 |
| rs34147598 | 2 | 162822349 | T | C | 0.032 | -0.377 | 0.076 | 6.92E-07 | 0.0087 | 29.011 |
| rs138237447 | 3 | 70440238 | T | A | 0.015 | 0.505 | 0.114 | 9.77E-06 | 0.0075 | 24.874 |
| rs7650572 | 3 | 171501558 | A | G | 0.823 | -0.152 | 0.032 | 2.40E-06 | 0.0067 | 22.192 |
| rs28550727 | 4 | 180520424 | T | C | 0.010 | -0.591 | 0.128 | 4.07E-06 | 0.0067 | 22.378 |
| rs12647106 | 4 | 4337988 | A | G | 0.290 | -0.129 | 0.028 | 2.75E-06 | 0.0069 | 22.848 |
| rs575968615 | 4 | 170490927 | G | A | 0.017 | -0.474 | 0.106 | 7.41E-06 | 0.0076 | 25.117 |
| rs74480769 | 5 | 40972211 | G | A | 0.032 | -0.510 | 0.073 | 3.39E-12 | 0.0159 | 53.425 |
| rs6864050 | 5 | 76672960 | T | C | 0.295 | 0.124 | 0.028 | 6.92E-06 | 0.0064 | 21.357 |
| rs1157603 | 7 | 8517556 | A | G | 0.985 | 0.481 | 0.108 | 8.91E-06 | 0.0069 | 23.030 |
| rs11775501 | 8 | 101465070 | C | T | 0.341 | -0.125 | 0.027 | 2.82E-06 | 0.0070 | 23.156 |
| rs79920736 | 8 | 129408584 | C | T | 0.078 | -0.213 | 0.046 | 3.98E-06 | 0.0065 | 21.625 |
| rs55747605 | 9 | 16677509 | A | T | 0.088 | -0.196 | 0.044 | 8.71E-06 | 0.0062 | 20.437 |
| rs10973731 | 9 | 38293885 | C | A | 0.156 | 0.169 | 0.035 | 1.32E-06 | 0.0075 | 25.013 |
| rs113266389 | 10 | 6565474 | C | T | 0.025 | 0.373 | 0.081 | 4.57E-06 | 0.0069 | 22.815 |
| rs35516176 | 10 | 81722059 | T | A | 0.060 | 0.270 | 0.060 | 7.41E-06 | 0.0082 | 27.383 |
| rs11839354 | 13 | 40977804 | A | C | 0.251 | -0.124 | 0.028 | 9.12E-06 | 0.0058 | 19.270 |
| rs8025499 | 15 | 89189984 | C | T | 0.473 | 0.113 | 0.025 | 6.17E-06 | 0.0064 | 21.251 |
| rs117454577 | 16 | 2281967 | T | C | 0.026 | -0.382 | 0.086 | 9.77E-06 | 0.0073 | 24.125 |
| rs117506641 | 16 | 56693581 | C | G | 0.027 | -0.388 | 0.081 | 1.74E-06 | 0.0078 | 25.795 |
| rs9989454 | 17 | 21826038 | C | T | 0.279 | -0.124 | 0.028 | 7.94E-06 | 0.0062 | 20.459 |
| rs8079914 | 17 | 7937533 | A | G | 0.705 | -0.122 | 0.027 | 8.32E-06 | 0.0062 | 20.638 |
| rs78309177 | 17 | 52912221 | A | G | 0.034 | -0.321 | 0.071 | 5.62E-06 | 0.0067 | 22.263 |
| rs4795433 | 17 | 26716821 | T | C | 0.510 | 0.119 | 0.025 | 1.15E-06 | 0.0071 | 23.516 |
| rs72967818 | 18 | 72033508 | A | G | 0.139 | 0.171 | 0.036 | 2.14E-06 | 0.0070 | 23.312 |
| rs62143206 | 19 | 54326212 | T | G | 0.213 | 0.262 | 0.030 | 1.26E-18 | 0.0230 | 77.677 |
| rs73090279 | 20 | 8407019 | A | G | 0.022 | 0.389 | 0.087 | 7.41E-06 | 0.0066 | 21.840 |
| rs2829624 | 21 | 26569831 | T | C | 0.256 | 0.133 | 0.029 | 4.90E-06 | 0.0067 | 22.336 |

Chr, chromosome; EAF, Effect allele frequency; Pos, position; SE, standard error; SNP, single nucleotide polymorphism. The threshold was set at $p < 1 \times 10^{-5}$.

**Supplementary Table 5.** Characteristics of selected SNPs for neuralized E3 ubiquitin-protein ligase 1.

| SNP | Chr | Pos. | Effect allele | Other allele | EAF | Beta | SE | $p$ | $R^2$ | F statistic |
|---|---|---|---|---|---|---|---|---|---|---|
| rs548834381 | 1 | 227684581 | T | C | 0.434 | 0.121 | 0.027 | 9.12E-06 | 0.0072 | 23.860 |
| rs61813832 | 1 | 156882950 | T | C | 0.039 | 0.295 | 0.066 | 7.24E-06 | 0.0065 | 21.459 |
| rs7580559 | 2 | 45449950 | C | T | 0.534 | 0.112 | 0.025 | 9.77E-06 | 0.0063 | 20.840 |
| rs13173656 | 5 | 163505869 | T | C | 0.098 | 0.186 | 0.042 | 7.41E-06 | 0.0061 | 20.213 |
| rs183040236 | 5 | 126178997 | T | C | 0.041 | -0.280 | 0.063 | 8.91E-06 | 0.0062 | 20.643 |
| rs6451674 | 5 | 43110754 | T | C | 0.676 | 0.121 | 0.027 | 5.13E-06 | 0.0064 | 21.393 |
| rs9276427 | 6 | 32711857 | C | T | 0.493 | 0.116 | 0.025 | 2.29E-06 | 0.0068 | 22.497 |
| rs12202773 | 6 | 100824250 | A | G | 0.098 | 0.189 | 0.041 | 4.79E-06 | 0.0063 | 21.023 |
| rs6936531 | 6 | 2729530 | A | G | 0.917 | 0.207 | 0.045 | 3.89E-06 | 0.0065 | 21.583 |
| rs17683330 | 7 | 16736345 | G | A | 0.407 | 0.125 | 0.027 | 3.55E-06 | 0.0075 | 24.913 |
| rs117915747 | 7 | 62001515 | C | T | 0.022 | -0.433 | 0.096 | 6.61E-06 | 0.0082 | 27.376 |
| rs2299255 | 7 | 94938786 | C | T | 0.130 | 0.272 | 0.037 | 2.29E-13 | 0.0167 | 55.878 |
| rs115722675 | 7 | 45591193 | A | G | 0.031 | 0.328 | 0.072 | 5.01E-06 | 0.0065 | 21.421 |
| rs7383801 | 7 | 142340054 | T | G | 0.031 | -0.321 | 0.072 | 7.41E-06 | 0.0062 | 20.595 |
| rs6993770 | 8 | 106581528 | T | A | 0.282 | 0.129 | 0.027 | 2.69E-06 | 0.0067 | 22.290 |
| rs2543061 | 8 | 39831647 | G | T | 0.772 | 0.138 | 0.030 | 3.63E-06 | 0.0067 | 22.294 |
| rs77563269 | 9 | 92253311 | G | C | 0.018 | -0.435 | 0.095 | 4.90E-06 | 0.0068 | 22.447 |
| rs116968700 | 9 | 79915537 | G | A | 0.028 | -0.343 | 0.078 | 9.55E-06 | 0.0064 | 21.277 |
| rs2096372 | 10 | 129487469 | A | T | 0.982 | 0.429 | 0.095 | 6.61E-06 | 0.0064 | 21.362 |
| rs34226858 | 11 | 26176125 | G | T | 0.391 | 0.130 | 0.026 | 4.79E-07 | 0.0081 | 26.899 |
| rs9567814 | 13 | 47810394 | T | C | 0.109 | -0.206 | 0.042 | 7.76E-07 | 0.0082 | 27.240 |
| rs187150569 | 16 | 10189376 | C | T | 0.008 | 0.640 | 0.137 | 2.95E-06 | 0.0068 | 22.665 |
| rs148533624 | 16 | 2072874 | A | C | 0.021 | 0.425 | 0.087 | 1.12E-06 | 0.0074 | 24.604 |
| rs6070532 | 20 | 57171698 | A | C | 0.118 | -0.174 | 0.038 | 4.07E-06 | 0.0063 | 20.916 |
| rs112408513 | 20 | 45775895 | T | G | 0.011 | -0.565 | 0.126 | 7.59E-06 | 0.0072 | 24.001 |

Chr, chromosome; EAF, Effect allele frequency; Pos, position; SE, standard error; SNP, single nucleotide polymorphism. The threshold was set at $p < 1 \times 10^{-5}$.

**Supplementary Table 6.** Characteristics of selected SNPs for prolactin.

| SNP | Chr | Pos. | Effect allele | Other allele | EAF | Beta | SE | $p$ | $R^2$ | F statistic |
|---|---|---|---|---|---|---|---|---|---|---|
| rs9699592 | 1 | 6788985 | G | A | 0.578 | 0.112 | 0.025 | 9.55E-06 | 0.0061 | 20.278 |
| rs12145632 | 1 | 247393142 | C | T | 0.162 | -0.155 | 0.034 | 5.13E-06 | 0.0065 | 21.615 |
| rs6546916 | 2 | 74872278 | C | A | 0.928 | 0.238 | 0.051 | 3.47E-06 | 0.0075 | 25.060 |
| rs17885909 | 2 | 155331020 | A | G | 0.156 | -0.151 | 0.034 | 9.33E-06 | 0.0060 | 19.909 |
| rs2302153 | 2 | 234847823 | C | A | 0.203 | 0.140 | 0.031 | 4.90E-06 | 0.0063 | 21.081 |
| rs13402525 | 2 | 28314858 | T | G | 0.640 | -0.119 | 0.026 | 3.72E-06 | 0.0065 | 21.535 |
| rs7627092 | 3 | 116478181 | C | G | 0.309 | 0.120 | 0.026 | 5.25E-06 | 0.0061 | 20.300 |
| rs11717594 | 3 | 118201375 | A | G | 0.027 | -0.347 | 0.077 | 7.08E-06 | 0.0063 | 20.952 |
| rs10051894 | 5 | 149159985 | A | G | 0.456 | 0.119 | 0.026 | 2.88E-06 | 0.0071 | 23.456 |
| rs113682140 | 5 | 32752151 | C | T | 0.236 | 0.140 | 0.029 | 1.91E-06 | 0.0070 | 23.421 |
| rs6899064 | 5 | 60940718 | A | G | 0.179 | -0.155 | 0.032 | 1.70E-06 | 0.0071 | 23.520 |
| rs9467170 | 6 | 24452754 | A | G | 0.336 | 0.119 | 0.026 | 5.89E-06 | 0.0064 | 21.128 |
| rs17062048 | 6 | 133294400 | C | T | 0.031 | 0.335 | 0.073 | 4.47E-06 | 0.0068 | 22.497 |
| rs11155993 | 6 | 154942072 | T | G | 0.205 | 0.139 | 0.031 | 7.24E-06 | 0.0063 | 20.757 |
| rs10950441 | 7 | 13207343 | G | A | 0.285 | 0.120 | 0.027 | 9.12E-06 | 0.0059 | 19.620 |
| rs79971189 | 7 | 42406078 | T | C | 0.014 | -0.509 | 0.109 | 3.02E-06 | 0.0070 | 23.310 |
| rs142120150 | 8 | 21315016 | C | G | 0.057 | -0.264 | 0.060 | 9.55E-06 | 0.0075 | 24.819 |
| rs72671779 | 8 | 102461870 | G | A | 0.086 | 0.227 | 0.049 | 4.37E-06 | 0.0081 | 26.852 |
| rs1157007 | 9 | 91535433 | T | C | 0.573 | -0.117 | 0.026 | 5.13E-06 | 0.0067 | 22.174 |
| rs7091050 | 10 | 2188690 | C | T | 0.463 | 0.111 | 0.025 | 7.59E-06 | 0.0062 | 20.488 |
| rs10995455 | 10 | 64936361 | A | G | 0.310 | 0.124 | 0.027 | 5.37E-06 | 0.0066 | 21.990 |
| rs11815780 | 10 | 6409333 | A | G | 0.045 | -0.302 | 0.064 | 2.57E-06 | 0.0078 | 25.884 |
| rs12779423 | 10 | 133351511 | A | G | 0.106 | 0.178 | 0.040 | 9.55E-06 | 0.0060 | 19.868 |
| rs11025062 | 11 | 19237979 | T | C | 0.514 | -0.117 | 0.025 | 4.47E-06 | 0.0068 | 22.602 |
| rs17124538 | 11 | 120783369 | G | A | 0.050 | -0.275 | 0.059 | 2.82E-06 | 0.0072 | 24.016 |
| rs61942975 | 12 | 88074484 | T | C | 0.065 | 0.251 | 0.054 | 3.31E-06 | 0.0077 | 25.510 |
| rs142333252 | 14 | 42070338 | G | A | 0.045 | -0.321 | 0.065 | 6.61E-07 | 0.0088 | 29.413 |
| rs1875938 | 16 | 10612442 | G | C | 0.185 | 0.166 | 0.033 | 3.47E-07 | 0.0083 | 27.695 |
| rs138645734 | 17 | 10655160 | C | A | 0.021 | -0.432 | 0.095 | 5.89E-06 | 0.0079 | 26.122 |
| rs117268622 | 19 | 48295037 | T | C | 0.029 | -0.363 | 0.081 | 6.61E-06 | 0.0073 | 24.411 |
| rs7249614 | 19 | 43637890 | G | A | 0.578 | -0.120 | 0.027 | 6.03E-06 | 0.0070 | 23.261 |
| rs2867491 | 20 | 41286644 | T | A | 0.299 | 0.121 | 0.027 | 8.13E-06 | 0.0061 | 20.332 |
| rs3729555 | 20 | 61594493 | A | G | 0.328 | -0.122 | 0.027 | 5.25E-06 | 0.0066 | 21.754 |

Chr, chromosome; EAF, Effect allele frequency; Pos, position; SE, standard error; SNP, single nucleotide polymorphism. The threshold was set at $p < 1\times10^{-5}$.

**Supplementary Table 7.** Characteristics of selected SNPs for Fc receptor-like protein 4.

| SNP | Chr | Pos. | Effect allele | Other allele | EAF | Beta | SE | $p$ | $R^2$ | F statistic |
|---|---|---|---|---|---|---|---|---|---|---|
| rs3850533 | 1 | 20061456 | C | T | 0.247 | 0.137 | 0.029 | 1.95E-06 | 0.0070 | 23.203 |
| rs76661224 | 1 | 210590022 | A | G | 0.072 | 0.215 | 0.048 | 7.41E-06 | 0.0062 | 20.584 |
| rs11582663 | 1 | 157559122 | T | C | 0.144 | -1.133 | 0.030 | 1.00E-200 | 0.3169 | 1530.602 |
| rs1609331 | 2 | 184556456 | A | G | 0.536 | 0.111 | 0.025 | 8.32E-06 | 0.0061 | 20.157 |
| rs6436653 | 2 | 227972708 | G | A | 0.613 | -0.113 | 0.026 | 9.33E-06 | 0.0061 | 20.211 |
| rs73104894 | 2 | 239544749 | A | G | 0.019 | -0.461 | 0.092 | 4.79E-07 | 0.0080 | 26.544 |
| rs76470538 | 3 | 102579094 | C | T | 0.027 | -0.349 | 0.077 | 5.89E-06 | 0.0065 | 21.458 |
| rs76866641 | 3 | 35950517 | A | G | 0.022 | -0.399 | 0.089 | 7.59E-06 | 0.0069 | 22.927 |
| rs17676863 | 4 | 54610788 | T | A | 0.028 | 0.369 | 0.081 | 5.01E-06 | 0.0075 | 25.030 |
| rs13189930 | 5 | 14727882 | A | C | 0.219 | -0.136 | 0.031 | 9.33E-06 | 0.0063 | 20.849 |
| rs2973719 | 5 | 177801274 | C | T | 0.265 | 0.123 | 0.028 | 9.55E-06 | 0.0059 | 19.600 |
| rs150083591 | 6 | 141850357 | T | C | 0.024 | 0.437 | 0.090 | 1.32E-06 | 0.0090 | 29.966 |
| rs762808 | 6 | 32797466 | A | G | 0.052 | 0.250 | 0.056 | 8.51E-06 | 0.0061 | 20.354 |
| rs76383287 | 6 | 43177353 | A | G | 0.103 | -0.179 | 0.040 | 9.77E-06 | 0.0059 | 19.579 |
| rs116995988 | 6 | 162877862 | C | T | 0.025 | 0.391 | 0.080 | 1.10E-06 | 0.0074 | 24.726 |
| rs116921833 | 7 | 153895185 | T | C | 0.011 | -0.605 | 0.128 | 2.09E-06 | 0.0077 | 25.725 |
| rs9648088 | 7 | 46659313 | T | C | 0.220 | -0.145 | 0.031 | 3.24E-06 | 0.0072 | 23.910 |
| rs13257111 | 8 | 26582563 | A | G | 0.591 | -0.120 | 0.026 | 3.89E-06 | 0.0069 | 22.941 |
| rs2974279 | 8 | 88075043 | C | T | 0.640 | -0.121 | 0.026 | 4.47E-06 | 0.0067 | 22.328 |
| rs700089 | 9 | 125874636 | G | A | 0.950 | -0.255 | 0.058 | 9.55E-06 | 0.0062 | 20.578 |
| rs112726374 | 9 | 36985873 | T | C | 0.037 | -0.321 | 0.065 | 8.91E-07 | 0.0073 | 24.357 |
| rs10968633 | 9 | 28517171 | T | C | 0.192 | -0.160 | 0.036 | 9.55E-06 | 0.0079 | 26.369 |
| rs568952649 | 11 | 94912324 | C | T | 0.014 | 0.538 | 0.118 | 5.25E-06 | 0.0081 | 27.087 |
| rs10744541 | 12 | 1607334 | A | G | 0.652 | 0.118 | 0.026 | 5.89E-06 | 0.0063 | 21.001 |
| rs143328393 | 13 | 83919602 | T | G | 0.026 | -0.370 | 0.080 | 3.31E-06 | 0.0068 | 22.704 |
| rs41307104 | 14 | 55835961 | C | G | 0.017 | -0.535 | 0.102 | 1.51E-07 | 0.0093 | 31.080 |
| rs3809562 | 15 | 71148408 | G | A | 0.579 | 0.113 | 0.025 | 6.03E-06 | 0.0062 | 20.744 |
| rs67181813 | 16 | 84413537 | C | G | 0.106 | -0.197 | 0.040 | 9.55E-07 | 0.0074 | 24.515 |
| rs554926389 | 17 | 9953082 | C | T | 0.017 | -0.499 | 0.103 | 1.29E-06 | 0.0085 | 28.124 |
| rs112638217 | 18 | 46632188 | C | T | 0.012 | -0.530 | 0.115 | 4.37E-06 | 0.0068 | 22.745 |
| rs17801029 | 19 | 45050756 | C | T | 0.026 | -0.360 | 0.078 | 4.37E-06 | 0.0066 | 21.929 |

Chr, chromosome; EAF, Effect allele frequency; Pos, position; SE, standard error; SNP, single nucleotide polymorphism. The threshold was set at $p < 1 \times 10^{-5}$.

**Supplementary Table 8.** Characteristics of selected SNPs for AD.

| SNP | Trait | Chr | Pos. | Effect allele | Other allele | EAF | Beta | SE | $p$ | $R^2$ | F statistic |
|---|---|---|---|---|---|---|---|---|---|---|---|
| rs679515 | AD | 1 | 207750568 | C | T | 0.172 | -0.151 | 0.018 | 1.55E-16 | 0.0065 | 415.785 |
| rs6733839 | AD | 2 | 127892810 | T | C | 0.382 | 0.169 | 0.015 | 4.02E-28 | 0.0135 | 876.955 |
| rs114812713 | AD | 6 | 41034000 | C | G | 0.019 | 0.298 | 0.043 | 4.47E-12 | 0.0033 | 211.220 |
| rs34665982 | AD | 6 | 32560306 | C | T | 0.301 | -0.097 | 0.017 | 5.8E-09 | 0.0039 | 252.620 |
| rs9381563 | AD | 6 | 47432637 | T | C | 0.644 | -0.082 | 0.015 | 2.93E-08 | 0.0031 | 198.105 |
| rs11767557 | AD | 7 | 143109139 | C | T | 0.803 | -0.103 | 0.018 | 1.56E-08 | 0.0033 | 214.198 |
| rs867230 | AD | 8 | 27468503 | A | C | 0.607 | 0.133 | 0.016 | 3.49E-17 | 0.0085 | 546.801 |
| rs73223431 | AD | 8 | 27219987 | T | C | 0.367 | 0.094 | 0.015 | 8.34E-10 | 0.0041 | 261.118 |
| rs11257242 | AD | 10 | 11721119 | G | C | 0.367 | 0.084 | 0.015 | 4.64E-08 | 0.0033 | 210.831 |
| rs1582763 | AD | 11 | 60021948 | A | G | 0.351 | -0.123 | 0.015 | 1.19E-16 | 0.0069 | 445.182 |
| rs3851179 | AD | 11 | 85868640 | C | T | 0.361 | 0.120 | 0.015 | 5.81E-16 | 0.0066 | 425.934 |
| rs3740688 | AD | 11 | 47380340 | T | G | 0.553 | 0.094 | 0.014 | 9.7E-11 | 0.0043 | 277.456 |
| rs12590654 | AD | 14 | 92938855 | A | G | 0.337 | -0.091 | 0.016 | 8.73E-09 | 0.0037 | 235.164 |
| rs72654445 | AD | 19 | 45417200 | A | G | 0.010 | -0.543 | 0.081 | 2.27E-11 | 0.0061 | 389.606 |
| rs7412 | AD | 19 | 45412079 | T | C | 0.072 | -0.467 | 0.031 | 6.4E-53 | 0.0292 | 1923.980 |
| rs1081105 | AD | 19 | 45412955 | C | A | 0.974 | 0.942 | 0.044 | 1.5E-103 | 0.0451 | 3019.937 |
| rs12151021 | AD | 19 | 1050874 | G | A | 0.319 | -0.107 | 0.017 | 2.56E-10 | 0.0050 | 320.277 |
| rs111278137 | AD | 19 | 45215081 | A | G | 0.021 | -0.474 | 0.071 | 3.2E-11 | 0.0093 | 597.580 |
| rs147711004 | AD | 19 | 45337918 | A | G | 0.028 | 1.135 | 0.037 | 1E-200 | 0.0702 | 4824.058 |
| rs139136389 | AD | 19 | 45427136 | T | C | 0.020 | -0.494 | 0.085 | 6.43E-09 | 0.0094 | 607.758 |
| rs150685845 | AD | 19 | 45675180 | G | A | 0.988 | 0.556 | 0.065 | 6.62E-18 | 0.0076 | 491.785 |

AD, Alzheimer's disease; Chr, chromosome; EAF, Effect allele frequency; Pos, position; SE, standard error; SNP, single nucleotide polymorphism. The threshold was set at $p < 5\times10^{-8}$.

**Supplementary Table 9.** Characteristics of selected SNPs for multiple sclerosis.

| SNP | Chr | Pos. | Effect allele | Other allele | EAF | Beta | SE | $p$ | $R^2$ | F statistic |
|---|---|---|---|---|---|---|---|---|---|---|
| rs10063294 | 5 | 35877505 | A | G | 0.529 | -0.099 | 0.016 | 1.13E-09 | 0.0049 | 568.834 |
| rs1014486 | 3 | 159691112 | C | T | 0.419 | 0.105 | 0.016 | 1.36E-10 | 0.0054 | 625.971 |
| rs1026916 | 17 | 40529835 | G | A | 0.652 | -0.130 | 0.017 | 1.02E-13 | 0.0076 | 890.047 |
| rs1077667 | 19 | 6668972 | T | C | 0.207 | -0.152 | 0.021 | 8.37E-13 | 0.0076 | 883.265 |
| rs10801908 | 1 | 117090493 | T | C | 0.120 | -0.215 | 0.026 | 3.54E-16 | 0.0097 | 1139.566 |
| rs1112718 | 10 | 94479107 | G | A | 0.407 | -0.106 | 0.017 | 2.46E-10 | 0.0054 | 626.895 |
| rs11256593 | 10 | 6117322 | T | C | 0.530 | 0.186 | 0.017 | 6.78E-27 | 0.0173 | 2038.135 |
| rs114872782 | 6 | 32241452 | T | C | 0.014 | -2.450 | 0.255 | 7.72E-22 | 0.1692 | 23577.340 |
| rs11666263 | 19 | 10590684 | G | A | 0.364 | -0.103 | 0.018 | 1.2E-08 | 0.0049 | 569.458 |
| rs11749040 | 5 | 40396425 | A | G | 0.128 | 0.197 | 0.023 | 3.54E-17 | 0.0087 | 1012.071 |
| rs1177228 | 2 | 61242410 | G | A | 0.722 | 0.107 | 0.019 | 8.57E-09 | 0.0046 | 538.596 |
| rs11809700 | 1 | 93152635 | T | C | 0.268 | 0.144 | 0.018 | 3.51E-15 | 0.0082 | 956.310 |
| rs12147246 | 14 | 103265844 | G | A | 0.654 | -0.099 | 0.017 | 4.29E-09 | 0.0045 | 519.580 |
| rs12365699 | 11 | 118743286 | A | G | 0.159 | -0.144 | 0.023 | 3.15E-10 | 0.0055 | 645.001 |
| rs12434551 | 14 | 69253364 | T | A | 0.456 | -0.104 | 0.016 | 1.83E-10 | 0.0054 | 623.553 |
| rs12478539 | 2 | 43355324 | C | G | 0.279 | -0.123 | 0.019 | 4.37E-11 | 0.0061 | 712.036 |
| rs1250551 | 10 | 81059335 | T | G | 0.366 | 0.116 | 0.017 | 2.66E-11 | 0.0062 | 724.179 |
| rs12612620 | 2 | 112488876 | A | G | 0.233 | 0.212 | 0.036 | 4.26E-09 | 0.0160 | 1885.159 |
| rs12925972 | 16 | 79111297 | C | T | 0.547 | 0.095 | 0.017 | 3.07E-08 | 0.0044 | 515.658 |
| rs13327021 | 3 | 27783015 | T | C | 0.350 | 0.115 | 0.017 | 1.73E-11 | 0.0060 | 703.581 |
| rs140522 | 22 | 50971266 | C | T | 0.671 | -0.111 | 0.018 | 2.85E-10 | 0.0054 | 628.367 |
| rs1465697 | 19 | 49837246 | T | C | 0.255 | 0.124 | 0.019 | 3.48E-11 | 0.0059 | 683.274 |
| rs17124032 | 14 | 88546009 | A | G | 0.071 | -0.217 | 0.032 | 7.08E-12 | 0.0062 | 724.597 |
| rs1738074 | 6 | 159465977 | C | T | 0.582 | 0.114 | 0.017 | 9.91E-12 | 0.0063 | 733.588 |
| rs1860545 | 12 | 6446777 | A | G | 0.392 | 0.117 | 0.017 | 7.79E-12 | 0.0065 | 754.758 |
| rs2150879 | 17 | 57859210 | A | G | 0.559 | -0.104 | 0.016 | 3.29E-10 | 0.0053 | 615.515 |
| rs2248461 | 20 | 52792202 | A | G | 0.370 | -0.108 | 0.017 | 5.33E-10 | 0.0055 | 634.523 |
| rs2317231 | 1 | 157686337 | T | G | 0.450 | -0.101 | 0.017 | 1.9E-09 | 0.0050 | 582.686 |
| rs2546890 | 5 | 158759900 | G | A | 0.475 | -0.117 | 0.016 | 1.04E-12 | 0.0068 | 795.841 |
| rs2681424 | 3 | 121769522 | C | T | 0.504 | -0.121 | 0.017 | 2.71E-13 | 0.0073 | 856.112 |
| rs2857700 | 6 | 31572481 | C | T | 0.867 | -0.767 | 0.024 | 1E-200 | 0.1356 | 18163.960 |
| rs28703878 | 8 | 79417222 | G | A | 0.277 | 0.134 | 0.021 | 4.51E-10 | 0.0072 | 835.067 |
| rs34695601 | 14 | 76014298 | C | T | 0.264 | -0.109 | 0.020 | 3.16E-08 | 0.0047 | 541.420 |
| rs354033 | 7 | 149289464 | A | G | 0.250 | -0.108 | 0.019 | 1.21E-08 | 0.0044 | 508.237 |
| rs35486093 | 1 | 85729820 | G | A | 0.093 | 0.179 | 0.028 | 1.6E-10 | 0.0054 | 633.773 |
| rs35540610 | 2 | 231121829 | C | T | 0.246 | 0.135 | 0.019 | 2.88E-12 | 0.0068 | 789.494 |

| SNP | Chr | Pos | | | EAF | | SE | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| rs35703946 | 16 | 86021505 | A | G | 0.163 | -0.173 | 0.029 | 1.94E-09 | 0.0081 | 948.333 |
| rs3809627 | 16 | 30103160 | A | C | 0.400 | -0.097 | 0.018 | 3.25E-08 | 0.0045 | 524.901 |
| rs415759 | 16 | 1066917 | C | T | 0.186 | 0.119 | 0.022 | 4.76E-08 | 0.0043 | 497.112 |
| rs4325907 | 3 | 101749022 | T | C | 0.643 | -0.099 | 0.017 | 3.68E-09 | 0.0045 | 525.974 |
| rs438613 | 3 | 28072086 | C | T | 0.470 | 0.138 | 0.017 | 9.43E-17 | 0.0095 | 1109.665 |
| rs478093 | 1 | 120255126 | G | A | 0.684 | 0.105 | 0.018 | 4.3E-09 | 0.0048 | 556.488 |
| rs4808760 | 19 | 18301979 | G | C | 0.293 | -0.135 | 0.019 | 4.84E-13 | 0.0075 | 874.419 |
| rs4896153 | 6 | 135833463 | A | T | 0.631 | -0.138 | 0.019 | 1.65E-13 | 0.0089 | 1041.312 |
| rs4939490 | 11 | 60793651 | G | C | 0.397 | 0.137 | 0.017 | 4.25E-15 | 0.0089 | 1044.446 |
| rs4947255 | 6 | 32207483 | T | C | 0.035 | -0.552 | 0.056 | 2.54E-23 | 0.0203 | 2404.728 |
| rs55970742 | 7 | 2441337 | T | C | 0.674 | -0.100 | 0.018 | 2.05E-08 | 0.0044 | 515.255 |
| rs56232455 | 11 | 321235 | A | G | 0.487 | 0.158 | 0.028 | 1.78E-08 | 0.0125 | 1470.438 |
| rs58546351 | 6 | 32483611 | G | A | 0.008 | -1.894 | 0.053 | 1E-200 | 0.0559 | 6857.161 |
| rs59655222 | 1 | 200875897 | C | T | 0.298 | -0.123 | 0.019 | 3.76E-11 | 0.0064 | 740.138 |
| rs6032662 | 20 | 44734310 | T | C | 0.756 | -0.134 | 0.018 | 2.85E-13 | 0.0066 | 770.427 |
| rs62420820 | 6 | 137438057 | A | G | 0.238 | 0.137 | 0.019 | 2.5E-13 | 0.0068 | 796.445 |
| rs6496663 | 15 | 90887584 | C | A | 0.295 | 0.101 | 0.018 | 2.78E-08 | 0.0042 | 489.348 |
| rs6670198 | 1 | 2520527 | C | T | 0.346 | -0.145 | 0.018 | 2.03E-16 | 0.0095 | 1113.184 |
| rs6763437 | 3 | 119145390 | A | G | 0.041 | -0.779 | 0.132 | 3.72E-09 | 0.0477 | 5800.974 |
| rs6990534 | 8 | 128814091 | G | A | 0.710 | 0.107 | 0.018 | 3.6E-09 | 0.0047 | 550.312 |
| rs701006 | 12 | 58106836 | G | A | 0.600 | 0.114 | 0.017 | 1.35E-11 | 0.0062 | 725.038 |
| rs7190580 | 16 | 11403470 | G | A | 0.711 | -0.098 | 0.018 | 4.64E-08 | 0.0040 | 459.280 |
| rs7200146 | 16 | 11213449 | T | G | 0.657 | -0.171 | 0.017 | 7E-24 | 0.0131 | 1541.765 |
| rs7207542 | 17 | 45697549 | G | C | 0.497 | 0.109 | 0.017 | 4.67E-11 | 0.0059 | 689.002 |
| rs72928038 | 6 | 90976768 | A | G | 0.174 | 0.161 | 0.025 | 9.01E-11 | 0.0074 | 862.915 |
| rs743771 | 6 | 32976909 | A | C | 0.466 | -0.099 | 0.016 | 8.55E-10 | 0.0049 | 572.214 |
| rs74449127 | 1 | 101290432 | G | A | 0.292 | -0.197 | 0.026 | 1.36E-14 | 0.0160 | 1888.336 |
| rs7592560 | 2 | 68647001 | A | G | 0.549 | 0.104 | 0.017 | 2.87E-10 | 0.0054 | 624.710 |
| rs7855251 | 9 | 100868189 | C | T | 0.256 | -0.110 | 0.020 | 4.23E-08 | 0.0046 | 536.698 |
| rs7975763 | 12 | 123604053 | T | C | 0.210 | 0.121 | 0.021 | 7.8E-09 | 0.0049 | 566.386 |
| rs9277647 | 6 | 33083750 | T | C | 0.190 | -0.214 | 0.021 | 5.47E-24 | 0.0140 | 1649.409 |
| rs9393975 | 6 | 29802217 | A | T | 0.177 | -0.766 | 0.043 | 1.49E-70 | 0.1710 | 23891.210 |
| rs9591325 | 13 | 50811220 | C | T | 0.068 | -0.212 | 0.034 | 4.16E-10 | 0.0057 | 663.126 |
| rs9610458 | 22 | 22205353 | T | C | 0.522 | 0.114 | 0.017 | 4.57E-12 | 0.0065 | 758.871 |
| rs9955954 | 18 | 56348044 | G | A | 0.236 | -0.110 | 0.019 | 1.54E-08 | 0.0044 | 508.117 |
| rs9992763 | 4 | 109058718 | T | G | 0.568 | -0.090 | 0.016 | 4.51E-08 | 0.0040 | 462.626 |

Chr, chromosome; EAF, Effect allele frequency; MS, multiple sclerosis; Pos, position; SE, standard error; SNP, single nucleotide polymorphism. The threshold was set at $p < 5 \times 10^{-8}$.

**Supplementary Table 10.** Characteristics of selected SNPs for epilepsy.

| SNP | Chr | Pos. | Effect allele | Other allele | EAF | Beta | SE | $p$ | $R^2$ | F statistic |
|---|---|---|---|---|---|---|---|---|---|---|
| rs6432877 | 2 | 166998767 | G | C | 0.255 | 0.063 | 0.009 | 1.7E-13 | 0.0015 | 68.739 |
| rs4671319 | 2 | 57950346 | A | G | 0.542 | -0.042 | 0.007 | 8.07E-09 | 0.0009 | 39.123 |
| rs4638568 | 16 | 50045839 | A | G | 0.061 | -0.086 | 0.016 | 4E-08 | 0.0008 | 37.861 |

Chr, chromosome; EAF, Effect allele frequency; Pos, position; SE, standard error; SNP, single nucleotide polymorphism. The threshold was set at $p < 5 \times 10^{-8}$.

**Supplementary Table 11.** Characteristics of selected SNPs for ischemic stroke.

| SNP | Chr | Pos. | Effect allele | Other allele | EAF | Beta | SE | $p$ | $R^2$ | F statistic |
|---|---|---|---|---|---|---|---|---|---|---|
| rs2758612 | 1 | 156205301 | C | T | 0.355 | -0.065 | 0.011 | 3.68E-09 | 0.0020 | 861.196 |
| rs34311906 | 4 | 113732090 | C | T | 0.402 | 0.065 | 0.011 | 1.07E-08 | 0.0020 | 893.805 |
| rs2634074 | 4 | 111677041 | A | T | 0.788 | -0.094 | 0.012 | 5.9E-15 | 0.0030 | 1307.924 |
| rs2066864 | 4 | 155525695 | A | G | 0.245 | 0.063 | 0.012 | 3.51E-08 | 0.0015 | 656.118 |
| rs11242678 | 6 | 1337180 | T | C | 0.255 | 0.072 | 0.011 | 2.7E-10 | 0.0020 | 876.276 |
| rs2107595 | 7 | 19049388 | A | G | 0.167 | 0.088 | 0.013 | 2.33E-11 | 0.0022 | 956.463 |
| rs473238 | 11 | 102700360 | C | T | 0.867 | -0.083 | 0.015 | 1.65E-08 | 0.0016 | 700.583 |
| rs3184504 | 12 | 111884608 | C | T | 0.528 | -0.078 | 0.010 | 1.23E-14 | 0.0030 | 1335.950 |
| rs4942561 | 13 | 47209347 | T | G | 0.759 | 0.066 | 0.012 | 1.77E-08 | 0.0016 | 692.194 |

Chr, chromosome; EAF, Effect allele frequency; Pos, position; SE, standard error; SNP, single nucleotide polymorphism. The threshold was set at $p < 5\times10^{-8}$.

**Supplementary Table 12.** Characteristics of selected SNPs for migraine.

| SNP | Chr | Pos. | Effect allele | Other allele | EAF | Beta | SE | $p$ | $R^2$ | F statistic |
|---|---|---|---|---|---|---|---|---|---|---|
| rs11172113 | 12 | 57527283 | C | T | 0.415 | -0.107 | 0.005 | 1.38E-90 | 0.0055 | 4859.749 |
| rs4759276 | 12 | 57526646 | A | G | 0.392 | -0.104 | 0.005 | 7.05E-83 | 0.0052 | 4539.210 |
| rs4759275 | 12 | 57525756 | A | G | 0.426 | -0.097 | 0.005 | 7.31E-74 | 0.0046 | 4018.044 |
| rs10218452 | 1 | 3075597 | G | A | 0.229 | 0.110 | 0.006 | 7.26E-71 | 0.0043 | 3747.233 |
| rs7518255 | 1 | 3086464 | A | G | 0.224 | 0.108 | 0.006 | 1.35E-70 | 0.0040 | 3527.335 |
| rs10797381 | 1 | 3072482 | A | T | 0.229 | 0.109 | 0.006 | 4.13E-70 | 0.0042 | 3704.242 |
| rs2075968 | 1 | 3081241 | T | C | 0.225 | 0.107 | 0.006 | 6.49E-70 | 0.0040 | 3512.754 |
| rs61759167 | 1 | 3091587 | T | C | 0.224 | 0.108 | 0.006 | 2.82E-69 | 0.0040 | 3533.697 |
| rs10467124 | 12 | 57519694 | C | G | 0.429 | -0.093 | 0.005 | 6.77E-69 | 0.0042 | 3707.791 |
| rs2376495 | 1 | 3095126 | G | C | 0.224 | 0.108 | 0.006 | 7.76E-69 | 0.0041 | 3552.668 |
| rs11587518 | 1 | 3096925 | A | T | 0.224 | 0.108 | 0.006 | 9.23E-69 | 0.0041 | 3551.699 |
| rs28594467 | 1 | 3097051 | T | C | 0.224 | 0.108 | 0.006 | 9.96E-69 | 0.0041 | 3552.248 |
| rs56304645 | 1 | 3085186 | T | C | 0.231 | 0.106 | 0.006 | 1.59E-68 | 0.0040 | 3468.542 |
| rs1393064 | 1 | 3099138 | C | G | 0.223 | 0.109 | 0.006 | 2.77E-68 | 0.0041 | 3595.500 |
| rs11172111 | 12 | 57515804 | G | T | 0.425 | -0.093 | 0.005 | 3.00E-68 | 0.0043 | 3728.150 |
| rs11172110 | 12 | 57515769 | C | T | 0.429 | -0.092 | 0.005 | 3.86E-68 | 0.0042 | 3664.627 |
| rs12298170 | 12 | 57515363 | G | A | 0.430 | -0.092 | 0.005 | 1.19E-67 | 0.0041 | 3611.042 |
| rs10876963 | 12 | 57514554 | C | T | 0.430 | -0.092 | 0.005 | 1.36E-67 | 0.0041 | 3613.244 |
| rs12322902 | 12 | 57513866 | G | A | 0.431 | -0.092 | 0.005 | 2.80E-67 | 0.0042 | 3645.527 |
| rs12309413 | 12 | 57513879 | G | C | 0.432 | -0.092 | 0.005 | 1.22E-66 | 0.0041 | 3620.639 |
| rs10909886 | 1 | 3066761 | T | A | 0.232 | 0.109 | 0.006 | 6.06E-66 | 0.0042 | 3698.620 |
| rs61759161 | 1 | 3065568 | T | C | 0.229 | 0.110 | 0.006 | 2.85E-65 | 0.0043 | 3734.556 |
| rs4257011 | 12 | 57528197 | A | G | 0.350 | -0.092 | 0.006 | 5.95E-63 | 0.0039 | 3404.314 |
| rs10747776 | 12 | 57528679 | A | G | 0.350 | -0.092 | 0.006 | 7.82E-63 | 0.0039 | 3395.784 |

Chr, chromosome; EAF, Effect allele frequency; Pos, position; SE, standard error; SNP, single nucleotide polymorphism. The threshold was set at $p < 1 \times 10^{-60}$.

**Table S13.** Mendelian randomization results of possible plasma proteins on Alzheimer's diseases.

| Trait | nSNPs | Method | OR (95%CI) | $p$ | Q pval | Intercept pval | Global pval |
|---|---|---|---|---|---|---|---|
| Leucine-rich repeat neuronal protein 1 | 22 | IVW | 2.217 (1.850, 2.656) | 6.24E-18 | 5.66E-193 | | |
| | | MR Egger | 2.902 (2.413, 3.489) | 2.09E-10 | | 3.67E-04 | |
| | | MR-PRESSO | 2.189 (1.835, 2.611) | 6.79E-09 | | | <0.001 |
| | | Weighted median | 2.372 (1.888, 2.980) | 1.22E-13 | | | |
| | | Weighted mode | 2.771 (2.624, 2.925) | 2.90E-21 | | | |
| Vacuolar protein sorting-associated protein 29 | 22 | IVW | 0.806 (0.766, 0.849) | 4.64E-16 | 2.83E-06 | | |
| | | MR Egger | 0.755 (0.718, 0.793) | 5.65E-10 | | 4.76E-04 | |
| | | MR-PRESSO | 0.824 (0.781, 0.869) | 1.40E-07 | | | <0.001 |
| | | Weighted median | 0.765 (0.737, 0.795) | 7.86E-44 | | | |
| | | Weighted mode | 0.759 (0.731, 0.788) | 2.22E-12 | | | |
| Protein S100-A13 | 22 | IVW | 0.500 (0.413, 0.605) | 1.33E-12 | 2.54E-196 | | |
| | | MR Egger | 0.349 (0.305, 0.400) | 1.98E-12 | | 2.60E-07 | |
| | | MR-PRESSO | 0.514 (0.427, 0.618) | 2.66E-07 | | | <0.001 |
| | | Weighted median | 0.736 (0.627, 0.862) | 1.55E-04 | | | |
| | | Weighted mode | 0.381 (0.359, 0.405) | 3.39E-19 | | | |
| Cardiotrophin-1 | 20 | IVW | 2.556 (1.860, 3.512) | 7.23E-09 | 4.86E-310 | | |
| | | MR Egger | 4.496 (3.235, 6.249) | 4.78E-08 | | 2.41E-04 | |
| | | MR-PRESSO | 2.556 (1.860, 3.512) | 1.42E-05 | | | <0.001 |
| | | Weighted median | 1.030 (0.932, 1.138) | 0.561 | | | |
| | | Weighted mode | 0.966 (0.853, 1.095) | 0.598 | | | |
| Proteasome activator complex subunit 1 | 18 | IVW | 0.777 (0.696, 0.867) | 6.92E-06 | 4.21E-17 | | |
| | | MR Egger | 0.659 (0.580, 0.748) | 8.63E-06 | | 3.42E-03 | |
| | | MR-PRESSO | 0.793 (0.714, 0.882) | 3.5E-04 | | | <0.001 |
| | | Weighted median | 0.745 (0.655, 0.847) | 6.75E-06 | | | |
| | | Weighted mode | 0.645 (0.603, 0.690) | 3.91E-10 | | | |
| MAP kinase-activated protein kinase 5 | 25 | IVW | 1.083 (1.042, 1.125) | 3.94E-05 | 5.76E-04 | | |
| | | MR Egger | 1.124 (1.059, 1.194) | 8.21E-04 | | 0.131 | |
| | | MR-PRESSO | 1.085 (1.036, 1.137) | 1.75E-03 | | | <0.001 |
| | | Weighted median | 1.099 (1.029, 1.173) | 4.70E-03 | | | |
| | | Weighted mode | 1.178 (1.102, 1.260) | 6.65E-05 | | | |

AD, Alzheimer's disease; CI, confidence interval; IVW, inverse-variance weighted; MR-PRESSO, Mendelian randomization-Pleiotropy Residual Sum and Outlier, nSNPs, number of single nucleotide polymorphisms; OR, odds ratio; Q_pval, p-value of the Cochran Q statistic.

**Supplementary Table 14.** STROBE-MR reporting guidelines

| Relevant section | Item | Instruction | Location addressed in this article |
|---|---|---|---|
| TITLE and ABSTRACT | TITLE and ABSTRACT | Indicate Mendelian randomization as the study's design in the title and/or the abstract. | Title and abstract |
| INTRODUCTION | Background | Explain the scientific background and rationale for the reported study. Is causality between exposure and outcome plausible?<br>Justify why MR is a helpful method to address the study question. | Introduction |
| | Objectives | State specific objectives clearly, including pre-specified causal hypotheses (if any). | Introduction |
| METHODS | Study design and data sources | Present key elements of study design early in the paper.<br>Consider including a table listing sources of data for all phases of the study. For each data source contributing to the analysis, describe the following:<br>a) Describe the study design and the underlying population from which it was drawn.<br>Describe also the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection, if available.<br>b) Give the eligibility criteria, and the sources and methods of selection of participants.<br>c) Explain how the analyzed sample size was arrived at.<br>d) Describe measurement, quality and selection of genetic variants.<br>e) For each exposure, outcome and other relevant variables, describe methods of assessment and, in the case of diseases, the diagnostic criteria used.<br>f) Provide details of ethics committee approval and participant informed consent, if relevant. | a) Abstract, Introduction, Methods, Figure 1, Table 1<br>b) Methods<br>c) Methods<br>d) Methods<br>e) Methods<br>f) Methods |
| | Assumptions | Explicitly state assumptions for the main analysis (e.g., relevance, exclusion, independence, homogeneity) as well assumptions for any additional or sensitivity analysis. | Methods, Figure 1 |
| | Statistical methods: main analysis | Describe statistical methods and statistics used.<br>a) Describe how quantitative variables were handled in the analyses (i.e., scale, units, model).<br>b) Describe the process for identifying genetic variants and weights to be included in the analyses (i.e., independence and model). Consider a flow diagram.<br>c) Describe the MR estimator, e.g., two-stage least squares, Wald ratio, and related statistics.<br>Detail the included covariates and, in case of two-sample MR, whether the same covariate set was used for adjustment in the two samples.<br>d) Explain how missing data were addressed.<br>e) If applicable, say how multiple testing was dealt with | a) Methods<br>b) Methods<br>c) Methods<br>d) Methods<br>e) Methods |
| | Assessment of assumptions | Describe any methods used to assess the assumptions or justify their validity | Methods |
| | Sensitivity analyses | Describe any sensitivity analyses or additional analyses performed. | Methods |
| | Software and | a) Name statistical software and package(s), including version and settings used; b) | Methods |

| | | | |
|---|---|---|---|
| | pre-registration | State whether the study protocol and details were pre-registered (as well as when and where). | |
| RESULTS | Descriptive data | a) Report the numbers of individuals at each stage of included studies and reasons for exclusion. Consider use of a flow diagram.<br>b) Report summary statistics for phenotypic exposure(s), outcome(s) and other relevant variables (e.g., means, standard deviations, proportions).<br>c) If the data sources include meta-analyses of previous studies, provide the number of studies, their reported ancestry, if available, and assessments of heterogeneity across these studies. Consider using a supplementary table for each data source.<br>d) For two-sample Mendelian randomization:<br>i. Provide information on the similarity of the genetic variant exposure associations between the exposure and outcome samples.<br>ii. Provide information on extent of sample overlap between the exposure and outcome data sources | a) Methods, Figure 1, Table 1<br>b) Supplementary Tables<br>c) N/A<br>d) Methods<br> i. N/A<br> ii. N/A |
| | Main results | a) Report the associations between genetic variant and exposure, and between genetic variant and outcome, preferably on an interpretable scale (e.g., comparing 25th and 75th percentile of allele count or genetic risk score, if individual-level data available).<br>b) Report causal effect estimate between exposure and outcome, and the measures of uncertainty from the MR analysis. Use an intuitive scale, such as odds ratio, or relative risk, per standard deviation difference.<br>c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time-period.<br>d) Consider any plots to visualize results (e.g., forest plot, scatterplot of associations between genetic variants and outcome versus between genetic variants and exposure) | a) N/A, no individual level data available<br>b) Results, Supplementary Tables<br>c) N/A<br>d) N/A |
| | Assessment of assumptions | a) Assess the validity of the assumptions.<br>b) Report any additional statistics (e.g., assessments of heterogeneity, such as $I^2$, Q statistic) | a) Methods, Results, Supplementary Tables<br>b) Results, Table 2 |
| | Sensitivity and additional analyses | a) Use sensitivity analyses to assess the robustness of the main results to violations of the assumptions.<br>b) Report results from other sensitivity analyses (e.g., replication study with different dataset, analyses of subgroups, validation of instrument(s), simulations, etc.).<br>c) Report any assessment of direction of causality (e.g., bidirectional MR).<br>d) When relevant, report and compare with estimates from non-MR analyses.<br>e) Consider any additional plots to visualize results (e.g., leave-one-out analyses). | a) Results, Table 2<br>b) Results<br>c) Results, Figure 1, and Supplementary Table S1<br>d) Introduction, Discussion<br>e) N/A |
| DISCUSSION | Key results | Summarize key results with reference to study objectives. | Discussion |
| | Limitations | Discuss limitations of the study, taking into account the validity of the MR assumptions, other sources of potential bias, and imprecision. Discuss both direction and magnitude of any potential bias, and any efforts to address them. | Methods, Discussion |
| | Interpretation | a) Give a cautious overall interpretation of results considering objectives and | a) Discussion |

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|---|---|---|---|
| | | limitations. | b) Discussion |
| | | Compare with results from other relevant studies. | c) Abstract, Discussion |
| | | b) Discuss underlying biological mechanisms that could be modelled by using the genetic variants to assess the relationship between the exposure and the outcome. | |
| | | c) Discuss whether the results have clinical or policy relevance, and whether interventions could have the same size effect. | |
| | Generalizability | Discuss the generalizability of the study results (a) to other populations (i.e., external validity), | a) Discussion |
| | | | b) Discussion |
| | | (b) across other exposure periods/timings, and (c) across other levels of exposure. | c) N/A |
| OTHER INFORMATION | Funding | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study or studies on which the present article is based. | Study Funding |
| | Data and data sharing | Present data used to perform all analyses or report where and how the data can be accessed. State whether statistical code is publicly accessible and if so, where. | Methods, Table 1, acknowledgment |
| | Conflicts of Interest | All authors should declare all potential conflicts of interest. | Disclosure |

STROBE-MR, Strengthening the Reporting of Observational Studies in Epidemiology-Mendelian Randomization.