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Corresponding author(s): Y.M. Ruigrok and M.K. Bakker

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Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see Authors & Referees and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☒	☐	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	No software was used for data collection.
Data analysis	R 3.2.2 and 3.6.1. For creating plots, and running R-based programs SAIGE, FUSION, and GARFIELD. (https://www.r-project.org) plink 1.90 for genotype QC and genetic risk score (GRS) analysis. (https://www.cog-genomics.org/plink2/) SAIGE 0.29.3 for genome-wide logistic mixed model association analysis. (https://github.com/weizhouUMICH/SAIGE) GCTA v1.91.1beta as wrapper for COJO (http://cnsgenomics.com/software/gcta/) GCTA v1.92.2beta as wrapper for mtCOJO and GSMR (http://cnsgenomics.com/software/gcta/) SMR 0.712 (linux, http://cnsgenomics.com/software/smr/) FUSION (no version) for TWAS analysis. (https://github.com/gusevlab/fusion_twas) LDSC v1.0.0 for population stratification estimate, genetic correlation analysis, SNP heritability estimate, and heritability enrichment analyses. (https://github.com/bulik/ldsc) GARFIELD v2 for functional enrichment analysis. (https://www.ebi.ac.uk/birney-srv/GARFIELD/) METAL release 2011-03-25 for meta-analysis of genome-wide association analyses per stratum. (http://csg.sph.umich.edu/abecasis/Metal/) POPCORN 0.9.9 for trans-ancestry genetic correlation analysis. (https://github.com/brielin/Popcorn) eCAVIAR v2.2 (http://genetics.cs.ucla.edu/caviar/) MAGMA v1.06 (https://ctg.cncr.nl/software/magma) SumHer is integrated in ldak5 (linux, http://dougspeed.com/sumher/)

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

Summary statistics for the Stage 1 and Stage 2 GWAS meta analyses, as well as summary statistics for the ruptured IA versus controls, unruptured IA versus controls, and the analysis including only East Asian participants can be accessed using doi: 10.6084/m9.figshare.11303372. And through the cerebrovascular disease knowledge portal http://www.cerebrovascularportal.org.

The following datasets have been accessed and used.

Database of genotypes and phenotypes (dbGaP): https://dbgap.ncbi.nlm.nih.gov
Health and Retirement Study (HRS) genotype data (dbGaP accession code phs000428.v2.p2)
Atherosclerosis Risk in Communities (ARIC) genotype data (dbGaP accession code phs000280.v5.p1)
Genetic Association Information Network (GAIN) genotype data (dbGaP accession code phs000021.v3.p2)
Schizophrenia controls, not included in the GAIN study (nonGAIN, dbGaP accession code phs000167.v1.p1)

European Genome-Phenome Archive (EGA): https://ega-archive.org
Genotypes from the Busselton cohort (EGA accession code EGAD00000000076)
Genotypes from Netherlands, Finland and Italy (EGAD00010000288)
Genotypes from National blood donors cohort (EGAD00000000023 and EGAD00010000290)
Genotypes from 1958 British birth cohort (EGAD00000000021)

UK Biobank summary statistics from the Neale lab (http://www.nealelab.is/uk-biobank)
SMR reference data (https://cnsgenomics.com/software/smr/#eQTLsummarydata)
LDSC reference data (https://github.com/bulik/ldsc)
Mouse brain single-cell RNAseq data for LDSC (Supplementary Table 4 of Skene, N.G. et al. Genetic identification of brain cell types underlying schizophrenia. Nat Genet 50, 825-833 (2018).)
Mouse brain vasculature single-cell RNQseq data for LDSC. Published as dataset in: He, L. et al. Single-cell RNA sequencing of mouse brain and lung vascular and vessel-associated cell types. Sci Data 5, 180160 (2018).
TWAS reference data (http://gusevlab.org/projects/fusion/#reference-functional-data)
eCAVIAR reference data (Downloaded from GTEx resource: https://storage.googleapis.com/gtex_analysis_v7/single_tissue_eqtl_data/GTEx_Analysis_v7_eQTL_all_associations.tar.gz)

Access to summary statistics of the Aortic Abdominal Aneurysms (AAA), arteriovenous malformations (AVM), intracerebral hemorrhage (ICH), ischemic stroke (IS) and cervical artery dissection studies are specified in their respective publications:
AAA: Jones, G.T. et al. Meta-Analysis of Genome-Wide Association Studies for Abdominal Aortic Aneurysm Identifies Four New Disease-Specific Risk Loci. Circ Res 120, 341-353 (2017).
AVM: Weinsheimer, S. et al. Genome-wide association study of sporadic brain arteriovenous malformations. J Neurol Neurosurg Psychiatry 87, 916-23 (2016).
ICH: Woo, D. et al. Meta-analysis of genome-wide association studies identifies 1q22 as a susceptibility locus for intracerebral hemorrhage. Am J Hum Genet 94, 511-21 (2014).
IS: Malik, R. et al. Multiancestry genome-wide association study of 520,000 subjects identifies 32 loci associated with stroke and stroke subtypes. Nat Genet 50, 524-537 (2018).
Cervical artery dissection: Debette, S. et al. Common variation in PHACTR1 is associated with susceptibility to cervical artery dissection. Nat Genet 47, 78-83 (2015).

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	Sample sizes per cohort, stratum, and used in each meta analysis, are shown in Table 2 and Supplementary Table 1. In some instances, in particular when converting observed scale heritability to the liability scale, effective sample size is a more appropriate measure for sample size. The calculation for this is described in the Supplementary Note, section Analysis rationale and parameters. In instances where effective sample size is used, ascertainment (the fraction of cases in the sample) is set at 0.5.
Data exclusions	A description of quality control (QC) metrics, is described in the Supplementary Note, section Quality control parameters. The recruitment methods, including inclusion and exclusion criteria are described briefly in the Online Methods, section Recruitment and diagnosis and in detail in the Supplementary Note, section Cohort description.

Replication	No replication was performed
Randomization	Cases and controls were defined by disease status (intracranial aneurysm and/or subarachnoid hemorrhage), and could therefore not be randomized. Control datasets were matched based on genotyping platform and population, creating strata that were as homogeneous as possible. Extensive (QC) was performed to exclude population and batch outliers, as described in the Supplementary Note, section Quality control parameters. We used a mixed model, including genetic relationship matrix to account for population stratification and batch effect, and used principal components we included in the association analyses to further account for this. Sex was used as covariate to account for sex-specific confounding due to differences in prevalence between sexes.
Blinding	Blinding was not applicable, since groups were defined by disease status.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology
☒	☐ Animals and other organisms
☐	☒ Human research participants
☒	☐ Clinical data

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Human research participants

Policy information about studies involving human research participants

Population characteristics	An overview of number of cases and controls, sex distribution, and genotyping platform is given in Supplementary Table 1. The age of the participants was not registered for most of the cohorts included in this study.
Recruitment	The recruitment methods, including inclusion and exclusion criteria are described briefly in the Online Methods, section Recruitment and diagnosis and in detail in the Supplementary Note, section Cohort description. Given this recruitment method, we see two potential forms of bias. The first and largest source of potential bias is caused by the fact that there is no routine screening for intracranial aneurysms. This leads to an imbalance toward the inclusion of more subarachnoid hemorrhage cases, compared to unruptured intracranial aneurysm cases. It is therefore important to realize that the presented results for a large part represent the genetics of aneurysmal subarachnoid hemorrhage. Second, the most severe cases of subarachnoid hemorrhage are more likely to die before reaching a hospital, and therefore less likely to be included in the study. This could lead to an underrepresentation of severe cases. However, this is the not case for the included cohort studies (UK Biobank, Biobank Japan, HUNT study, China Kadoorie Biobank), where the cases were recruited before the clinical events. Since these cohort studies represent a large portion of the study population, we expect the effect of this potential bias to be small.
Ethics oversight	Local Data Access Committees reviewed and accepted the protocols for data collection and use for each cohort. Guidelines for the study procedure were provided by the Biobank Research Ethics Committee of the University Medical Center Utrecht (TCBio 17-087). The local data access and ethical committee who approved collection and use of genetic data are shown below -@neurIST Rotterdam: Medisch Ethische Toetsings Commissie Erasmus MC (METC) Barcelona (both centers): Research Committee of the Hospital Clinic de Barcelona Oxford and Sheffield: Central Office for Research Ethics Committes (COREC) NHS Geneva: Commission centrale d'éthique de la recherché sur l'être humain de la république et canton de Genève -ARIC NHLBI Data Access Committee (through dbGaP) -Busselton GABRIEL Consortium Data Access Committee. (through EGA) -Utrecht 1 University Medical Center Utrecht Ethics Committee -Netherlands (EGA) Wellcome Trust Case-Control Consortium Data Access Committee. (through EGA)

-Utrecht 2
University Medical Center Utrecht Ethics Committee
-Doetinchem Cohort Study
Scientific Advisory Group of the Netherlands National Institute for Public Health and the Environment
-Project MinE
Project MinE GWAS Consortium
-French Canadian
Comité d'éthique de la recherche du Centre hospitalier de l'Université de Montréal and McGill University ethics
-Finland (EGA)
Wellcome Trust Case-Control Consortium Data Access Committee. (through EGA)
-Finland
The ethics committee of Kuopio University Hospital and Helsinki University Hospital
-NFBC1966
Ethics Committee of Northern Ostrobotnia Hospital District, Finland
-ICAN
Institutional Review Boards (Comité consultatif sur le traitement de l'information en matière de recherche dans le domaine de la santé, Commission Nationale de l'Informatique et des Libertés) and Groupe Nantais d'Ethique dans le Domaine de la Santé (GNEDS)
-PREGO
Research Ethics Committee (CPP of Nantes)
-GAIN
NHLBI Data Access Committee (through dbGaP)
-FIA
University of Cincinatti ethics committee
-nonGAIN
NHLBI Data Access Committee (through dbGaP)
-Poland
Institutional review board of the Jagiellonian University.
-NBS
Wellcome Trust Case-Control Consortium Data Access Committee. (through EGA)
-UK Biobank
UK Biobank Data Access Committee
-GOSH controls
Central London REC 3 committee
-GOSH cases
Central London REC 3 committee
-NBS+1958BBC
Wellcome Trust Case-Control Consortium Data Access Committee. (through EGA)
-HUNT study
The Norwegian Data Inspectorate, the Norwegian Board of Health, and the Regional Committee for Ethics in Medical Research
-China Kadoorie Biobank
Oxford University ethical committee and the China National CDC
-Biobank Japan
Research ethics committees at the Institute of Medical Science, the University of Tokyo

Note that full information on the approval of the study protocol must also be provided in the manuscript.