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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 our Editorial Policies 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	Not applicable.
Data analysis	We used the following publicly available software for processing of whole-genome sequence data: BWA 0.7.10 mem, https://github.com/lh3/bwa Picard tools 1.117, https://broadinstitute.github.io/picard/ SAMtools 1.3, http://samtools.github.io/ Bedtools v2.25.0-76-g5e7c696z, https://github.com/arq5x/bedtools2/ GraphTyper 1.3, https://github.com/DecodeGenetics/graphtyper Variant Effect Predictor https://github.com/Ensembl/ensembl-vep

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 and 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

The sequence variants from the Icelandic population whole-genome sequence data have been deposited at the European Variant Archive under accession PRJEB15197. GWAS summary statistics for association with P<1×10−6 are available in Supplementary Data. The authors declare that the data supporting the

findings of this study are available within the article, it supplementary files, and upon request.

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	We had available audiometric measures for 11,484 subjects as a part of the deCODE health study and for 22,212 subjects obtained at the National Institute of Hearing and Speech in Iceland (NIHSI). Information on self-reported hearing difficulty was available for 393,921 participants of the UK Biobank of European ancestry.
Data exclusions	Audiometric measures obtained at the NISHI for subjects that had participated in the deCODE health study were excluded from that dataset.
Replication	In this study we meta-analyzed three datasets. The results for common variants were mainly driven by the UK Biobank dataset and 73% of the associations replicate in the Icelandic datasets and the effect sizes show high correlatation between the datasets.
Randomization	No randomization was used.
Blinding	Not relevant.

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 and archaeology
☒	☐ Animals and other organisms
☐	☒ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

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	For the deCODE health study subjects, the mean age is 55.4 (14.5 SD) and 43.6% are male. For the NIHSI subjects, the mean age is 48.0 (32.4 SD) and 55.5% are male. For the UK Biobank dataset, the mean age is 56.5 (8.1 SD) and 45.6% are men.
Recruitment	The deCODE health study is a population-based study in Iceland that is designed to improve our understanding of rare loss of function mutations and other potentially high impact mutations. Participants in the deCODE health study are a mixture of volunteers and carriers of rare predicted high impact mutations. The NIHSI dataset is skewed towards those with hearing impairment, because patients with hearing problems are referred to NIHSI. We therefore used patients with hearing impairment as cases in the NIHSI dataset and designated Icelanders with no hearing data available as population controls.
Ethics oversight	The Icelandic Data Protection Authority and the National Bioethics Committee

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