Supplementary Online Content

Writing Committee for the ENIGMA-CNV Working Group. Association of copy number variation of the 15q11.2 BP1-BP2 region with cortical and subcortical morphology and cognition. *JAMA Psychiatry*. Published online October 30, 2019. doi:10.1001/jamapsychiatry.2019.3779

outcome measures, split into UK Biobank, ENIGMA, and deCODE Genetics populations

eFigure 6. Forest plot of the observed effects (regression coefficients) from the linear regression analyses of 15q11.2 BP1-BP2 copy number on the primary outcome measures, split into UK Biobank, ENIGMA, and deCODE Genetics populations

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix 1. Brain to cognition and mediation analyses

We ran a series of linear regressions, with the (residualized, normalized) brain measures as predictors, and the (residualized, normalized) cognitive task performance measures as outcomes. The results are shown below, under the header ´Path B´. The significance threshold adopted here, and indicated in bold in the display items, is the same as for the main neuroimaging analyses, p-value<$4.7x10^{-4}$.

We further carried out mediation analyses, to couple the imaging findings to the behavioral findings, with the R package *mediation* v4.4.7. Please see eTable 12 for the sample sizes per task. We report the proportion of the total effect of the 15q11.2 (BP1-2) CNV on cognitive task performance ("Path C") mediated by the brain measures ("Path AB"), with p-values calculated through quasi-Bayesian approximation using 5000 simulations. On the following pages are the results, per task. Given the exploratory, follow-up nature of these analyses, and to give some indication of trends in the data in spite of low statistical power for mediation analyses, we indicate nominal significant (p-value<.05) findings in the tables in bold, and demarcate nominally significant regions on the cortical maps with bold lines.

The tables below (e13-S19) provide the results for the primary neuroimaging measures (global measures, plus subcortical measures). The "Path B" column indicates the regression coefficient from the linear regressions predicting cognition from the brain measures. The other columns, to the right, indicate the results from mediation analyses, with proportion of the effect of the CNV on cognition mediated by these measures and associated p-values for the 15q11.2 (BP1-2) CNV deletion carriers versus non-carriers ("Del v NC), duplication versus non-carriers "Dup vs NC") and the dosage analyses ("Dosage").

The brain maps reflect the results from the same analyses, for the regional cortical brain measures. The left column ("Path B") shows the relation between brain features and cognition, with the first and third row indicating the regression coefficients (blue indicates negative effects, red positive) and the second and fourth row indicating the associated -log10 p-values (more yellow values indicate greater significance). The brain maps to the right show the results from the mediation analyses, with the first and third row indicating the proportion mediated by these measures, and the second and fourth row indicating the associated p-values.

eTable 12. Available sample sizes per task, per carrier group, for the analyses linking the neuroimaging measures to the cognitive measures.

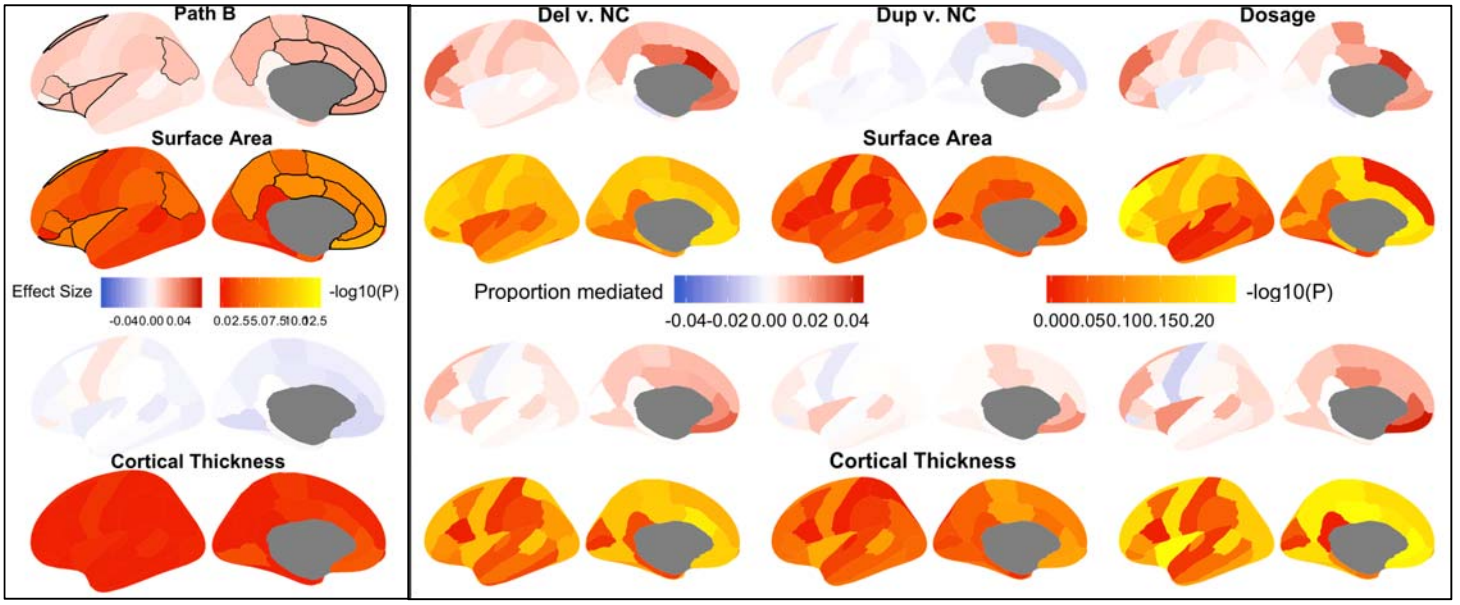
Task	Deletion carriers	Non-carriers	Duplication carriers
Pairs Matching	103	30936	116
Reaction Time	103	31022	116
Fluid Intelligence	35	10508	28
Digit Span	10	3109	5
Symbol Substitution	60	16203	54
Trail Making A	50	14401	48
Trail Making B	50	14401	48

Pairs Matching

eTable 13. Results from the linear regression of the pairs matching task performance on the primary brain outcome measures, ("Path B"), and the mediation analyses ("Del v NC", "Dup v NC", and "Dosage").

	Path B		Del v NC		Dup v NC		Dosage	
Feature	Estimate (SE)	P-value	Prop. mediated	P-value	Prop. mediated	P-value	Prop. mediated	P-value
Accumbens	0.01 (5.7e-03)	0.06	0.02	0.65	-2.2e-03	0.83	0.01	0.58
Caudate	4.1e-04 (5.7e-03)	0.94	2.8e-04	0.97	2.3e-04	0.95	9.6e-05	0.97
Pallidum	-7.4e-03 (5.7e-03)	0.19	-3.0e-03	0.74	-5.4e-04	0.91	-4.4e-03	0.68
Putamen	2.8e-03 (5.7e-03)	0.62	2.3e-03	0.86	2.3e-05	0.99	1.2e-03	0.87
Thalamus	2.7e-03 (5.7e-03)	0.63	1.3e-03	0.89	4.3e-04	0.91	2.0e-03	0.86
Amygdala	-3.2e-03 (5.7e-03)	0.58	-5.5e-04	0.91	6.5e-05	0.97	-2.3e-04	0.92
Hippocampus	3.4e-04 (5.7e-03)	0.95	1.2e-03	0.92	1.2e-04	0.96	-2.7e-05	0.99
Surface Area	**0.03 (5.7e-03)**	**3.9e-08**	0.08	0.59	-3.5e-03	0.93	0.04	0.55
Thickness	-6.2e-03 (5.7e-03)	0.27	9.1e-03	0.72	3.4e-03	0.86	0.01	0.74
ICV	**0.03 (5.7e-03)**	**6.7e-06**	-0.02	0.67	-0.04	0.79	-0.05	0.55

Note: Del=deletion carriers, NC=non-carriers, Dup=duplication carriers, SE=standard error, ICV=intracranial volume. Brain structures passing the significance threshold are indicated in bold.



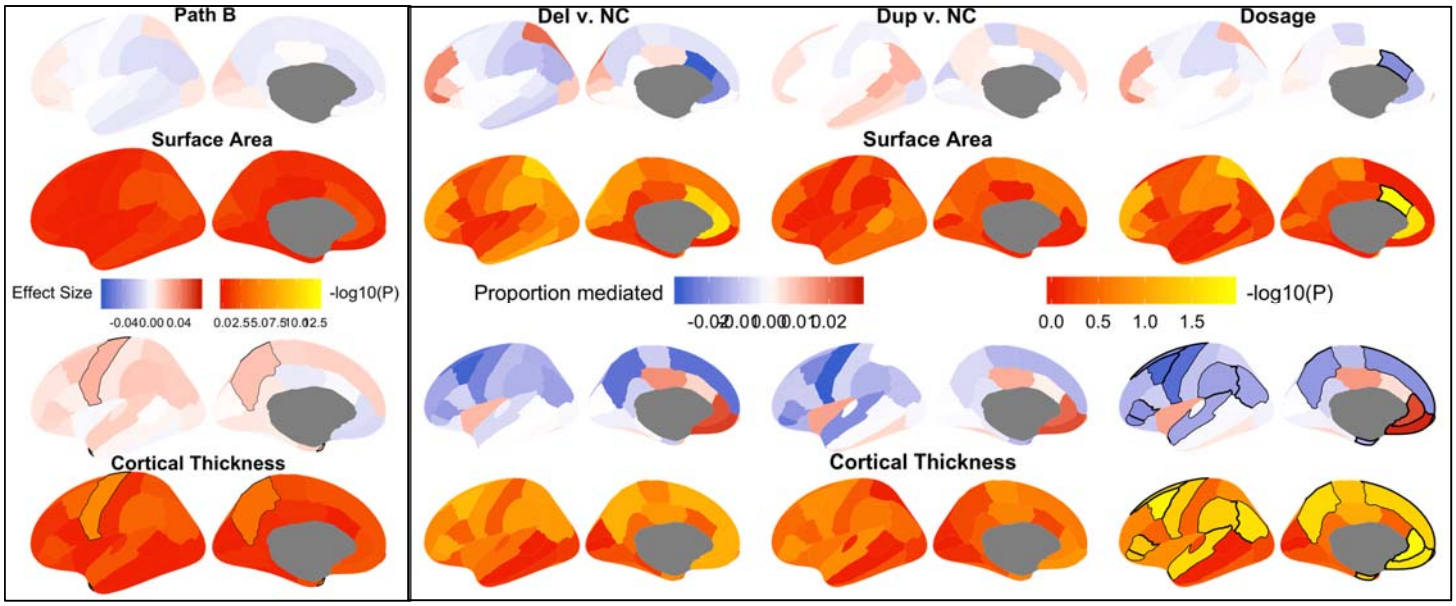
eFigure 7. Results from the linear regression of cognition (right, 'Path B') and mediation analyses (left) on regional surface area (top two rows) and cortical thickness (bottom two rows). The first and third row display the effect sizes (beta coefficient for the linear regression, proportion mediated for the mediation analyses), the second and fourth row show the statistical significance in –log10 of the p-value. Black demarcations around a brain region indicates that it passes the significance threshold with thicker lines indicating more significant findings. Note: column names indicate the comparisons. Del=deletion carriers, NC=non-carriers, Dup=duplication carriers.

Reaction time

eTable 14. Results from the linear regression of the reaction time task performance on the primary brain outcome measures, ("Path B"), and the mediation analyses ("Del v NC", "Dup v NC", and "Dosage").

	Path B		Del v NC		Dup v NC		Dosage	
Feature	Estimate (SE)	P-value	Prop. mediated	P-value	Prop. mediated	P-value	Prop. mediated	P-value
Accumbens	-4.1e-03 (5.7e-03)	0.47	-6.6e-03	0.51	6.4e-04	0.78	-2.5e-03	0.46
Caudate	-2.9e-03 (5.7e-03)	0.61	-2.6e-03	0.65	1.1e-03	0.74	-1.5e-04	0.85
Pallidum	0.01 (5.7e-03)	0.02	8.4e-03	0.23	5.1e-03	0.47	7.8e-03	0.16
Putamen	-1.0e-03 (5.7e-03)	0.86	-1.4e-03	0.81	-2.3e-06	1.00	-3.9e-04	0.88
Thalamus	**0.04 (5.7e-03)**	**4.5e-11**	0.04	0.09	0.02	0.42	0.04	0.03
Amygdala	-8.8e-03 (5.7e-03)	0.12	-4.8e-03	0.38	6.5e-04	0.82	-1.4e-03	0.65
Hippocampus	4.6e-03 (5.7e-03)	0.42	4.1e-03	0.43	1.2e-03	0.69	3.1e-03	0.51
Surface Area	-5.6e-03 (5.7e-03)	0.32	-0.01	0.32	1.0e-03	0.72	-3.8e-03	0.32
Thickness	0.01 (5.7e-03)	0.06	-0.02	0.11	-0.02	0.14	-0.02	0.07
ICV	**0.02 (5.7e-03)**	**8.1e-05**	-0.02	0.18	-0.03	0.17	**-0.03**	**0.02**

Note: Del=deletion carriers, NC=non-carriers, Dup=duplication carriers, SE=standard error, ICV=intracranial volume. Brain structures passing the significance threshold are indicated in bold.



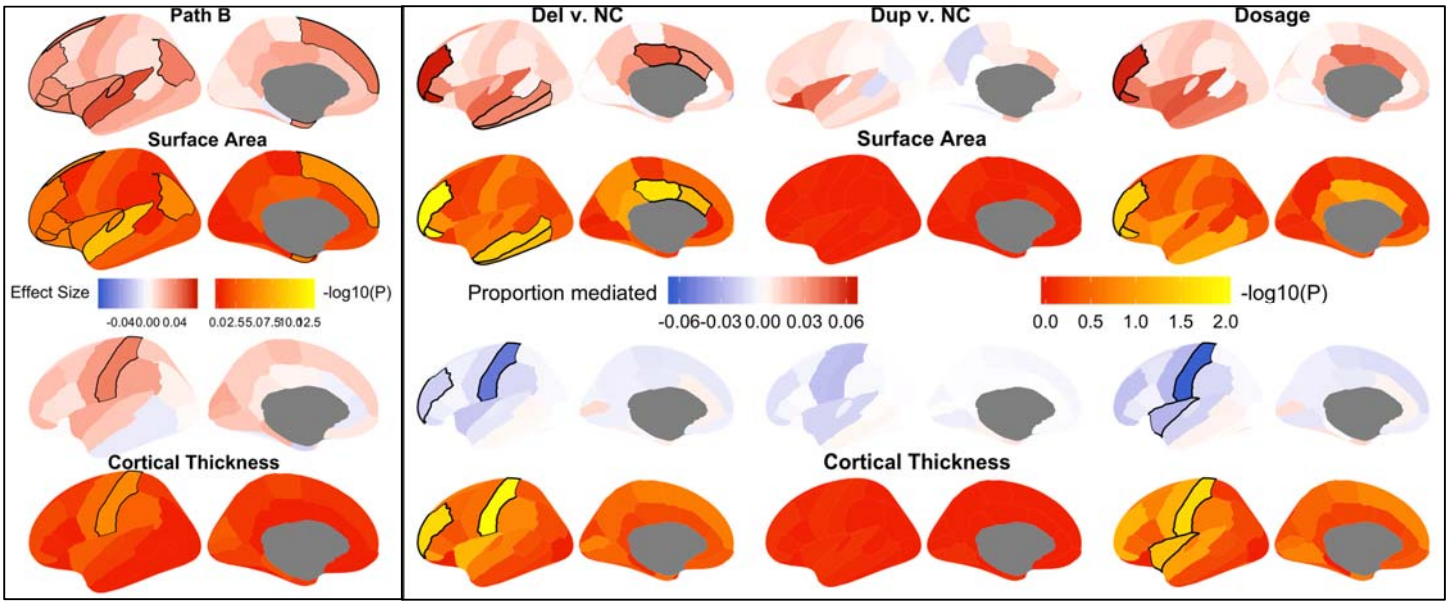
eFigure 8. Results from the linear regression of cognition (right, 'Path B') and mediation analyses (left) on regional surface area (top two rows) and cortical thickness (bottom two rows). The first and third row display the effect sizes (beta coefficient for the linear regression, proportion mediated for the mediation analyses), the second and fourth row show the statistical significance in –log10 of the p-value. Black demarcations around a brain region indicates that it passes the significance threshold with thicker lines indicating more significant findings. Note: column names indicate the comparisons. Del=deletion carriers, NC=non-carriers, Dup=duplication carriers.

Intelligence

eTable 15. Results from the linear regression of the intelligence measure on the primary brain outcome measures, ("Path B"), and the mediation analyses ("Del v NC", "Dup v NC", and "Dosage").

	Path B		Del v NC		Dup v NC		Dosage	
Feature	Estimate (SE)	P-value	Prop. mediated	P-value	Prop. mediated	P-value	Prop. mediated	P-value
Accumbens	0.01 (9.7e-03)	0.18	1.9e-03	0.60	-3.4e-03	0.80	-1.0e-03	0.78
Caudate	-4.8e-03 (9.8e-03)	0.62	-6.3e-03	0.60	2.2e-03	0.85	-2.4e-03	0.62
Pallidum	-4.9e-03 (9.8e-03)	0.62	-4.0e-03	0.59	-9.6e-04	0.91	-5.9e-03	0.52
Putamen	-8.9e-03 (9.8e-03)	0.36	-8.9e-03	0.37	1.9e-03	0.84	-4.0e-03	0.41
Thalamus	0.02 (9.7e-03)	0.13	6.6e-03	0.22	2.1e-03	0.85	8.4e-03	0.25
Amygdala	-0.01 (9.6e-03)	0.16	8.7e-04	0.76	-8.9e-04	0.91	-4.2e-04	0.89
Hippocampus	4.5e-03 (9.7e-03)	0.64	5.7e-04	0.77	4.0e-04	0.93	1.1e-03	0.72
Surface Area	**0.05 (9.7e-03)**	**1.6e-06**	**0.04**	**0.03**	0.01	0.79	**0.04**	**0.04**
Thickness	0.02 (9.8e-03)	0.02	**-0.02**	**0.04**	-0.02	0.73	**-0.02**	**0.04**
ICV	**0.15 (9.7e-03)**	**3.5e-56**	-0.05	0.35	7.6e-03	0.95	-0.06	0.38

Note: Del=deletion carriers, NC=non-carriers, Dup=duplication carriers, SE=standard error, ICV=intracranial volume. Brain structures passing the significance threshold are indicated in bold.



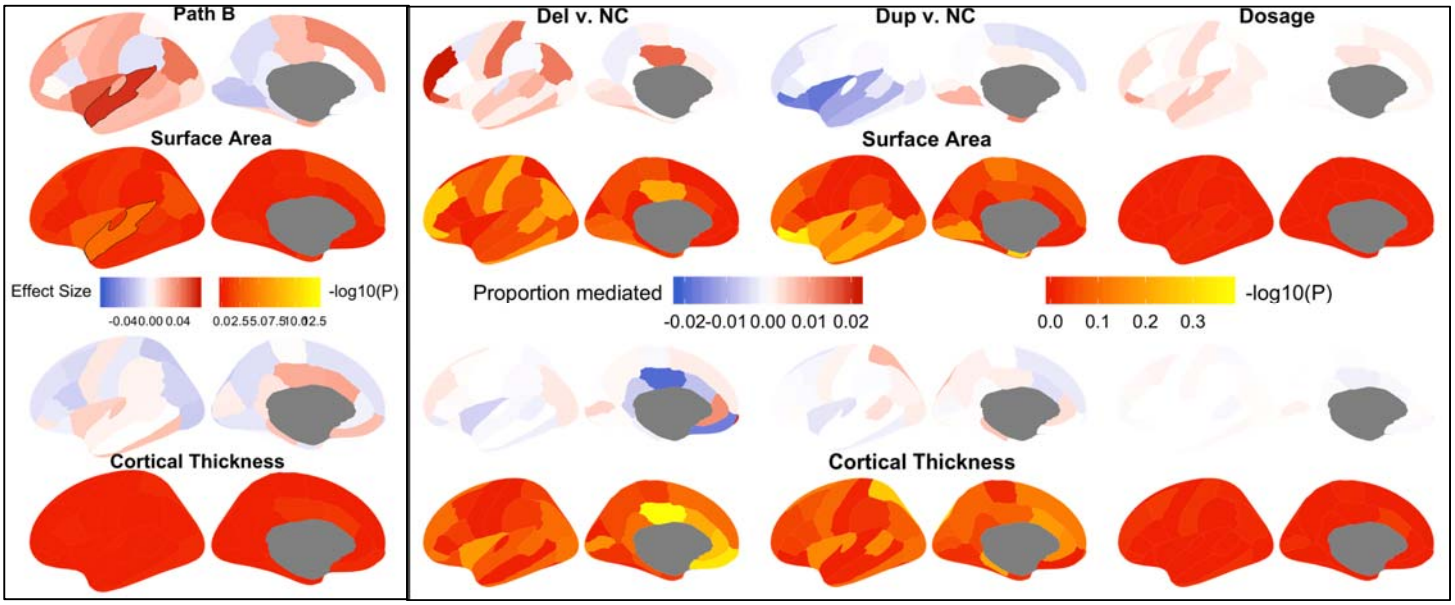
eFigure 9. Results from the linear regression of cognition (right, 'Path B') and mediation analyses (left) on regional surface area (top two rows) and cortical thickness (bottom two rows). The first and third row display the effect sizes (beta coefficient for the linear regression, proportion mediated for the mediation analyses), the second and fourth row show the statistical significance in –log10 of the p-value. Black demarcations around a brain region indicates that it passes the significance threshold with thicker lines indicating more significant findings. Note: column names indicate the comparisons. Del=deletion carriers, NC=non-carriers, Dup=duplication carriers.

Digit span

eTable 16. Results from the linear regression of the digit span task performance on the primary brain outcome measures, ("Path B"), and the mediation analyses ("Del v NC", "Dup v NC", and "Dosage").

	Path B		Del v NC		Dup v NC		Dosage	
Feature	Estimate (SE)	P-value	Prop. mediated	P-value	Prop. mediated	P-value	Prop. mediated	P-value
Accumbens	-4.5e-03 (0.02)	0.80	-3.7e-04	0.94	-4.4e-04	0.92	-1.5e-04	0.98
Caudate	0.03 (0.02)	0.13	0.05	0.30	-9.5e-03	0.52	0.02	0.91
Pallidum	-1.4e-03 (0.02)	0.94	-8.4e-04	0.96	1.1e-03	0.88	1.3e-03	0.97
Putamen	-0.02 (0.02)	0.35	-0.01	0.55	1.2e-03	0.85	-1.1e-03	0.95
Thalamus	5.2e-03 (0.02)	0.77	9.5e-04	0.88	-5.1e-03	0.76	2.0e-03	0.94
Amygdala	0.03 (0.02)	0.14	-1.6e-03	0.91	-0.02	0.29	1.5e-03	0.96
Hippocampus	0.03 (0.02)	0.10	7.7e-04	0.94	-8.5e-03	0.58	9.5e-05	0.99
Surface Area	0.04 (0.02)	0.05	0.03	0.32	-0.01	0.53	7.8e-03	0.93
Thickness	4.3e-04 (0.02)	0.98	-5.2e-04	0.94	-1.4e-04	0.96	2.6e-04	0.96
ICV	**0.11 (0.02)**	**8.2e-10**	-0.05	0.53	0.08	0.27	-0.02	0.93

Note: Del=deletion carriers, NC=non-carriers, Dup=duplication carriers, SE=standard error, ICV=intracranial volume. Brain structures passing the significance threshold are indicated in bold.



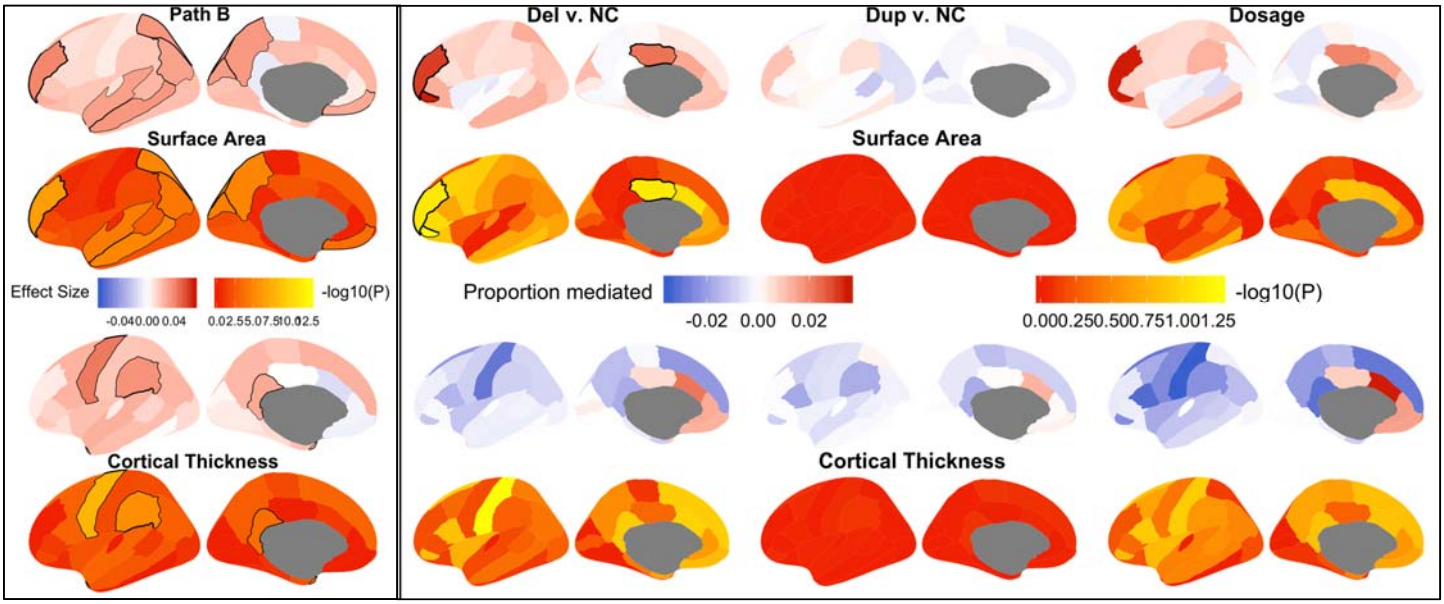
eFigure 10. Results from the linear regression of cognition (right, 'Path B') and mediation analyses (left) on regional surface area (top two rows) and cortical thickness (bottom two rows). The first and third row display the effect sizes (beta coefficient for the linear regression, proportion mediated for the mediation analyses), the second and fourth row show the statistical significance in –log10 of the p-value. Black demarcations around a brain region indicates that it passes the significance threshold with thicker lines indicating more significant findings. Note: column names indicate the comparisons. Del=deletion carriers, NC=non-carriers, Dup=duplication carriers.

Symbol substitution

eTable 17. Results from the linear regression of the symbol substitution task performance on the primary brain outcome measures, ("Path B"), and the mediation analyses ("Del v NC", "Dup v NC", and "Dosage").

	Path B		Del v NC		Dup v NC		Dosage	
Feature	Estimate (SE)	P-value	Prop. mediated	P-value	Prop. mediated	P-value	Prop. mediated	P-value
Accumbens	0.03 (7.8e-03)	5.6e-04	0.04	0.05	-7.3e-03	0.86	0.02	0.16
Caudate	2.0e-03 (7.9e-03)	0.80	7.6e-04	0.85	-5.0e-04	0.97	-1.1e-04	0.94
Pallidum	8.1e-03 (7.8e-03)	0.30	2.0e-03	0.61	4.1e-04	0.96	5.2e-03	0.51
Putamen	**0.03 (7.9e-03)**	**4.6e-05**	0.03	0.11	7.1e-04	0.99	0.02	0.31
Thalamus	**0.06 (7.8e-03)**	**2.6e-14**	0.04	0.17	0.01	0.89	0.05	0.20
Amygdala	0.01 (7.8e-03)	0.17	6.9e-03	0.29	2.6e-05	0.99	4.4e-03	0.47
Hippocampus	**0.03 (7.8e-03)**	**3.6e-05**	0.02	0.10	2.5e-03	0.93	0.02	0.26
Surface Area	**0.06 (7.8e-03)**	**4.2e-13**	0.07	0.06	-3.2e-03	0.96	0.05	0.16
Thickness	0.02 (7.9e-03)	2.6e-03	-0.02	0.15	-6.0e-03	0.89	-0.02	0.19
ICV	**0.06 (7.9e-03)**	**1.7e-12**	-0.03	0.32	-8.8e-03	0.90	-0.03	0.30

Note: Del=deletion carriers, NC=non-carriers, Dup=duplication carriers, SE=standard error, ICV=intracranial volume. Brain structures passing the significance threshold are indicated in bold.



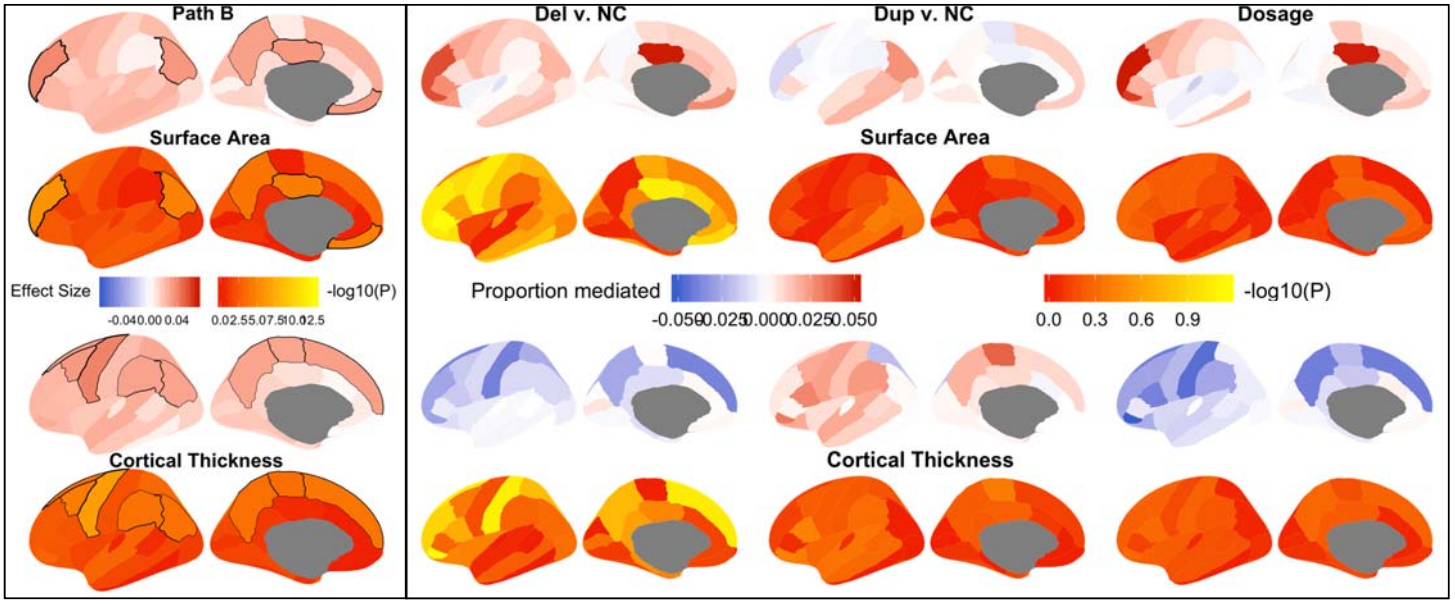
eFigure 11. Results from the linear regression of cognition (right, 'Path B') and mediation analyses (left) on regional surface area (top two rows) and cortical thickness (bottom two rows). The first and third row display the effect sizes (beta coefficient for the linear regression, proportion mediated for the mediation analyses), the second and fourth row show the statistical significance in –log10 of the p-value. Black demarcations around a brain region indicates that it passes the significance threshold with thicker lines indicating more significant findings. Note: column names indicate the comparisons. Del=deletion carriers, NC=non-carriers, Dup=duplication carriers.

Trail making A

eTable 18. Results from the linear regression of the trail making A task performance on the primary brain outcome measures, ("Path B"), and the mediation analyses ("Del v NC", "Dup v NC", and "Dosage").

	Path B		Del v NC		Dup v NC		Dosage	
Feature	Estimate (SE)	P-value	Prop. mediated	P-value	Prop. mediated	P-value	Prop. mediated	P-value
Accumbens	0.02 (8.3e-03)	7.1e-03	0.03	0.06	0.01	0.54	0.01	0.59
Caudate	**0.04 (8.4e-03)**	**3.3e-05**	0.03	0.11	0.05	0.37	-3.0e-04	0.99
Pallidum	-1.7e-04 (8.3e-03)	0.98	-1.1e-04	0.95	-1.2e-04	0.96	3.8e-04	0.93
Putamen	**0.03 (8.4e-03)**	**3.2e-04**	0.02	0.22	-3.0e-03	0.90	0.02	0.63
Thalamus	**0.05 (8.3e-03)**	**4.4e-09**	0.04	0.13	-0.04	0.52	0.07	0.46
Amygdala	0.01 (8.3e-03)	0.14	0.01	0.22	3.4e-04	0.94	8.2e-03	0.58
Hippocampus	**0.03 (8.3e-03)**	**2.9e-05**	0.03	0.12	-0.01	0.71	0.04	0.52
Surface Area	**0.05 (8.3e-03)**	**2.7e-08**	0.06	0.06	0.02	0.68	0.05	0.55
Thickness	**0.04 (8.4e-03)**	**1.6e-05**	-0.03	0.16	0.02	0.51	-0.04	0.54
ICV	**0.05 (8.4e-03)**	**2.6e-09**	-0.02	0.41	0.02	0.69	-0.02	0.68

Note: Del=deletion carriers, NC=non-carriers, Dup=duplication carriers, SE=standard error, ICV=intracranial volume. Brain structures passing the significance threshold are indicated in bold.



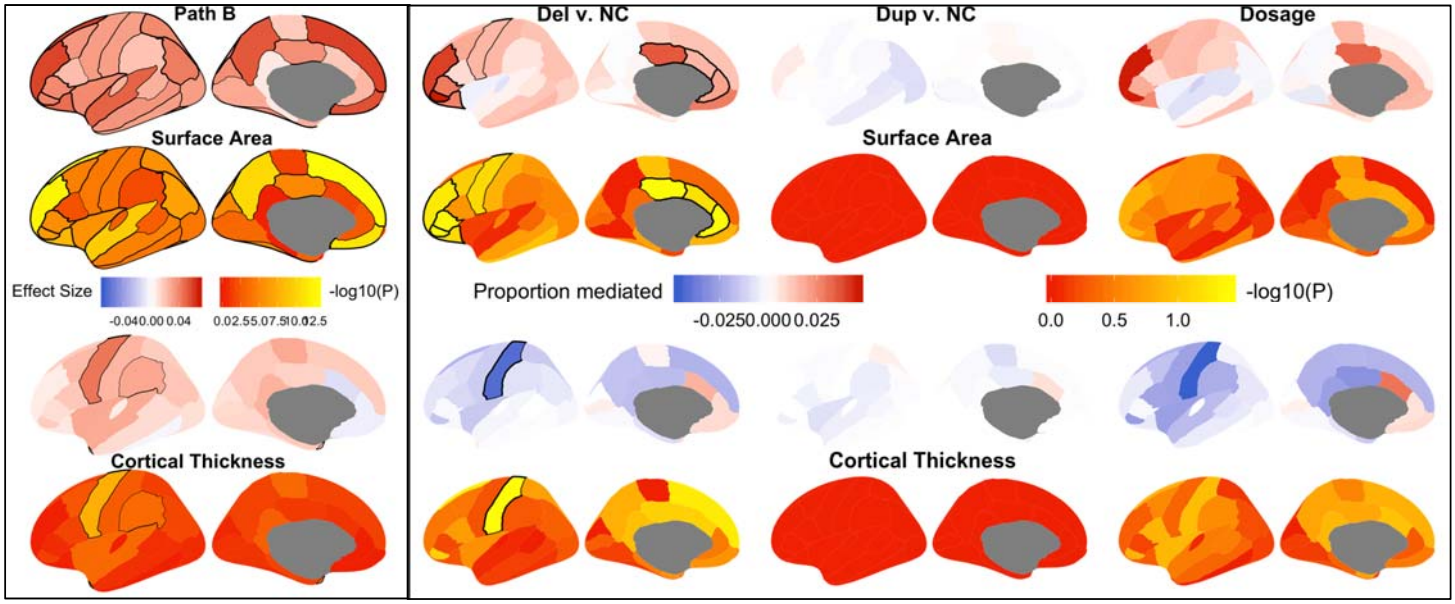
eFigure 12. Results from the linear regression of cognition (right, 'Path B') and mediation analyses (left) on regional surface area (top two rows) and cortical thickness (bottom two rows). The first and third row display the effect sizes (beta coefficient for the linear regression, proportion mediated for the mediation analyses), the second and fourth row show the statistical significance in –log10 of the p-value. Black demarcations around a brain region indicates that it passes the significance threshold with thicker lines indicating more significant findings. Note: column names indicate the comparisons. Del=deletion carriers, NC=non-carriers, Dup=duplication carriers.

Trail making B

eTable 19. Results from the linear regression of the trail making B task performance on the primary brain outcome measures, ("Path B"), and the mediation analyses ("Del v NC", "Dup v NC", and "Dosage").

	Path B		Del v NC		Dup v NC		Dosage	
Feature	Estimate (SE)	P-value	Prop. mediated	P-value	Prop. mediated	P-value	Prop. mediated	P-value
Accumbens	**0.03 (8.3e-03)**	**1.4e-04**	**0.04**	**0.03**	-3.3e-03	0.96	0.02	0.36
Caudate	0.02 (8.4e-03)	5.2e-03	0.02	0.07	-8.1e-03	0.95	-2.8e-04	0.97
Pallidum	-6.9e-04 (8.3e-03)	0.93	-2.6e-04	0.90	-3.7e-05	0.98	-1.2e-04	0.95
Putamen	0.03 (8.4e-03)	1.9e-03	0.01	0.20	1.7e-03	0.94	0.01	0.39
Thalamus	**0.06 (8.3e-03)**	**1.1e-12**	0.05	0.09	0.01	0.92	0.07	0.12
Amygdala	0.01 (8.3e-03)	0.12	9.6e-03	0.20	2.0e-04	0.96	6.4e-03	0.39
Hippocampus	**0.03 (8.3e-03)**	**3.7e-05**	0.03	0.09	3.4e-03	0.93	0.03	0.21
Surface Area	**0.08 (8.3e-03)**	**1.5e-21**	**0.10**	**0.04**	-2.6e-04	1.00	0.07	0.18
Thickness	0.03 (8.4e-03)	9.8e-04	-0.02	0.13	-1.4e-03	0.96	-0.03	0.19
ICV	**0.10 (8.4e-03)**	**2.4e-31**	-0.04	0.42	-3.1e-03	0.98	-0.05	0.42

Note: Del=deletion carriers, NC=non-carriers, Dup=duplication carriers, SE=standard error, ICV=intracranial volume. Brain structures passing the significance threshold are indicated in bold.



eFigure 13. Results from the linear regression of cognition (right, 'Path B') and mediation analyses (left) on regional surface area (top two rows) and cortical thickness (bottom two rows). The first and third row display the effect sizes (beta coefficient for the linear regression, proportion mediated for the mediation analyses), the second and fourth row show the statistical significance in –log10 of the p-value. Black demarcations around a brain region indicates that it passes the significance threshold with thicker lines indicating more significant findings. Note: column names indicate the comparisons. Del=deletion carriers, NC=non-carriers, Dup=duplication carriers.

eAppendix 2. Additional funding information

1000BRAINS: The 1000BRAINS study was funded by the Institute of Neuroscience and Medicine, Research Center Juelich, Germany. We thank the Heinz Nixdorf Foundation (Germany) for the generous support of the Heinz Nixdorf Recall Study on which 1000BRAINS is based. We also thank the scientists and the study staff of the Heinz Nixdorf Recall Study and 1000BRAINS. Funding was also granted by the Initiative and Networking Fund of the Helmholtz Association (Caspers) and the European Union's Horizon 2020 Research and Innovation Program under Grant Agreement 785907 (Human Brain Project SGA2; Amunts, Caspers, Cichon).

Brainscale: The Brainscale study was supported by the Netherlands Organization for Scientific Research MagW 480-04-004 (Boomsma), 51.02.060 (Hilleke Hulshoff Pol), 668.772 (Boomsma & Hulshoff Pol); NWO/SPI 56-464-14192 (Boomsma), the European Research Council (ERC-230374) (Boomsma), High Potential Grant Utrecht University (Hulshoff Pol), NWO Brain and Cognition 433-09-220 (Hulshoff Pol).

Betula: The Betula study was funded by the Knut and Alice Wallenberg (KAW) foundation. The Freesurfer segmentations on the Betula sample was performed on resources provided by the Swedish National Infrastructure for Computing (SNIC) at HPC2N in Umeå, Sweden.

Brain Imaging Genetics (BIG): This work makes use of the BIG database, first established in Nijmegen, The Netherlands, in 2007. This resource is now part of Cognomics (www.cognomics.nl), a joint initiative by researchers from the Donders Centre for Cognitive Neuroimaging, the Human Genetics and Cognitive Neuroscience departments of the Radboud university medical centre and the Max Planck Institute for Psycholinguistics in Nijmegen. The Cognomics Initiative has received supported from the participating departments and centres and from external grants, i.e. the Biobanking and Biomolecular Resources Research Infrastructure (Netherlands) (BBMRI-NL), the Hersenstichting Nederland, and the Netherlands Organisation for Scientific Research (NWO). The research leading to these results also receives funding from the NWO Gravitation grant 'Language in Interaction', the European Community's Seventh Framework Programme (FP7/2007–2013) under grant agreements n° 602450 (IMAGEMEND), n°278948 (TACTICS), and n°602805 (Aggressotype) as well as from the European Community's Horizon 2020 programme under grant agreement n° 643051 (MiND) and from ERC-2010-AdG 268800-NEUROSCHEMA. In addition, the work was supported by a grant for the ENIGMA Consortium (grant number U54 EB020403) from the BD2K Initiative of a cross-NIH partnership.

deCODE genetics: deCODE genetics acknowledges support from the Innovative Medicines Initiative Joint Undertaking under grant agreements' no. 115008 (NEWMEDS) and no. 115300 (EUAIMS) of which resources are composed of EFPIA in-kind contribution and financial contribution from the European Union's Seventh Framework Programme (EU-FP7/2007-2013), EU-

FP7 funded grant no. 602450 (IMAGEMEND) and EU funded FP7-People-2011-IAPP grant agreement no. 286213 (PsychDPC).

ECHO-DEFINE: The ECHO study acknowledges funding from a Medical Research Council (MRC) Centre Grant to Owen (G0801418), the Wellcome Trust (Institutional Strategic Support Fund (ISSF) to van den Bree and Clinical Research Training Fellowship to Doherty), the Waterloo Foundation (WF 918-1234 to van den Bree), the Baily Thomas Charitable Fund (2315/1 to van den Bree), National Institute of Mental Health (NIMH 5UO1MH101724 to van den Bree and Owen), the IMAGINE-ID study (funded by MRC (MR/N022572/1 to van den Bree and Owen)). The DEFINE study was supported by a Wellcome Trust Strategic Award (100202/Z/12/Z) to Owen.

ENIGMA: ENIGMA is supported in part by NIH grants U54 EB20403, R01MH116147, and R56AG058854.

EPIGEN-Dublin: The EPIGEN-Dublin cohort was supported by a Science Foundation Ireland Research Frontiers Programme award (08/RFP/GEN1538).

EPIGEN-UK (Sisodiya): The work was partly undertaken at UCLH/UCL, which received a proportion of funding from the UK Department of Health's NIHR Biomedical Research Centres funding scheme. We are grateful to the Wolfson Trust and the Epilepsy Society for supporting the Epilepsy Society MRI scanner.

GOBS: The GOBS study data collection was supported in part by the National Institutes of Health (NIH) grants: R01 MH078143, R01 MH078111 and R01 MH083824 with work conducted in part in facilities constructed under the support of NIH grant C06 RR020547.

HUBIN: The HUBIN study was financed by the Swedish Research Council (K2010-62X-15078-07-2, K2012-61X-15078-09-3, K2015-62X-15077-12-3, 2017-00949), the regional agreement on medical training and clinical research between Stockholm County Council and the Karolinska Institutet.

HUNT: The HUNT Study is a collaboration between HUNT Research Centre (Faculty of Medicine and Movement Sciences, NTNU – Norwegian University of Science and Technology), Nord-Trøndelag County Council, Central Norway Health Authority, and the Norwegian Institute of Public Health. HUNT-MRI was funded by the Liaison Committee between the Central Norway Regional Health Authority and the Norwegian University of Science and Technology, and the Norwegian National Advisory Unit for functional MRI.

IMAGEN: This work received support from the following sources: the European Union-funded FP6 Integrated Project IMAGEN (Reinforcement-related behaviour in normal brain function and psychopathology) (LSHM-CT-2007-037286), the Horizon 2020 funded ERC Advanced Grant 'STRATIFY' (Brain network based stratification of reinforcement-related disorders) (695313), ERANID (Understanding the Interplay between Cultural, Biological

and Subjective Factors in Drug Use Pathways) (PR-ST-0416-10004), BRIDGET (JPND: BRain Imaging, cognition Dementia and next generation GEnomics) (MR/N027558/1), the FP7 projects IMAGEMEND(602450; IMAging GEnetics for MENtal Disorders) and MATRICS (603016), the Innovative Medicine Initiative Project EU-AIMS (115300-2), the Medical Research Council Grant 'c-VEDA' (Consortium on Vulnerability to Externalizing Disorders and Addictions) (MR/N000390/1), the Swedish Research Council FORMAS, the Medical Research Council, the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London, the Bundesministeriumfür Bildung und Forschung (BMBF grants 01GS08152; 01EV0711; eMED SysAlc01ZX1311A; Forschungsnetz AERIAL 01EE1406A, 01EE1406B), the Deutsche Forschungsgemeinschaft (DFG grants, SM 80/7-2, SFB 940/2), the Medical Research Foundation and Medical research council (grant MR/R00465X/1). Further support was provided by grants from: ANR (project AF12-NEUR0008-01 – WM2NA, and ANR-12-SAMA-0004), the Fondation de France, the Fondation pour la Recherche Médicale, the Mission Interministérielle de Lutte-contre-les-Drogues-et-les-Conduites-Addictives (MILDECA), the Fondation pour la Recherche Médicale (DPA20140629802), the Fondation de l'Avenir, Paris Sud University IDEX 2012; the National Institutes of Health, Science Foundation Ireland (16/ERCD/3797), U.S.A. (Axon, Testosterone and Mental Health during Adolescence; RO1 MH085772-01A1), and by NIH Consortium grant U54 EB020403, supported by a cross-NIH alliance that funds Big Data to Knowledge Centres of Excellence.

NCNG: NCNG sample collection was supported by grants from the Bergen Research Foundation and the University of Bergen, the Dr Einar Martens Fund, the K.G. Jebsen Foundation, the Research Council of Norway, to le Hellard, Steen and Espeseth. The Bergen group was supported by grants from the Western Norway Regional Health Authority (Grant 911593 to AL, Grant 911397 and 911687 to AJL).

NTR: The NTR cohort was supported by the Netherlands Organization for Scientific Research (NWO), MW904-61-193 (de Geus & Boomsma), MaGW-nr: 400-07- 080 (van 't Ent), MagW 480-04-004 (Boomsma), NWO/SPI 56-464-14192 (Boomsma), the European Research Council, ERC-230374 (Boomsma), and Amsterdam Neuroscience. Funding for genotyping was obtained from the National Institutes of Health (NIMH U24 MH068457-06; Grand Opportunity grants 1RC2 MH089951, and 1RC2 MH089995); the Avera Institute for Human Genetics, Sioux Falls, South Dakota (USA). Part of the genotyping and analyses were funded by the Genetic Association Information Network (GAIN) of the Foundation for the National Institutes of Health.

OATS: The Older Australian Twins Study (OATS) is funded by NHMRC Program Grant ID1045325 and the NHMRC/Australian Research Council Strategic Award (ID401162). Twins Research Australia was supported by the NHRMC Enabling Grant 310667. We also thank the OATS participants and Research Team.

Osaka: Osaka study was supported by the Brain Mapping by Integrated Neurotechnologies for Disease Studies (Brain/MINDS: Grant Number JP18dm0207006), Brain/MINDS & beyond studies (Grant Number JP19dm0307002) and Health and Labor Sciences Research Grants for Comprehensive Research on Persons with Disabilities (Grant Number H26-seishin-ippan-012) from the Japan Agency for Medical Research and Development (AMED), Grants-in-Aid for Scientific Research (KAKENHI; Grant Number JP25293250 and JP16H05375). Some computations were performed at the Research Center for Computational Science, Okazaki, Japan.

PAFIP: The PAFIP study was supported by Instituto de Salud Carlos III, FIS 00/3095, 01/3129, PI020499, PI060507, PI10/00183, the SENY Fundació Research Grant CI 2005-0308007, and the Fundación Marqués de Valdecilla API07/011. Biological samples from our cohort were stored at the Valdecilla Biobank and genotyping services were conducted at the Spanish “Centro Nacional de Genotipado” (CEGEN-ISCIII).

MCIC/COBRE is funded by the National Institutes of Health studies R01EB006841, P20GM103472, and P30GM122734.

PING: Data collection and sharing for the Pediatric Imaging, Neurocognition and Genetics (PING) Study (National Institutes of Health Grant RC2DA029475) were funded by the National Institute on Drug Abuse and the Eunice Kennedy Shriver National Institute of Child Health & Human Development. A full list of PING investigators is at http://pingstudy.ucsd.edu/investigators.html.

QTIM: The QTIM study was supported by the National Institute of Child Health and Human Development (R01 HD050735), and the National Health and Medical Research Council (NHMRC 486682, 1009064), Australia. Genotyping was supported by NHMRC (389875). Medland is supported in part by an NHRC fellowship (APP1103623).

SHIP: SHIP is part of the Community Medicine Research net of the University of Greifswald, Germany, which is funded by the Federal Ministry of Education and Research (grants no. 01ZZ9603, 01ZZ0103, and 01ZZ0403), the Ministry of Cultural Affairs and the Social Ministry of the Federal State of Mecklenburg-West Pomerania. Genome-wide SNP typing in SHIP and MRI scans in SHIP and SHIP-TREND have been supported by a joint grant from Siemens Healthineers, Erlangen, Germany and the Federal State of Mecklenburg-West Pomerania.

StrokeMRI: StrokeMRI was supported by the Norwegian ExtraFoundation for Health and Rehabilitation (2015/FO5146), the Research Council of Norway (249795, 262372), the South-Eastern Norway Regional Health Authority (2014097, 2015044, 2015073), and the Department of Psychology, University of Oslo.

Sydney MAS: The Sydney Memory and Aging Study (Sydney MAS) is funded by National and Health Medical Research Council (NHMRC) Program and

Project Grants (ID350833, ID568969, ID109308). We also thank the Sydney MAS participants and the Research Team.

SYS: The SYS Study is supported by Canadian Institutes of Health Research.

TOP: Centre of Excellence: RCN #23273. KG Jebsen: SKGJ-MED-008 and KG Jebsen: SKGJ-MED-002, RCN #. 226971. Part of this work was performed on the TSD (Tjeneste for Sensitive Data) facilities, owned by the University of Oslo, operated and developed by the TSD service group at the University of Oslo, IT-Department (USIT). (tsd-drift@usit.uio.no). The research leading to these results has received funding from the European Union Seventh Framework Programme (FP7-PEOPLE-2013-COFUND) under grant agreement n° 609020 - Scientia Fellows; the Research Council of Norway (RCN) # 276082 - A lifespan perspective on mental illness: toward precision medicine using multimodal brain imaging and genetics;

UCLA_UMCU: The UCLA_UMCU cohort comprises of 6 studies which were supported by National Alliance for Research in Schizophrenia and Affective Disorders (NARSAD) (20244 to Prof. Hillegers), The Netherlands Organisation for Health Research and Development (ZonMw) (908-02-123 to Prof. Hulshoff Pol), and Netherlands Organisation for Scientific Research (NWO 9120818 and NWO- VIDI 917-46-370 to Prof. Hulshoff Pol). The GROUP study was funded through the Geestkracht programme of the Dutch Health Research Council (ZonMw, grant number 10-000-1001), and matching funds from participating pharmaceutical companies (Lundbeck, AstraZeneca, Eli Lilly, Janssen Cilag) and universities and mental health care organizations (Amsterdam: Academic Psychiatric Centre of the Academic Medical Center and the mental health institutions: GGZ inGeest, Arkin, Dijk en Duin, GGZ Rivierduinen, Erasmus Medical Centre, GGZ Noord Holland Noord. Groningen: University Medical Center Groningen and the mental health institutions: Lentis, GGZ Friesland, GGZ Drenthe, Dimence, Mediant, GGNet Warnsveld, Yulius Dordrecht, and Parnassia psycho-medical center, The Hague. Maastricht: Maastricht University Medical Centre and the mental health institutions: GGzE, GGZ Breburg, GGZ Oost-Brabant, Vincent van Gogh voor Geestelijke Gezondheid, Mondriaan, Virenze riagg, Zuyderland GGZ, MET ggz, Universitair Centrum Sint- Jozef Kortenberg, CAPRI University of Antwerp, PC Ziekeren Sint-Truiden, PZ Sancta Maria Sint-Truiden, GGZ Overpelt, OPZ Rekem. Utrecht: University Medical Center Utrecht and the mental health institutions Altrecht, GGZ Centraal, and Delta.)

UKB: This work made use of data sharing from UKB (under project code 27412).

eMethods 1. Details on quality control of CNVs

The genotypes used in the current study were obtained by genotyping with commercially available platforms, performed at participating sites for each cohort (Supplement 2). In the case of cohorts primarily consisting of Asian and African individuals, a PFB-file was generated through PennCNV compile_pfb.pl and using all genotyping arrays from the cohort (Supplement 2).

Only samples with standard deviation (SD) of normalized intensity (LRR) <0.35, B allele frequency (BAF) drifting value <0.01 and wave factor value between -0.05 and 0.05 were included. Adjacent CNVs separated by a gap less than 20% of the combined length of the two CNVs were merged until no more gaps of <20% existed, and CNVs based on less than 15 SNPs were excluded.

CNVs overlapping the 15q11.2 (BP1-2) region were identified and visualized with the R package iPsychCNV SelectSamplesFromROI with parameters OverlapMin = 0 and OverlapMax = 5. To exclude false-positives, , LRR- and BAF-plots of the 15q11.2 distal region of all called 15q11.2 (BP1-2) carriers were generated with R package iPsychCNV StackPlot and visually inspected. As can be seen in eFigure 2, the 15q11.2 (BP1-2) region was covered well by all the arrays in the study. No false positives were identified.

For the UKB, CNVs were called similar to the ENIGMA cohorts. Anonymized genotyped data was downloaded as l2r & baf-files from the UKB data repository for chromosomes 1-22, X, Y, M & XY. In addition, SNP-files were downloaded. This data was stored and processed on a secure Unix server.

For the initial steps, the l2r- and baf-files were split into separate files for each individual containing both l2r and baf-values in 20 batches, each containing 25,000 individuals per batch. Subsequently, SNP-names were added to the files. CNVs were called in sub-batches of 1000 individuals per batch using PennCNV [57] and self-generated PFB- and GCC-model files (NCBI37/hg19) and affygw6.hmm. Subsequent filtering and visualization was done as for the main dataset above, except that the LRR_SD cut-off was set at 0.50 given that we observed reliable CNV calls within these ranges. We did not filter based on number of CNVs or genotype call rate. A total of 59 individuals were excluded from the entire UK biobank using this procedure. These filtering criteria could have been stricter. However, all individuals with structural MRI data and 15q11.2 CNVs were visualized and inspected without identification of false positives. This suggests that the stringency level was adequate, and thus we did not visually inspect the remaining 15q11.2 (BP1-2) CNV carriers in the full UKB dataset

eMethods 2. Details on cognitive task data processing

The *Pairs Matching* task (field 399), tested episodic memory, with six pairs of cards being shown for three seconds to participants, before being turned over, after which the participants were asked to identify the matching pairs. We used the total number of errors made. The *Reaction Time* task (field 20023), tested simple processing speed through twelve rounds of a game where participants had to click a button as quickly as possible when shown two matching cards. We used the mean reaction time. *Fluid Intelligence* (field 20016), tested reasoning and problem solving through thirteen verbal and numerical reasoning questions, which had to be answered within two minutes. We used the total number of correct answers. The *Digit Span* task (field 4282) tested numeric working memory by presenting progressively longer numbers to participants and asking them to recall these once the number had disappeared. We used the maximum number of digits correctly recalled. The Symbol Digit Substitution task (field 20195) tested complex processing speed through the matching of numbers to a set of symbols. We used the number of correct substitutions. The Trail Making A and B tasks (fields 20156 and 20157) tested visual attention by asking participants to connect scattered circles according to numbers (trail A) and to alternating numbers and letters (trail B). We used the time taken to complete these tests for our analyses. All data was recoded so that higher scores indicate higher performance.

eMethods 3. Description of additional control analyses

Both for comparison between groups (t-tests) and for dose response (linear regression), we performed a set of robustness and sensitivity analyses in the discovery cohort:

a) excluding individuals with an established psychiatric or neurodevelopmental diagnosis to verify that detected effects were not due to disease alone.

b) adults-only analyses excluding individuals below age 18 years.

c) A matched controls analysis was carried, in which the R package *Matchit* v2.4 was first used to match each CNV carrier with four non-carriers based on sex, age, and scanner site.

d) adding the first four genetic principal components as covariates to the analyses, to control for population structure effects,

e) checking for the role of age in our significant findings by rerunning the analyses with an interaction term between copy number and age.

f) checking for differences between men and women in our significant findings by rerunning the analyses with an interaction term between copy number and sex.

g) We analyzed the data for the UKB and the ENIGMA-CNV cohorts separately. This was to ensure that the single largest contributing cohort, the UKB, is comparable to the other cohorts, with respect to the observed effects of the CNV on the brain, thereby not unduly driving the results.

For a) through d) and (g), we first carried out the steps described above, and then re-ran the analyses identical to the main analyses. For e), we first residualized the raw measures for sex, scanner site and intracranial volume, followed by the inverse-normalization. After that, we ran a linear regression, with copy number, age, and copy number-by-age interaction term as predictors. For f) we did the same, but first residualizing for age, scanner site and ICV, and then running a linear regression with an interaction term between copy number and sex. Results for a) through f) are found in eTables 3-8. eFigure 3 further shows the results from analysis e) in the form of scatterplots. eFigure 4 shows the results from g) in the form of forest plots.

eTable 1. CNVs of interest

Individuals with a CNV with minimum overlap of 0.4 to these CNVs were excluded from the analysis. Coordinates are in Human Genome Build GRCh37/hg19.

CNV of Interest	Chr	Start	Stop	Length	source
1p36_GABRD	1	0	2500000	2500000	Kendall et al 2017
1q21_TAR	1	145394955	145807817	412862	Kendall et al 2017
1q21.1	1	146527987	147394444	866457	Kendall et al 2017
1q21.1_distalprox	1	145394955	147394444	1999489	Kendall et al 2017
2p16.3_NRXN1	2	50145643	51259674	1114031	Kendall et al 2017
2q11.2	2	96742409	97677516	935107	Kendall et al 2017
2q13_NHP1	2	110862716	110983948	121232	Kendall et al 2017
2q13	2	111394040	112012649	618609	Kendall et al 2017
2q21.1	2	131481308	131930677	449369	Kendall et al 2017
2q37_HDAC4	2	239716679	243199373	3482694	Kendall et al 2017
3q29	3	195720167	197354826	1634659	Kendall et al 2017
4p16.3_WH	4	1552030	2091303	539273	Kendall et al 2017
5q35_Sotos	5	175720924	177052594	1331670	Kendall et al 2017
6q16_SIM1	6	100836750	100911811	75061	Kendall et al 2017
7q11.23_WBS	7	72744915	74142892	1397977	Kendall et al 2017
7q11.23	7	75138294	76064412	926118	Kendall et al 2017
8p23.1	8	8098990	11872558	3773568	Kendall et al 2017
9q34_EHMT1	9	140513444	140730578	217134	Kendall et al 2017
10q11.22-23	10	49390199	51058796	1668597	Kendall et al 2017
10q23_NRG3_GRID1	10	82045472	88931651	6886179	Kendall et al 2017
11p11.2_EXT2	11	43940000	46020000	2080000	Kendall et al 2017
13q12.11 ZMYM5	13	20977806	21100012	122206	Kendall et al 2017
13q12.12	13	23555358	24884622	1329264	Kendall et al 2017
15q11.2	15	22805313	23094530	289217	Kendall et al 2017
15q11.2-13.1_BP1-2	15	22805313	28390339	5585026	Kendall et al 2017
15q13.1_BP3-4	15	29161368	30375967	1214599	Kendall et al 2017
15q11q13_BP3_BP5	15	29161368	32462776	3301408	Kendall et al 2017
15q13.3_BP4-BP5	15	31080645	32462776	1382131	Kendall et al 2017
15q13.3_BP4.5-BP5	15	32017070	32453068	435998	Kendall et al 2017
15q24	15	72900171	78151253	5251082	Kendall et al 2017
15q25	15	83219735	85722039	2502304	Kendall et al 2017
16p13.3_Rubinstein_Taybi_CREBBP	16	3775056	3930121	155065	Kendall et al 2017
16p13.11	16	15511655	16293689	782034	Kendall et al 2017
16p12.2-p11.2	16	21596415	28347808	6751393	Kendall et al 2017
16p12.1	16	21950135	22431889	481754	Kendall et al 2017
16p11.2_-_distal	16	28823196	29046783	223587	Kendall et al 2017
16p11.2_-_distal_large	16	28453196	29046783	593587	Sønderby et al 2018
16p11.2_entireregion	16	28453196	30200773	1747577	Sønderby et al 2018
16p11.2	16	29650840	30200773	549933	Kendall et al 2017
17p13.3_YWHAE	17	1247834	1303556	55722	Kendall et al 2017
17p13.3_PAFAH1B1	17	2496923	2588909	91986	Kendall et al 2017
17p12	17	14141387	15426961	1285574	Kendall et al 2017
17p11.2	17	16812771	20211017	3398246	Kendall et al 2017
17q11.2_NF1	17	29107491	30265075	1157584	Kendall et al 2017
17q12	17	34815904	36217432	1401528	Kendall et al 2017
17q21.31	17	43705356	44164691	459335	Kendall et al 2017
17q23.1q23.2	17	58302389	60289141	1986752	Kendall et al 2017
22q11_3Mb	22	19037332	21466726	2429394	Kendall et al 2017
22q11_distal	22	21920127	23653646	1733519	Kendall et al 2017
SHANK3	22	51113070	51171640	58570	Kendall et al 2017

Due to varying numbers of missingness per measure, and the exclusion of cohorts without carriers, final discovery sample size per primary outcome measure and per test varies. eTable 2 shows the final sample sizes.

eTable 2. Final sample size per primary outcome measure and per comparison in the discovery sample, after removing missing values and cohorts without 15q11.2 BP1-BP2 carriers

	Del v. NC		Dup v. NC		Dosage		
Feature	Del	NC	Dup	NC	Del	NC	Dup
Accumbens	144	40525	42539	186	140	39841	158
Caudate	144	40744	42724	187	140	40025	159
Pallidum	144	40624	42600	185	140	39907	157
Putamen	143	40588	42570	187	139	39871	159
Thalamus	144	40681	42660	187	140	39962	159
Amygdala	143	40653	42629	188	139	39935	160
Hippocampus	144	40659	42628	186	140	39943	158
Surface area	143	41047	43024	191	139	40343	164
Thickness	143	41049	43027	190	139	40346	164
ICV	146	41580	43560	192	142	40874	165

eTable 3. Results after excluding individuals with brain disorders

	Del v. NC		Dup v. NC		Dosage	
Feature	Cohen's D (SE)	P-value	Cohen's D (SE)	P-value	Estimate (SE)	P-value
Accumbens	-0.27 (0.09)	1.8e-03	-0.02 (8.7e-03)	0.82	0.11 (0.06)	0.06
Caudate	-0.08 (0.04)	0.35	-0.12 (0.06)	0.12	-0.04 (0.06)	0.48
Pallidum	-0.09 (0.05)	0.29	9.2e-03 (4.7e-03)	0.90	0.05 (0.06)	0.39
Putamen	-0.13 (0.06)	0.15	-0.05 (0.02)	0.53	0.05 (0.06)	0.4
Thalamus	-0.11 (0.06)	0.19	-0.05 (0.03)	0.51	0.04 (0.06)	0.52
Amygdala	-0.03 (0.01)	0.77	0.02 (0.01)	0.76	0.04 (0.06)	0.55
Hippocampus	-0.14 (0.07)	0.10	0.08 (0.04)	0.29	0.11 (0.06)	0.07
Surface area	**-0.32 (0.09)**	**2.7e-04**	-0.02 (9.8e-03)	0.80	0.12 (0.06)	0.04
Thickness	**0.36 (0.09)**	**3.8e-05**	-0.26 (0.07)	4.6e-04	**-0.27 (0.06)**	**5.1e-06**
ICV	0.18 (0.09)	0.04	-0.11 (0.06)	0.14	-0.14 (0.06)	0.02

Note: Del=deletion carriers, NC=non-carriers, Dup=duplication carriers, SE=standard error, ICV=intracranial volume. Multiple comparison corrected significant findings ($p<4.7 \times 10^{-4}$) are indicated in bold.

eTable 4. Results after excluding individuals younger than 18 years

Note: Del=deletion carriers, NC=non-carriers, Dup=duplication carriers, SE=standard error, ICV=intracranial volume. Multiple comparison corrected significant findings ($p<4.7 \times 10^{-4}$) are indicated in bold.

	Del v. NC		Dup v. NC		Dosage	
Feature	Cohen's D (SE)	P-value	Cohen's D (SE)	P-value	Estimate (SE)	P-value
Accumbens	**-0.33 (0.08)**	**8.3e-05**	-0.02 (0.01)	0.76	0.14 (0.06)	0.02
Caudate	-0.16 (0.08)	0.05	-0.11 (0.06)	0.13	0.02 (0.06)	0.74
Pallidum	-0.16 (0.08)	0.05	6.7e-03 (3.4e-03)	0.93	0.07 (0.06)	0.24
Putamen	-0.17 (0.09)	0.05	-0.07 (0.03)	0.39	0.04 (0.06)	0.49
Thalamus	-0.17 (0.08)	0.04	-0.05 (0.02)	0.55	0.06 (0.06)	0.28
Amygdala	-0.04 (0.02)	0.65	-2.8e-03 (1.4e-03)	0.97	0.03 (0.06)	0.62
Hippocampus	-0.15 (0.08)	0.07	0.07 (0.04)	0.36	0.11 (0.06)	0.06
Surface area	**-0.38 (0.09)**	**9.3e-06**	-0.03 (0.01)	0.72	0.15 (0.06)	9.9e-03
Thickness	**0.35 (0.09)**	**4.2e-05**	-0.22 (0.08)	4.4e-03	**-0.26 (0.06)**	**7.2e-06**
ICV	0.16 (0.08)	0.07	-0.09 (0.04)	0.25	-0.11 (0.06)	0.05

eTable 5. Results after matching each carrier with 4 noncarriers

	Del v. NC		Dup v. NC		Dosage	
Feature	Cohen's D (SE)	P-value	Cohen's D (SE)	P-value	Estimate (SE)	P-value
Accumbens	**-0.31 (0.08)**	**2.0e-04**	-0.04 (0.02)	0.60	0.11 (0.06)	0.05
Caudate	-0.11 (0.06)	0.17	-0.10 (0.05)	0.15	-0.03 (0.06)	0.58
Pallidum	-0.14 (0.07)	0.08	-0.02 (9.4e-03)	0.80	0.06 (0.06)	0.27
Putamen	-0.13 (0.06)	0.13	-0.09 (0.04)	0.24	0.03 (0.06)	0.65
Thalamus	-0.12 (0.06)	0.14	-0.07 (0.04)	0.30	0.03 (0.06)	0.61
Amygdala	-0.02 (0.01)	0.81	0.02 (0.01)	0.73	0.02 (0.06)	0.72
Hippocampus	-0.12 (0.06)	0.15	0.07 (0.04)	0.34	0.09 (0.06)	0.11
Surface area	**-0.34 (0.08)**	**3.9e-05**	-0.03 (0.01)	0.69	0.13 (0.06)	0.02
Thickness	**0.35 (0.08)**	**3.2e-05**	-0.24 (0.07)	1.1e-03	**-0.28 (0.06)**	**1.1e-06**
ICV	0.15 (0.08)	0.06	-0.10 (0.05)	0.18	-0.12 (0.06)	0.04

Note: Del=deletion carriers, NC=non-carriers, Dup=duplication carriers, SE=standard error, ICV=intracranial volume. Multiple comparison corrected significant findings ($p<4.7 \times 10^{-4}$) are indicated in bold.

eTable 6. Results after first regressing out 4 population components

	Del v. NC		Dup v. NC		Dosage	
Feature	Cohen's D (SE)	P-value	Cohen's D (SE)	P-value	Estimate (SE)	P-value
Accumbens	-0.28 (0.09)	1.1e-03	-0.04 (0.02)	0.61	0.1 (0.06)	0.09
Caudate	-0.16 (0.08)	0.06	-0.13 (0.07)	0.08	0 (0.06)	0.96
Pallidum	-0.14 (0.07)	0.11	-0.01 (5.7e-03)	0.88	0.06 (0.06)	0.33
Putamen	-0.09 (0.05)	0.28	-0.10 (0.05)	0.19	0.01 (0.06)	0.89
Thalamus	-0.15 (0.08)	0.09	-0.07 (0.04)	0.33	0.05 (0.06)	0.36
Amygdala	1.0e-02 (5.1e-03)	0.91	-0.03 (0.02)	0.69	-0.01 (0.06)	0.87
Hippocampus	-0.14 (0.07)	0.11	0.04 (0.02)	0.60	0.09 (0.06)	0.12
Surface area	**-0.33 (0.09)**	**1.4e-04**	-0.07 (0.03)	0.38	0.13 (0.06)	0.03
Thickness	**0.37 (0.09)**	**1.8e-05**	-0.21 (0.08)	5.7e-03	**-0.28 (0.06)**	**1.2e-06**
ICV	0.13 (0.07)	0.12	-0.05 (0.03)	0.47	-0.1 (0.06)	0.07

Note: Del=deletion carriers, NC=non-carriers, Dup=duplication carriers, SE=standard error, ICV=intracranial volume. Multiple comparison corrected significant findings ($p<4.7 \times 10^{-4}$) are indicated in bold.

eTable 7. Results of linear regression analyses including an interaction term between copy number and age

	Nucleus accumbens		Mean thickness		Total surface area	
Predictor	Coefficient (SE)	P-value	Coefficient (SE)	P-value	Coefficient (SE)	P-value
Copy number	0.147 (0.054)	6.8e-03	**-0.216 (0.054)**	**5.9e-05**	0.147 (0.054)	6.8e-03
Age	-0.013 (5.8e-03)	0.026	-0.012 (5.9e-03)	0.044	-5.5e-03 (6.0e-03)	0.354
Copy number * Age	2.4e-03 (2.9e-03)	0.407	5.6e-04 (2.9e-03)	0.849	4.1e-04 (3.0e-03)	0.892

Note: SE=standard error. Multiple comparison corrected significant findings ($p<4.7 \times 10^{-4}$) are indicated in bold.

eTable 8. Results of linear regression analyses including an interaction term between copy number and sex

	Nucleus accumbens		Mean thickness		Total surface area	
Predictor	Coefficient (SE)	P-value	Coefficient (SE)	P-value	Coefficient (SE)	P-value
Copy number	0.207 (0.079)	9.3e-03	**-0.294 (0.079)**	**2.1e-04**	0.221 (0.078)	4.4e-03
Sex	0.125 (0.22)	0.57	-0.067 (0.22)	0.759	-0.082 (0.215)	0.702
Copy number * Sex	-0.15 (0.11)	0.172	0.032 (0.11)	0.768	-0.146 (0.108)	0.176

Note: SE=standard error. Multiple comparison corrected significant findings ($p<4.7 \times 10^{-4}$) are indicated in bold.

eTable 9. Meta-analysis results from *t* tests and linear regression on each of the primary brain morphology measures without preresidualizing for ICV

	Del v. NC		Dup v. NC		Dosage	
Feature	Cohen's D (SE)	P-value	Cohen's D (SE)	P-value	Estimate (SE)	P-value
Accumbens	-0.28 (0.09)	1.1e-03	-0.04 (0.02)	0.61	0.1 (0.06)	0.09
Caudate	-0.16 (0.08)	0.06	-0.13 (0.07)	0.08	0 (0.06)	0.96
Pallidum	-0.14 (0.07)	0.11	-0.01 (5.7e-03)	0.88	0.06 (0.06)	0.33
Putamen	-0.09 (0.05)	0.28	-0.10 (0.05)	0.19	0.01 (0.06)	0.89
Thalamus	-0.15 (0.08)	0.09	-0.07 (0.04)	0.33	0.05 (0.06)	0.36
Amygdala	1.0e-02 (5.1e-03)	0.91	-0.03 (0.02)	0.69	-0.01 (0.06)	0.87
Hippocampus	-0.14 (0.07)	0.11	0.04 (0.02)	0.60	0.09 (0.06)	0.12
Surface area	**-0.33 (0.09)**	**1.4e-04**	-0.07 (0.03)	0.38	0.13 (0.06)	0.03
Thickness	**0.37 (0.09)**	**1.8e-05**	-0.21 (0.08)	5.7e-03	**-0.28 (0.06)**	**1.2e-06**
ICV	0.13 (0.07)	0.12	-0.05 (0.03)	0.47	-0.1 (0.06)	0.07

Note: Del=deletion carriers, NC=non-carriers, Dup=duplication carriers, SE=standard error, ICV=intracranial volume. Multiple comparison corrected significant findings ($p<4.7 \times 10^{-4}$) are indicated in bold.

eTable 10. Results from *t* tests and linear regression on each of the primary brain morphology measures for the discovery sample (ENIGMA and UK Biobank) (top) and the replication sample (deCODE Genetics) (bottom)

Discovery sample

	Del v. NC		Dup v. NC		Dosage	
Feature	Cohen's D (SE)	P-value	Cohen's D (SE)	P-value	Estimate (SE)	P-value
Accumbens	**-0.31 (0.08)**	**2.0e-04**	-0.02 (0.01)	0.79	0.13 (0.06)	0.03
Caudate	-0.13 (0.07)	0.13	-0.11 (0.06)	0.12	-0.01 (0.06)	0.8
Pallidum	-0.14 (0.07)	0.08	-0.02 (9.0e-03)	0.81	0.06 (0.06)	0.29
Putamen	-0.13 (0.07)	0.11	-0.08 (0.04)	0.26	0.03 (0.06)	0.59
Thalamus	-0.13 (0.07)	0.11	-0.06 (0.03)	0.43	0.04 (0.06)	0.46
Amygdala	-7.7e-03 (3.9e-03)	0.93	0.03 (0.02)	0.64	0.03 (0.06)	0.59
Hippocampus	-0.12 (0.06)	0.14	0.08 (0.04)	0.27	0.1 (0.06)	0.08
Surface area	**-0.35 (0.08)**	**3.3e-05**	-0.02 (8.2e-03)	0.82	0.14 (0.06)	0.01
Thickness	**0.33 (0.08)**	**6.9e-05**	-0.23 (0.07)	1.3e-03	**-0.26 (0.06)**	**6.1e-06**
ICV	0.15 (0.08)	0.07	-0.08 (0.04)	0.24	-0.1 (0.06)	0.06

Replication sample

	Del v. NC		Dup v. NC		Dosage	
Feature	Cohen's D (SE)	P-value	Cohen's D (SE)	P-value	Estimate (SE)	P-value
Accumbens	-0.20 (0.10)	0.13	0.03 (0.02)	0.77	0.09 (0.05)	0.23
Caudate	-0.03 (0.01)	0.84	0.12 (0.06)	0.22	0.09 (0.05)	0.26
Pallidum	-0.13 (0.07)	0.33	0.04 (0.02)	0.69	0.07 (0.04)	0.39
Putamen	0.03 (0.02)	0.81	-0.23 (0.10)	0.02	-0.16 (0.08)	0.04
Thalamus	0.06 (0.03)	0.63	-0.18 (0.09)	0.07	-0.14 (0.07)	0.07
Amygdala	-0.24 (0.12)	0.08	0.08 (0.04)	0.41	0.13 (0.07)	0.08
Hippocampus	-0.23 (0.12)	0.09	0.05 (0.03)	0.62	0.11 (0.06)	0.14
Surface area	**-0.58 (0.14)**	**1.4e-05**	-0.12 (0.06)	0.23	0.13 (0.07)	0.08
Thickness	0.42 (0.14)	1.8e-03	-0.09 (0.05)	0.36	-0.20 (0.08)	8.0e-03
ICV	-0.29 (0.14)	0.03	-0.03 (0.02)	0.75	0.08 (0.04)	0.28

Note: Del=deletion carriers, NC=non-carriers, Dup=duplication carriers, SE=standard error, ICV=intracranial volume. Multiple comparison corrected significant findings ($p<4.7 \times 10^{-4}$) are indicated in bold.

eTable 11. Full results from the regional cortical analyses, including the *t* tests (pairwise comparisons) and the general linear model (copy number dosage effects)

Results are split by measure and contrast, and with regions sorted alphabetically.

Region	Measure	Contrast	Estimate	SE	P
banks superior temporal	Area	Del v. NC	-7.2e-03	3.7e-03	0.93
caudal anterior cingulate	Area	Del v. NC	-0.42	0.08	4.0e-07
caudal middle frontal	Area	Del v. NC	-0.25	0.08	3.2e-03
cuneus	Area	Del v. NC	-0.16	0.08	0.05
entorhinal	Area	Del v. NC	-0.11	0.06	0.19
frontal pole	Area	Del v. NC	0.10	0.05	0.24
fusiform	Area	Del v. NC	-0.10	0.05	0.22
inferior parietal	Area	Del v. NC	-0.18	0.08	0.04
inferior temporal	Area	Del v. NC	-0.19	0.08	0.02
insula	Area	Del v. NC	0.07	0.04	0.41
isthmus cingulate	Area	Del v. NC	-0.09	0.05	0.28
lateral occipital	Area	Del v. NC	-0.20	0.08	0.02
lateral orbitofrontal	Area	Del v. NC	-0.26	0.08	1.9e-03
lingual	Area	Del v. NC	-0.06	0.03	0.46
medial orbito frontal	Area	Del v. NC	-0.15	0.08	0.08
middle temporal	Area	Del v. NC	-0.09	0.05	0.29
para central	Area	Del v. NC	-0.26	0.08	2.3e-03
parahippocampal	Area	Del v. NC	-0.33	0.08	8.0e-05
pars opercularis	Area	Del v. NC	-0.12	0.06	0.15
pars orbitalis	Area	Del v. NC	-0.42	0.08	5.5e-07
pars triangularis	Area	Del v. NC	-0.19	0.08	0.02
pericalcarine	Area	Del v. NC	-0.16	0.08	0.06
post central	Area	Del v. NC	-0.29	0.08	5.8e-04
posterior cingulate	Area	Del v. NC	-0.27	0.08	1.1e-03
pre central	Area	Del v. NC	-0.30	0.08	4.2e-04
precuneus	Area	Del v. NC	-0.19	0.08	0.03
rostral anterior cingulate	Area	Del v. NC	-0.27	0.08	1.2e-03
rostral middle frontal	Area	Del v. NC	-0.38	0.08	6.1e-06
superior frontal	Area	Del v. NC	-0.20	0.08	0.02
superior parietal	Area	Del v. NC	-0.23	0.08	5.5e-03
superior temporal	Area	Del v. NC	-0.02	0.01	0.79
supramarginal	Area	Del v. NC	-0.12	0.06	0.16
temporal pole	Area	Del v. NC	-0.16	0.08	0.06
transverse temporal	Area	Del v. NC	0.06	0.03	0.49
banks superior temporal	Area	Dup v. NC	-0.13	0.07	0.07
caudal anterior cingulate	Area	Dup v. NC	0.09	0.05	0.21
caudal middle frontal	Area	Dup v. NC	0.03	0.02	0.66
cuneus	Area	Dup v. NC	-0.04	0.02	0.54
entorhinal	Area	Dup v. NC	3.8e-03	2.0e-03	0.96
frontal pole	Area	Dup v. NC	-0.03	0.01	0.70
fusiform	Area	Dup v. NC	-0.07	0.03	0.36
inferior parietal	Area	Dup v. NC	-0.08	0.04	0.30
inferior temporal	Area	Dup v. NC	-0.07	0.04	0.31
insula	Area	Dup v. NC	0.01	6.7e-03	0.86
isthmus cingulate	Area	Dup v. NC	-0.08	0.04	0.29
lateral occipital	Area	Dup v. NC	-0.13	0.07	0.07
lateral orbitofrontal	Area	Dup v. NC	0.14	0.07	0.05
lingual	Area	Dup v. NC	-0.09	0.05	0.19
medial orbito frontal	Area	Dup v. NC	0.11	0.06	0.13
middle temporal	Area	Dup v. NC	-0.04	0.02	0.56
para central	Area	Dup v. NC	0.18	0.07	0.01
parahippocampal	Area	Dup v. NC	0.09	0.05	0.22

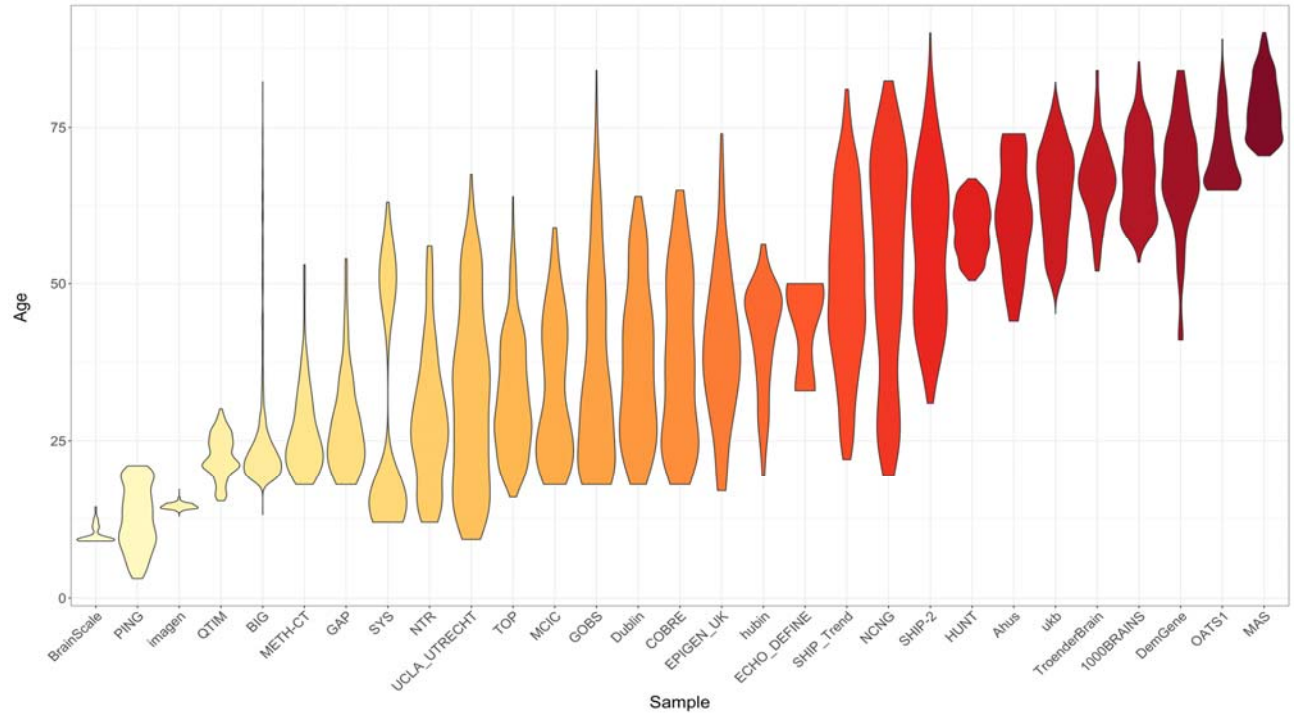
pars opercularis	Area	Dup v. NC	0.03	0.02	0.66
pars orbitalis	Area	Dup v. NC	0.14	0.07	0.06
pars triangularis	Area	Dup v. NC	0.07	0.04	0.32
pericalcarine	Area	Dup v. NC	0.02	0.01	0.75
post central	Area	Dup v. NC	0.07	0.04	0.33
posterior cingulate	Area	Dup v. NC	0.04	0.02	0.57
pre central	Area	Dup v. NC	-0.04	0.02	0.63
precuneus	Area	Dup v. NC	0.05	0.03	0.46
rostral anterior cingulate	Area	Dup v. NC	0.03	0.02	0.66
rostral middle frontal	Area	Dup v. NC	0.05	0.02	0.53
superior frontal	Area	Dup v. NC	-0.06	0.03	0.41
superior parietal	Area	Dup v. NC	0.04	0.02	0.54
superior temporal	Area	Dup v. NC	-0.03	0.02	0.69
supramarginal	Area	Dup v. NC	3.3e-03	1.7e-03	0.96
temporal pole	Area	Dup v. NC	-0.03	0.02	0.68
transverse temporal	Area	Dup v. NC	-0.08	0.04	0.30
banks superior temporal	Area	Dosage	-0.10	0.06	0.09
caudal anterior cingulate	Area	Dosage	0.27	0.06	4.4e-06
caudal middle frontal	Area	Dosage	0.13	0.06	0.03
cuneus	Area	Dosage	0.03	0.06	0.62
entorhinal	Area	Dosage	0.04	0.06	0.46
frontal pole	Area	Dosage	-0.07	0.06	0.26
fusiform	Area	Dosage	0.02	0.06	0.73
inferior parietal	Area	Dosage	0.05	0.06	0.35
inferior temporal	Area	Dosage	0.07	0.06	0.24
insula	Area	Dosage	0.0e+00	0.06	0.94
isthmus cingulate	Area	Dosage	-0.02	0.06	0.67
lateral occipital	Area	Dosage	0.0e+00	0.06	0.98
lateral orbitofrontal	Area	Dosage	0.17	0.06	2.8e-03
lingual	Area	Dosage	-0.01	0.06	0.88
medial orbito frontal	Area	Dosage	0.12	0.06	0.04
middle temporal	Area	Dosage	0.03	0.06	0.65
para central	Area	Dosage	0.23	0.06	9.8e-05
parahippocampal	Area	Dosage	0.23	0.06	4.8e-05
pars opercularis	Area	Dosage	0.09	0.06	0.11
pars orbitalis	Area	Dosage	0.24	0.06	3.8e-05
pars triangularis	Area	Dosage	0.10	0.06	0.09
pericalcarine	Area	Dosage	0.07	0.06	0.25
post central	Area	Dosage	0.18	0.06	2.1e-03
posterior cingulate	Area	Dosage	0.16	0.06	5.0e-03
pre central	Area	Dosage	0.09	0.06	0.12
precuneus	Area	Dosage	0.10	0.06	0.09
rostral anterior cingulate	Area	Dosage	0.11	0.06	0.06
rostral middle frontal	Area	Dosage	0.18	0.06	1.7e-03
superior frontal	Area	Dosage	0.03	0.06	0.61
superior parietal	Area	Dosage	0.14	0.06	0.02
superior temporal	Area	Dosage	0.0e+00	0.06	0.97
supramarginal	Area	Dosage	0.08	0.06	0.19
temporal pole	Area	Dosage	0.05	0.06	0.36
transverse temporal	Area	Dosage	-0.06	0.06	0.28
banks superior temporal	Thickness	Del v. NC	0.19	0.08	0.02
caudal anterior cingulate	Thickness	Del v. NC	0.20	0.08	0.01
caudal middle frontal	Thickness	Del v. NC	0.31	0.08	2.2e-04
cuneus	Thickness	Del v. NC	4.5e-03	2.3e-03	0.96
entorhinal	Thickness	Del v. NC	0.08	0.04	0.32
frontal pole	Thickness	Del v. NC	0.22	0.08	9.1e-03
fusiform	Thickness	Del v. NC	0.10	0.05	0.25
inferior parietal	Thickness	Del v. NC	0.20	0.08	0.01
inferior temporal	Thickness	Del v. NC	0.05	0.03	0.53
insula	Thickness	Del v. NC	0.25	0.08	3.5e-03

isthmus cingulate	Thickness	Del v. NC	0.24	0.08	4.4e-03
lateral occipital	Thickness	Del v. NC	0.09	0.05	0.29
lateral orbitofrontal	Thickness	Del v. NC	0.17	0.08	0.05
lingual	Thickness	Del v. NC	0.11	0.06	0.19
medial orbito frontal	Thickness	Del v. NC	0.24	0.08	4.2e-03
middle temporal	Thickness	Del v. NC	0.21	0.08	0.01
para central	Thickness	Del v. NC	0.15	0.08	0.08
parahippocampal	Thickness	Del v. NC	0.13	0.06	0.13
pars opercularis	Thickness	Del v. NC	0.30	0.08	3.8e-04
pars orbitalis	Thickness	Del v. NC	0.24	0.08	3.5e-03
pars triangularis	Thickness	Del v. NC	0.32	0.08	1.6e-04
pericalcarine	Thickness	Del v. NC	-0.06	0.03	0.45
post central	Thickness	Del v. NC	0.44	0.08	1.7e-07
posterior cingulate	Thickness	Del v. NC	0.30	0.08	4.3e-04
pre central	Thickness	Del v. NC	0.24	0.08	4.5e-03
precuneus	Thickness	Del v. NC	0.23	0.08	5.6e-03
rostral anterior cingulate	Thickness	Del v. NC	0.17	0.08	0.05
rostral middle frontal	Thickness	Del v. NC	0.43	0.08	3.0e-07
superior frontal	Thickness	Del v. NC	0.43	0.08	3.6e-07
superior parietal	Thickness	Del v. NC	0.25	0.08	2.5e-03
superior temporal	Thickness	Del v. NC	0.12	0.06	0.15
supramarginal	Thickness	Del v. NC	0.19	0.08	0.03
temporal pole	Thickness	Del v. NC	0.01	6.1e-03	0.89
transverse temporal	Thickness	Del v. NC	0.06	0.03	0.44
banks superior temporal	Thickness	Dup v. NC	-0.21	0.07	4.0e-03
caudal anterior cingulate	Thickness	Dup v. NC	-0.15	0.07	0.03
caudal middle frontal	Thickness	Dup v. NC	-0.21	0.07	3.0e-03
cuneus	Thickness	Dup v. NC	-0.11	0.06	0.13
entorhinal	Thickness	Dup v. NC	-0.15	0.07	0.04
frontal pole	Thickness	Dup v. NC	-0.23	0.07	1.4e-03
fusiform	Thickness	Dup v. NC	-0.21	0.07	4.1e-03
inferior parietal	Thickness	Dup v. NC	-0.13	0.06	0.08
inferior temporal	Thickness	Dup v. NC	-0.15	0.07	0.04
insula	Thickness	Dup v. NC	-0.28	0.07	1.9e-04
isthmus cingulate	Thickness	Dup v. NC	-0.10	0.05	0.17
lateral occipital	Thickness	Dup v. NC	-0.08	0.04	0.29
lateral orbitofrontal	Thickness	Dup v. NC	-0.24	0.07	9.8e-04
lingual	Thickness	Dup v. NC	-0.13	0.06	0.08
medial orbito frontal	Thickness	Dup v. NC	-0.22	0.07	2.2e-03
middle temporal	Thickness	Dup v. NC	-0.21	0.07	3.2e-03
para central	Thickness	Dup v. NC	-0.22	0.07	2.1e-03
parahippocampal	Thickness	Dup v. NC	-0.14	0.07	0.05
pars opercularis	Thickness	Dup v. NC	-0.26	0.07	3.3e-04
pars orbitalis	Thickness	Dup v. NC	-0.24	0.07	1.2e-03
pars triangularis	Thickness	Dup v. NC	-0.23	0.07	1.7e-03
pericalcarine	Thickness	Dup v. NC	-0.13	0.07	0.07
post central	Thickness	Dup v. NC	-0.27	0.07	2.3e-04
posterior cingulate	Thickness	Dup v. NC	-0.15	0.07	0.04
pre central	Thickness	Dup v. NC	-0.23	0.07	1.3e-03
precuneus	Thickness	Dup v. NC	-0.15	0.07	0.04
rostral anterior cingulate	Thickness	Dup v. NC	-0.24	0.07	1.2e-03
rostral middle frontal	Thickness	Dup v. NC	-0.23	0.07	1.7e-03
superior frontal	Thickness	Dup v. NC	-0.15	0.07	0.04
superior parietal	Thickness	Dup v. NC	-0.07	0.03	0.36
superior temporal	Thickness	Dup v. NC	-0.20	0.07	6.1e-03
supramarginal	Thickness	Dup v. NC	-0.15	0.07	0.04
temporal pole	Thickness	Dup v. NC	-0.15	0.07	0.04
transverse temporal	Thickness	Dup v. NC	-0.06	0.03	0.40
banks superior temporal	Thickness	Dosage	-0.20	0.06	4.1e-04
caudal anterior cingulate	Thickness	Dosage	-0.14	0.06	0.01

caudal middle frontal	Thickness	Dosage	-0.24	0.06	3.2e-05
cuneus	Thickness	Dosage	-0.05	0.06	0.37
entorhinal	Thickness	Dosage	-0.11	0.06	0.07
frontal pole	Thickness	Dosage	-0.22	0.06	1.6e-04
fusiform	Thickness	Dosage	-0.14	0.06	0.02
inferior parietal	Thickness	Dosage	-0.16	0.06	4.5e-03
inferior temporal	Thickness	Dosage	-0.10	0.06	0.07
insula	Thickness	Dosage	-0.27	0.06	3.1e-06
isthmus cingulate	Thickness	Dosage	-0.17	0.06	2.9e-03
lateral occipital	Thickness	Dosage	-0.09	0.06	0.11
lateral orbitofrontal	Thickness	Dosage	-0.22	0.06	1.4e-04
lingual	Thickness	Dosage	-0.09	0.06	0.12
medial orbito frontal	Thickness	Dosage	-0.23	0.06	5.9e-05
middle temporal	Thickness	Dosage	-0.18	0.06	2.0e-03
para central	Thickness	Dosage	-0.18	0.06	1.6e-03
parahippocampal	Thickness	Dosage	-0.14	0.06	0.02
pars opercularis	Thickness	Dosage	-0.28	0.06	8.6e-07
pars orbitalis	Thickness	Dosage	-0.24	0.06	2.6e-05
pars triangularis	Thickness	Dosage	-0.27	0.06	2.7e-06
pericalcarine	Thickness	Dosage	-0.02	0.06	0.77
post central	Thickness	Dosage	-0.34	0.06	4.0e-09
posterior cingulate	Thickness	Dosage	-0.20	0.06	5.2e-04
pre central	Thickness	Dosage	-0.22	0.06	1.4e-04
precuneus	Thickness	Dosage	-0.17	0.06	3.2e-03
rostral anterior cingulate	Thickness	Dosage	-0.18	0.06	1.6e-03
rostral middle frontal	Thickness	Dosage	-0.30	0.06	1.4e-07
superior frontal	Thickness	Dosage	-0.27	0.06	3.7e-06
superior parietal	Thickness	Dosage	-0.14	0.06	0.02
superior temporal	Thickness	Dosage	-0.16	0.06	5.6e-03
supramarginal	Thickness	Dosage	-0.16	0.06	4.9e-03
temporal pole	Thickness	Dosage	-0.06	0.06	0.29
transverse temporal	Thickness	Dosage	-0.07	0.06	0.22

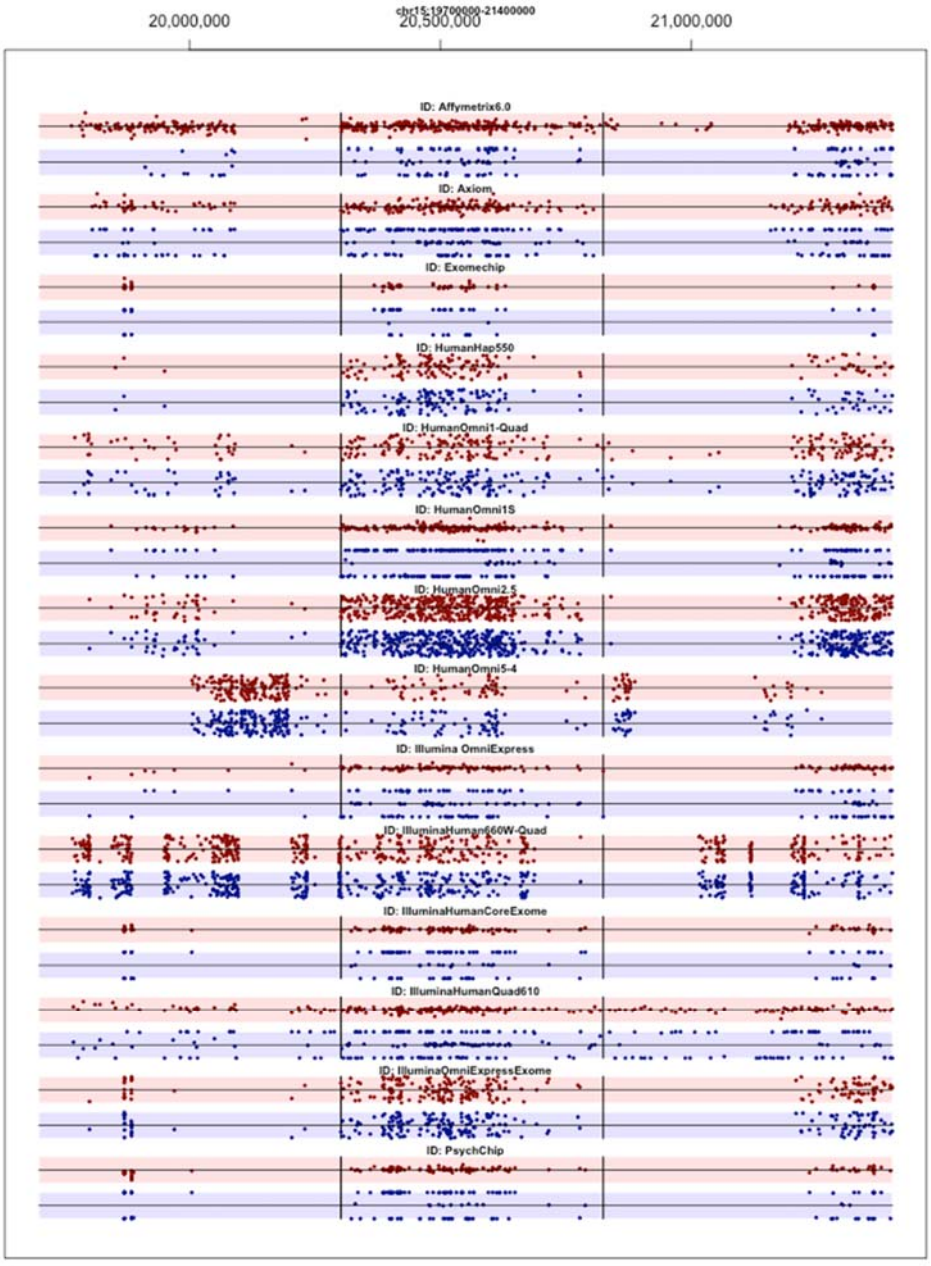
Note: Del=deletion carriers, NC=non-carriers, Dup=duplication carriers, SE=standard error.

eFigure 1. Age distribution per cohort contributing data to the current study, with age in years on the y-axis and cohort name on the x-axis



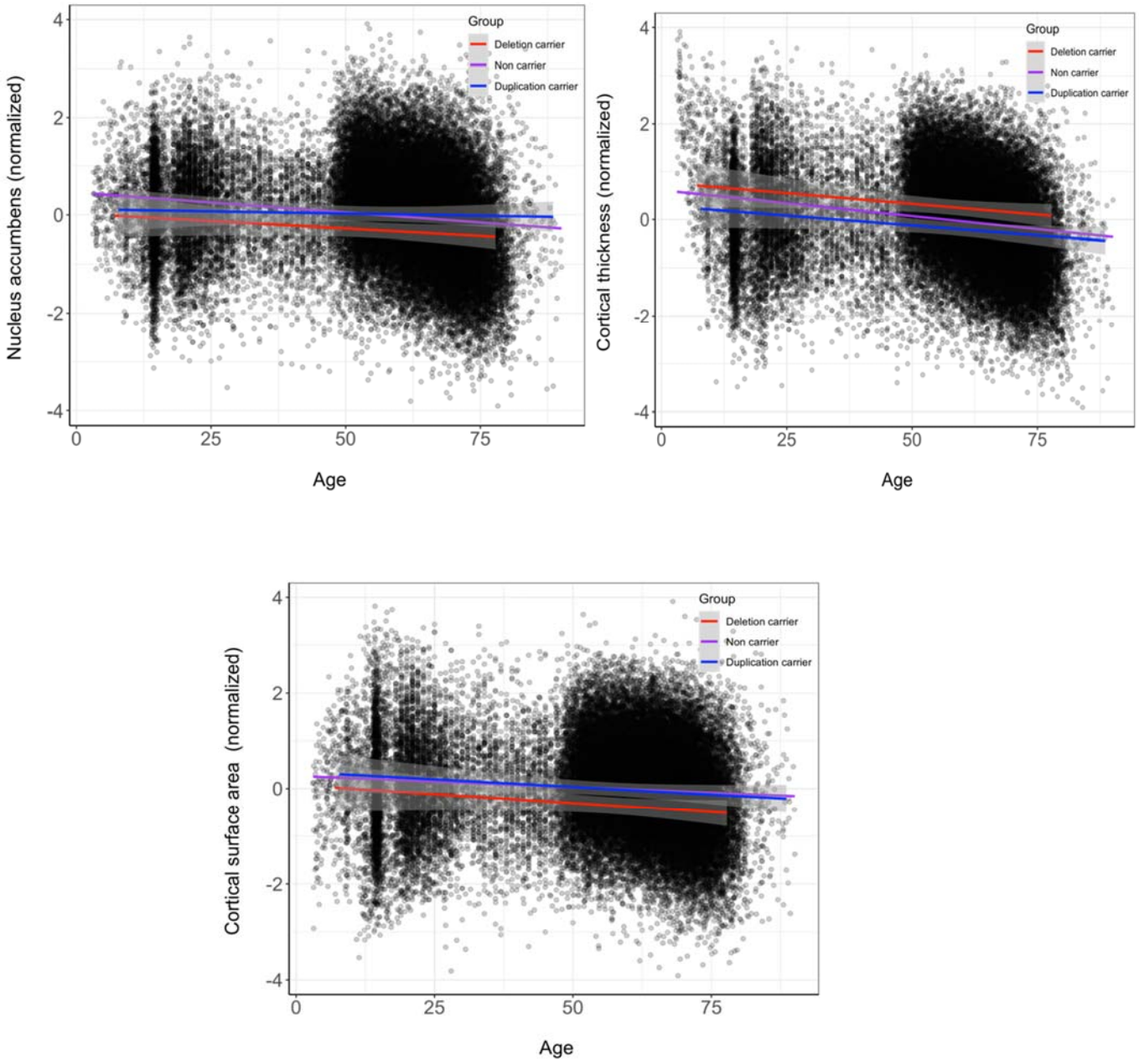
eFigure 2. Coverage of the 15q11.2 BP1-BP2 region by the arrays used across cohorts

Log R ratio is shown in red, B-allele Frequency in blue. The vertical black lines delimit the boundaries of the 15q11.2 (BP1-2) region. HumanHap550, HumanOmniQuad1-Quad, HumanOmni2.5, HumanOmni5-4, IlluminaHuman660-Quad, IlluminaOmniExpressExome are mock data, rest is based on real data. Coordinates are in NCBI36/hg18.

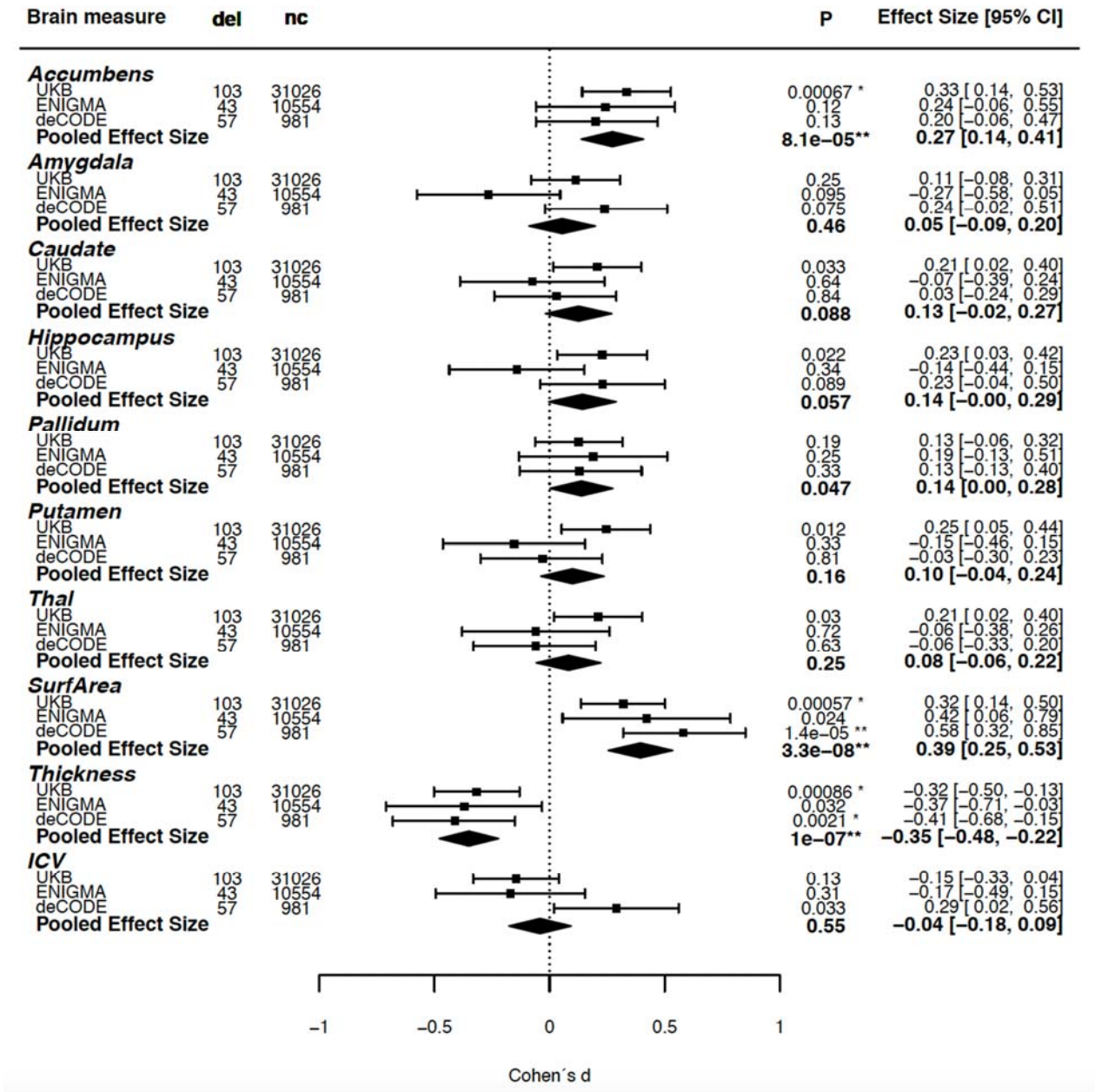


eFigure 3. Scatterplots of the relation between age and the significant primary outcome measures (nucleus accumbens, mean cortical thickness, and total surface area)

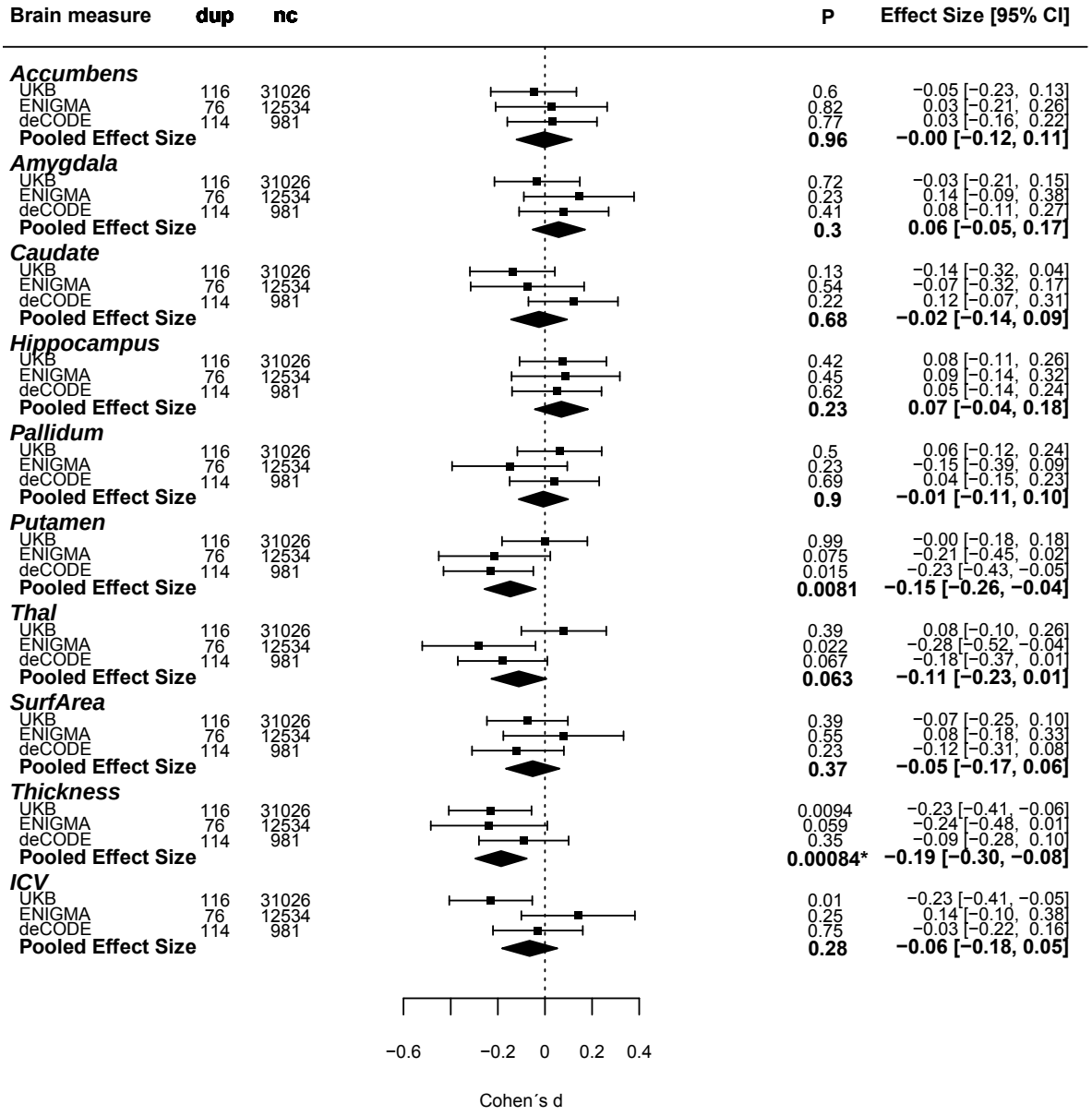
On the x-axis is age, and on the y-axis is the inverse-normalized brain measure, pre-residualized for sex, scanner site and intracranial volume. The three regression lines shown, representing the three carrier groups as indicated in the legend, were obtained from a linear regression of copy number, age, and their interaction.



eFigure 4. Forest plot of the observed effects (Cohen *d*) of the *t* test between 15q11.2 BP1-BP2 deletion carriers and noncarriers on the primary outcome measures, split into UK Biobank, ENIGMA, and deCODE Genetics populations



eFigure 5. Forest plot of the observed effects (Cohen *d*) of the *t* test between 15q11.2 BP1-BP2 duplication carriers and noncarriers on the primary outcome measures, split into UK Biobank, ENIGMA, and deCODE Genetics populations



eFigure 6. Forest plot of the observed effects (regression coefficients) from the linear regression analyses of 15q11.2 BP1-BP2 copy number on the primary outcome measures, split into UK Biobank, ENIGMA, and deCODE Genetics populations