Supplementary Figures and Figure Legends

S1: Demographics and analysis

Overview of demographics (left). Per cohort, an age distribution is displayed, based on mean and standard deviation of the age at baseline. Cohorts of European ancestry are displayed in green, non-European cohorts are displayed in yellow. On the right, the total number of included subjects is displayed and a pie-chart of the distribution of diagnostic groups (pink) in cohorts containing diagnostic groups and subjects not belonging to diagnostic groups – often healthy subjects (aqua). Overview of analysis pipeline (right).

S2: Correlations between change rates

Pearson correlations between rates of change in the largest adolescent cohort (left) and the largest cohort in older age (right). The size of the correlations is displayed by color and size of the circles.

S3: Phenotype and GWAS overview

Top row: Rates of change per cohort and estimated trajectories of rate of change with confidence intervals (in green) are displayed above. The size of the points represents the relative size of the cohorts. Only cohorts that satisfy N>75 and mean interval > 0.5 years are shown. The estimated trajectories of the volumes themselves are displayed below, for all subjects (solid line) and excluding diagnostic groups (dashed line). For genome-wide significant hits, a locus plot is displayed on the right when applicable. Locus plots were created with locus zoom (Pruim et al., 2010)
Bottom rows: Manhattan plots and QQ plots for age-independent, linear age-dependent and quadratic age-dependent GWASses.

S3A: Amygdala
S3B: Caudate
S3C: Cerebellum gray matter
S3D: Cerebellum white matter
S3E: Cerebral white matter
S3F: Cortex volume
S3G: Cortical thickness
S3H: Hippocampus
S3I: Lateral ventricles
S3J: Nucleus accumbens
S3K: Pallidum
S3L: Putamen
S3M: Surface area
S3N: Thalamus
S3O: Total brain

S4: eQTL and chromatin interaction mapping for genome-wide significant loci

Circos plots demonstrating the results of eQTL and chromatin interaction mapping for prioritized loci on chromosome 5, 12, 13, 16 and 21, respectively (A-E). The outermost layer depicts SNPs with a $P < 0.05$ in a Manhattan-style plot. SNPs in detected genomic locus are colored according to their r2 value to the most significant variant at the locus. Y-axis values range from 0 to the maximum –log10(P-value) of the SNPs. The second and third layer represent the chromosome ring, where the locus is colored in blue. Genes that are mapped only by chromatin interactions or only by eQTLs, are colored orange or green, respectively, and interactions are shown by ribbons.

S5: Top SNPs for genome-wide significant loci and genes

Age-(in)dependent effect of the significant SNPs/top-SNPs in significant gene. The top figure displays the estimated effect of the tested allele on the rate of change in each cohort against age (where applicable). The red line displays the estimated age-effect with 95% confidence interval from the meta-analysis/meta-regression. The bottom figure shows a visualization of the effect of the tested allele on the phenotype itself. The red line represents the lifespan trajectory for the carriers of the tested allele, the black line represents the lifespan trajectory of the carriers of the alternative allele. *When the top-SNP did not have a reference SNP cluster ID (rsID), the highest-ranked SNP that had an rsID was displayed.

S5A: *TMCO2* for thalamus change

S5B: *EPAS1* for cerebellum gray matter change
S5C: *PID1* for cerebellum gray matter change
S5D: *AC027309.1* for cortical thickness change
S5E: rs6864758 for surface area change
S5F: *TMEM30A* for putamen change
S5G: *STEAP1B* for total brain change
S5H: *TMC1* for cerebellum gray matter change
S5I: rs10674957 / *THRDE* for cerebellum white matter change
S5J: rs573983368 / *DACH1* for cerebral white matter change
S5K: rs72772740 / *GPR139* for lateral ventricle change
S5L: *ABR* for cortex volume change
S5M: *MYOCD-AS1* for cerebral white matter change
S5N: *PLCD3* for caudate change
S5O: *OR7D2* for cerebellar white matter change
S5P: *APOE* for amygdala change
S5Q: *APOE* for hippocampus change
S5R: rs449998 / *DSCAM* for nucleus accumbens change

S6: Lookup longitudinal versus cross-sectional GWAS

Expected versus actual overlap for the first top-1000 ranked genes. Results from age-independent analysis (red), linear age-dependent analysis (green) and quadratic age-dependent analysis (blue) are shown in one figure. Top-N ranks are marked for nominally (dots) or FDR-corrected (triangles) significance for over- or under representation of genes associated with brain structural rates of change amongst the top-N ranked genes for cross-sectional brain measures. For lateral ventricles and cerebellum gray and white matter, summary statistics for the cross-sectional phenotype were only available for left and right lateral and inferior lateral ventricle, and left and right cerebellum gray and white matter, separately. Therefore, for those measures we show curves for overlap with the separate cross-sectional phenotypes.

S7: Overlap with other phenotypes

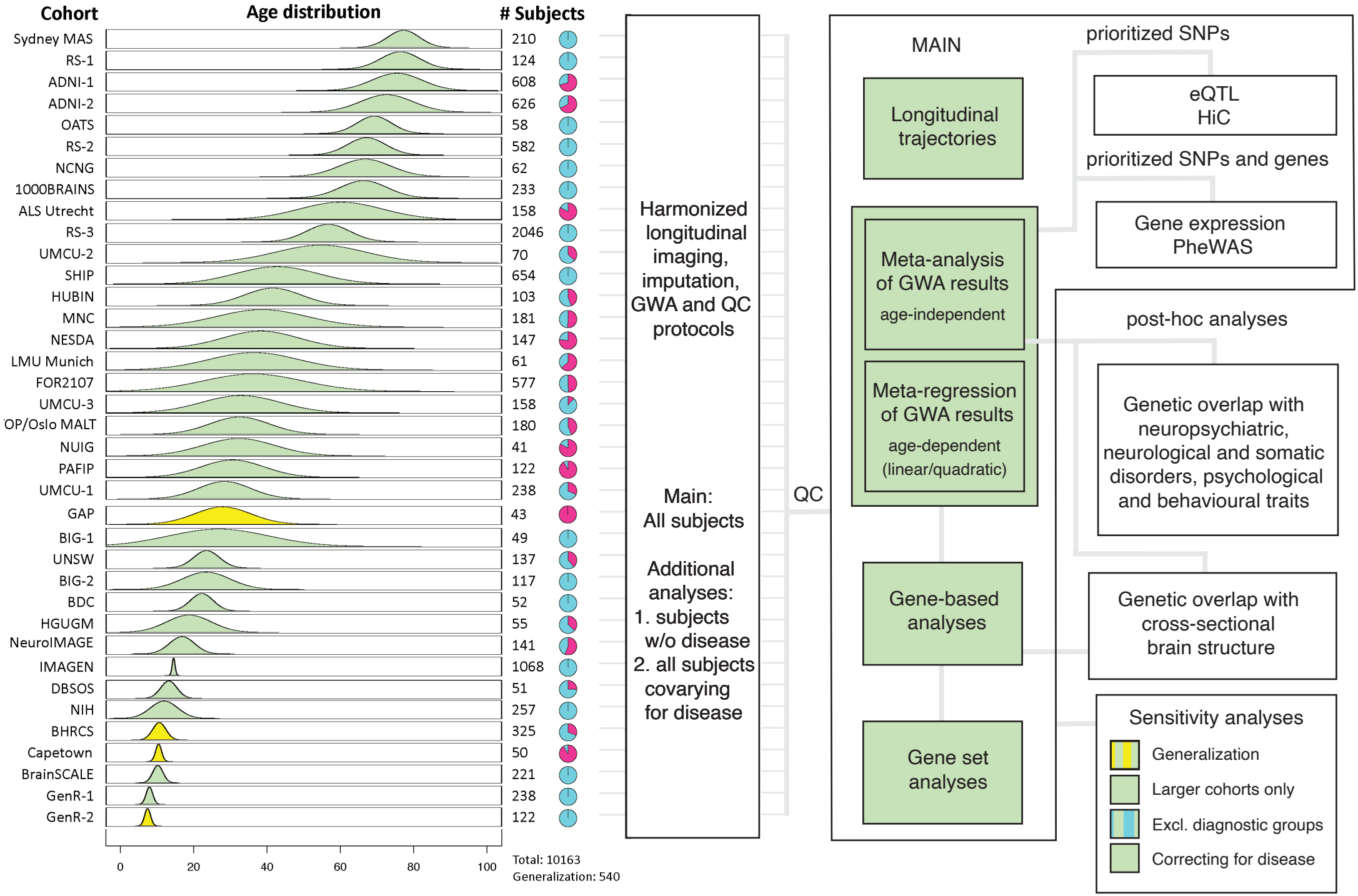
iSECA results for overlap between GWAS summary statistics of structural brain change with GWAS summary statistics of other phenotypes testing for pleiotropy (A), concordance (B) and discordance of effects (C). Pleiotropy results based on the subgroup excluding diagnostic groups are shown in (D). Colors display the significance level on a 10-log scale. Associations that are significant are marked with *.

S8: Gene expression for prioritized genes

Heatmaps display normalized expression value (zero mean normalization of log2 transformed expression) for prioritized genes, for expression in various tissue types (GTEx v8 RNAseq data; A) and expression at various ages (BrainSpan data B). Darker red means higher relative expression of that gene in each label, compared to a darker blue color in the same label. In the GTEx data three of the prioritized genes were not present (*DACH1*, *AC027309.1* and *MYOCD-AS1*) and in BrainSpan data two genes could not be identified (*AC027309.1* and *MYOCD-AS1*).

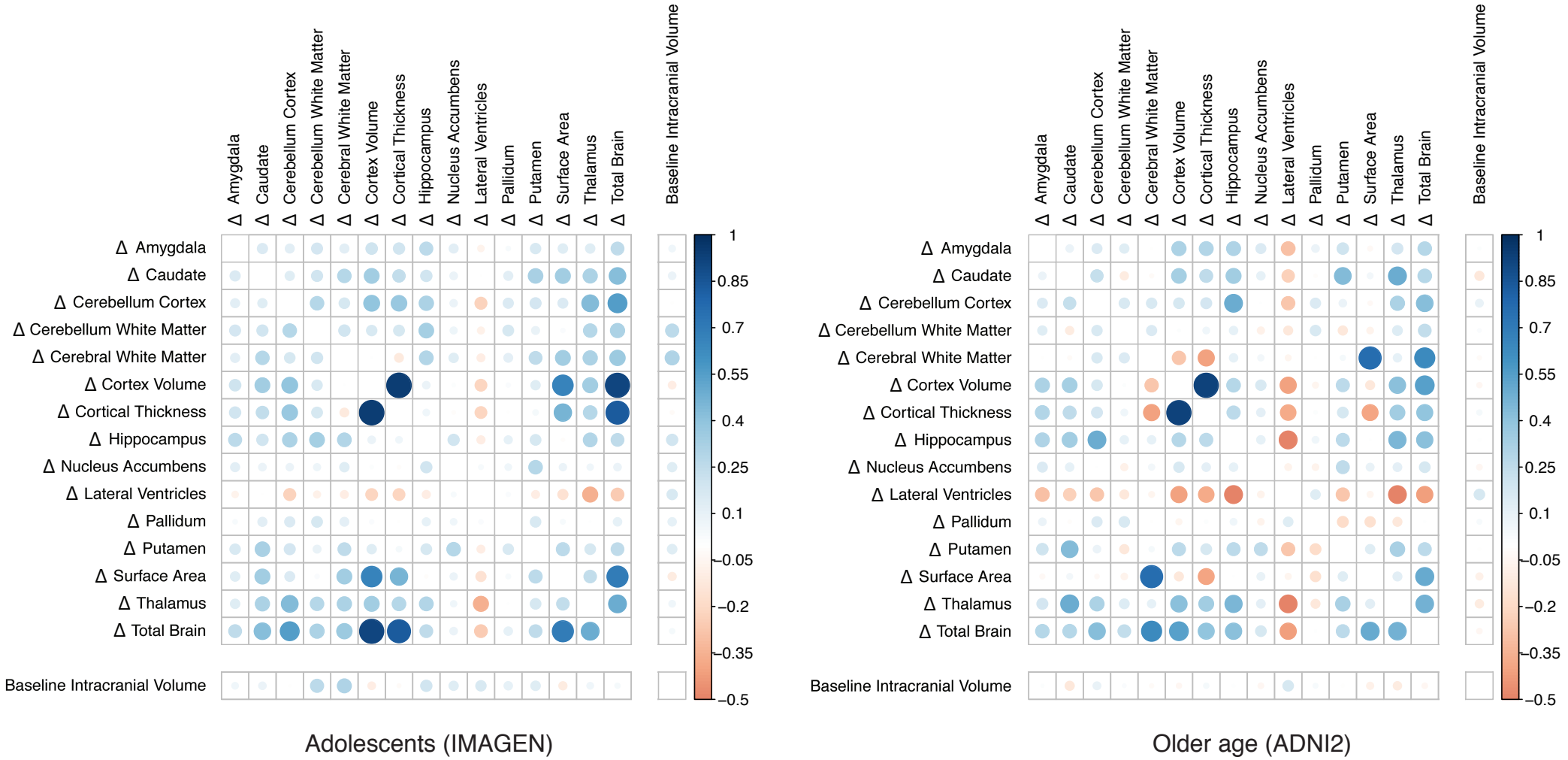
S9: PheWas results for study-wide significant genes *TMCO2* (A) and *GPR139* (B).

S1

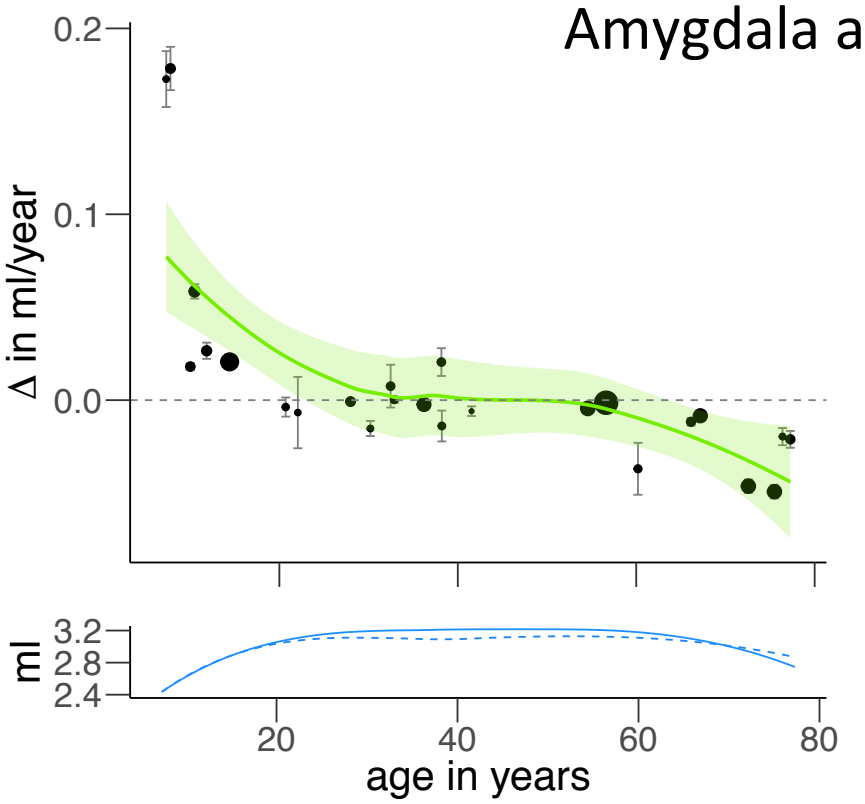

Cohort
Age distribution
Subjects
Sydney MAS 210
RS-1 124
ADNI-1 608
ADNI-2 626
OATS 58
RS-2 582
NCNG 62
1000BRAINS 233
ALS Utrecht 158
RS-3 2046
UMCU-2 70
SHIP 654
HUBIN 103
MNC 181
NESDA 147
LMU Munich 61
FOR2107 577
UMCU-3 158
OP/Oslo MALT 180
NUIG 41
PAFIP 122
UMCU-1 238
GAP 43
BIG-1 49
UNSW 137
BIG-2 117
BDC 52
HGUGM 55
NeuroIMAGE 141
IMAGEN 1068
DBSOS 51
NIH 257
BHRCS 325
Capetown 50
BrainSCALE 221
GenR-1 238
GenR-2 122
0 20 40 60 80 100
Total: 10163
Generalization: 540
Harmonized longitudinal imaging, imputation, GWA and QC protocols
Main: All subjects
Additional analyses: 1. subjects w/o disease 2. all subjects covarying for disease
QC
MAIN
Longitudinal trajectories
Meta-analysis of GWA results
age-independent
Meta-regression of GWA results
age-dependent (linear/quadratic)
Gene-based analyses
Gene set analyses
prioritized SNPs
eQTL
HiC
prioritized SNPs and genes
Gene expression
PheWAS
post-hoc analyses
Genetic overlap with neuropsychiatric, neurological and somatic disorders, psychological and behavioural traits
Genetic overlap with cross-sectional brain structure
Sensitivity analyses
Generalization
Larger cohorts only
Excl. diagnostic groups
Correcting for disease

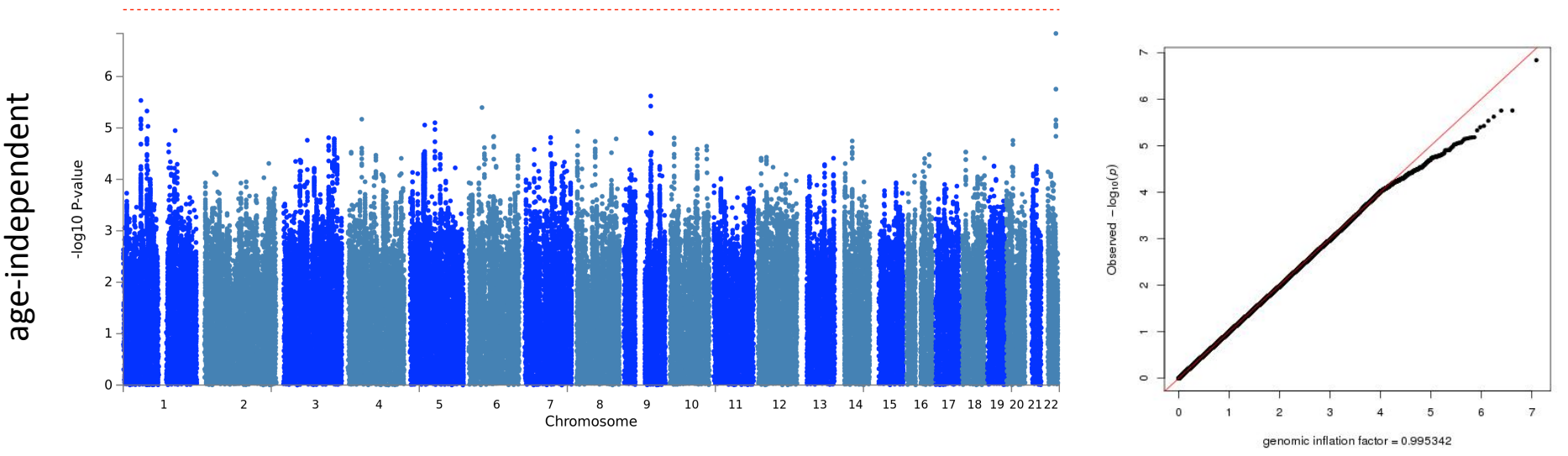
S2

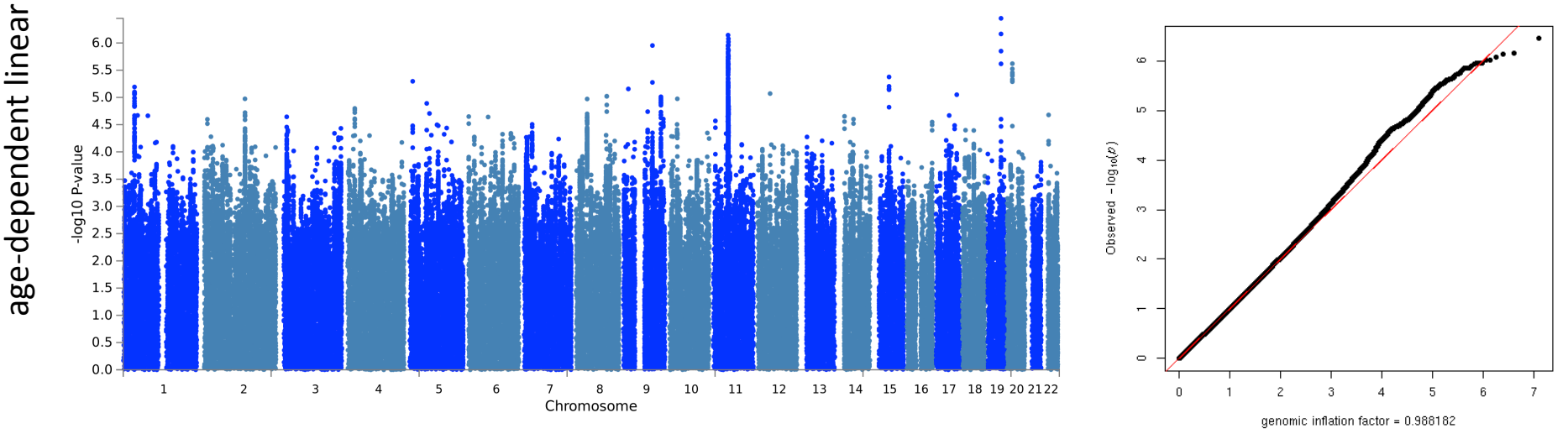
Correlations between rates of change

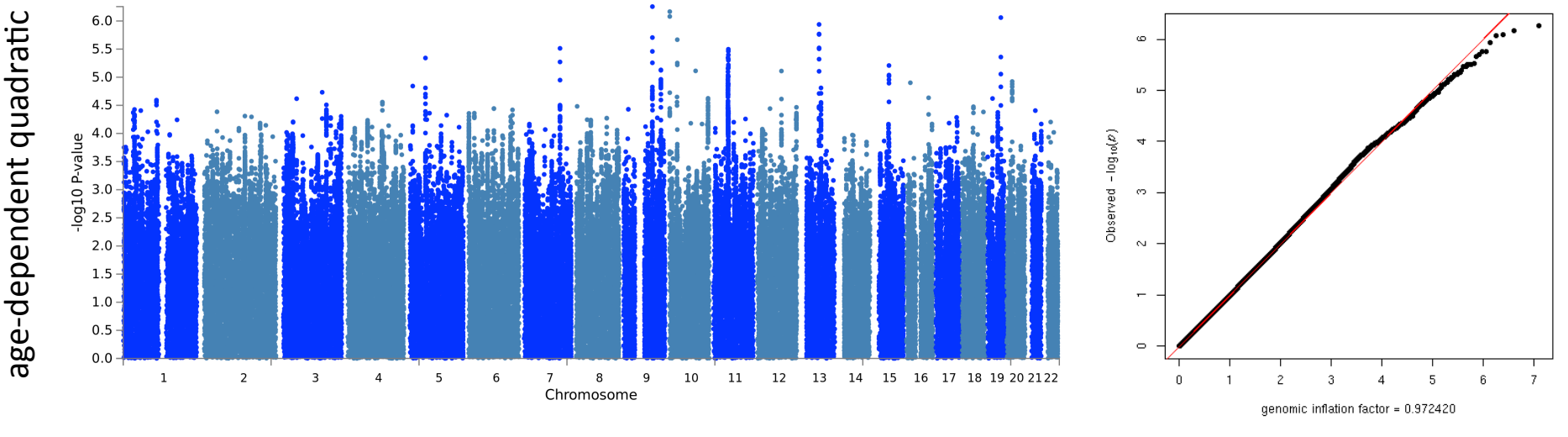


S3A

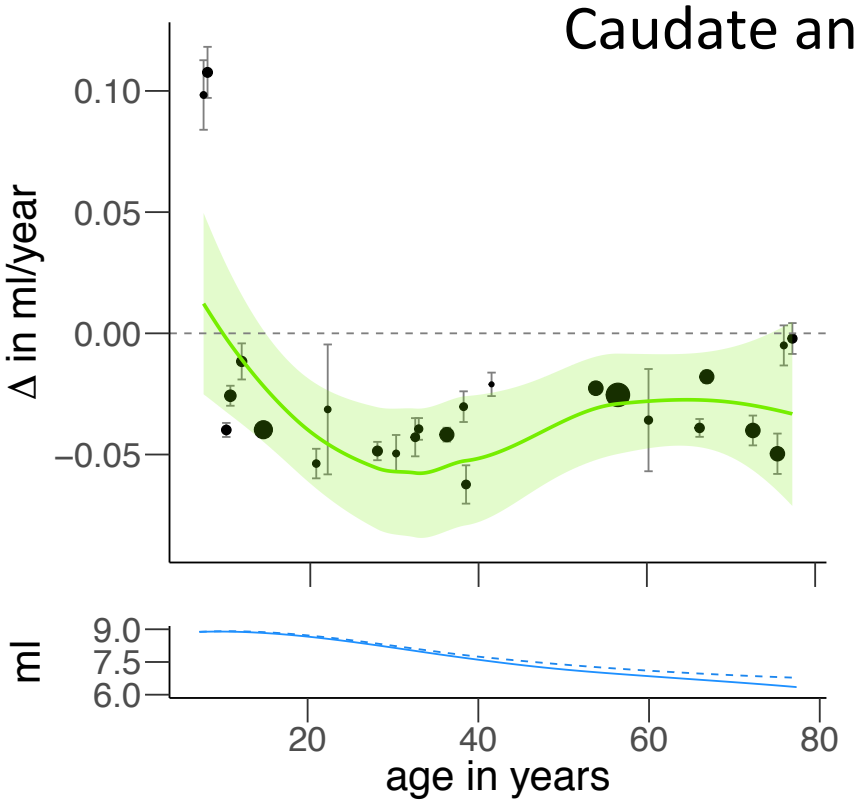

Amygdala annual change rate
Δ in ml/year
0.2
0.1
0.0
ml
3.2
2.8
2.4
20
40
60
80
age in years


age-independent
-log10 P-value
Chromosome
Observed −log10(p)
genomic inflation factor = 0.995342

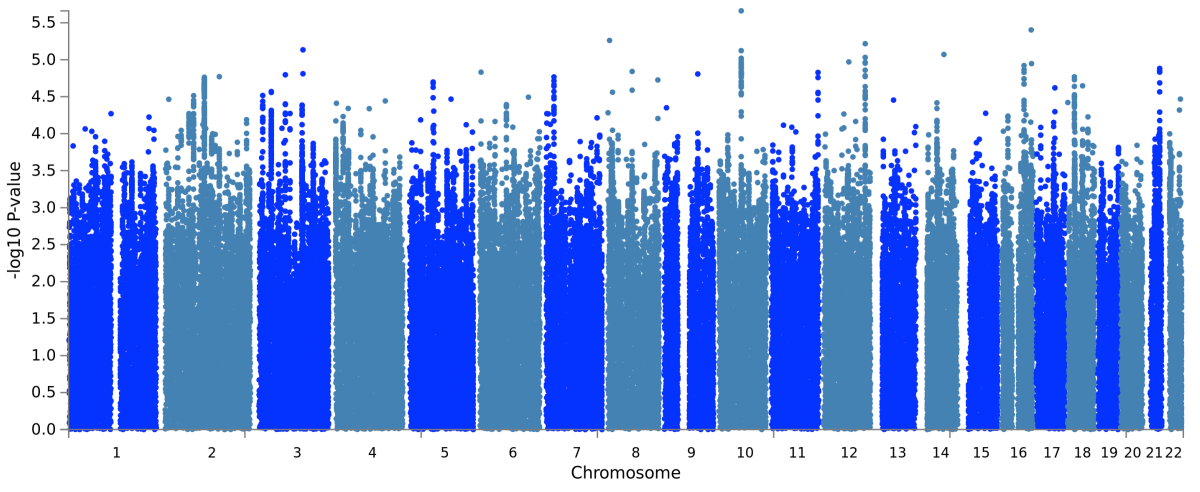

age-dependent linear
-log10 P-value
Chromosome
Observed −log10(p)
genomic inflation factor = 0.988182

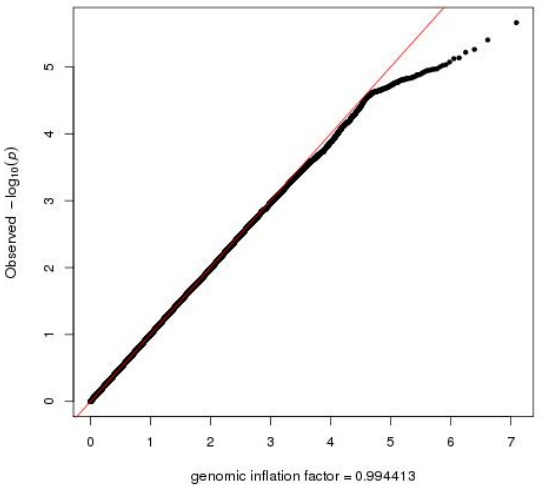

age-dependent quadratic
-log10 P-value
Chromosome
Observed −log10(p)
genomic inflation factor = 0.972420

S3B

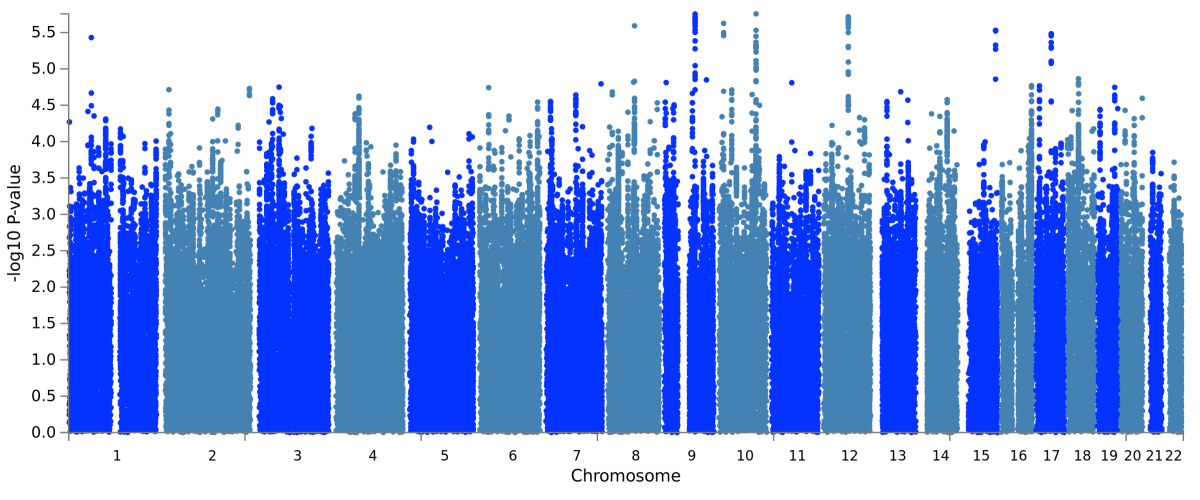


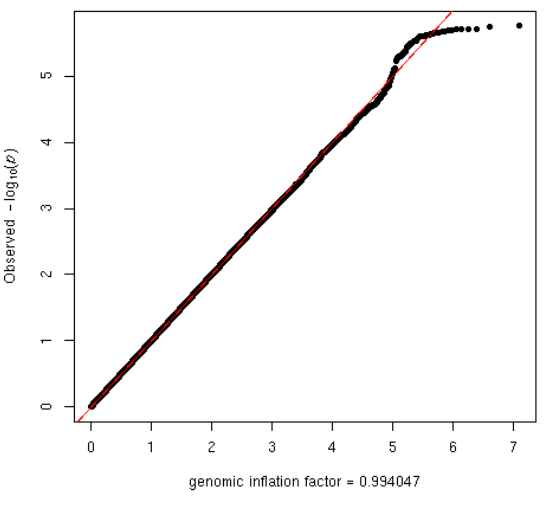
age-independent



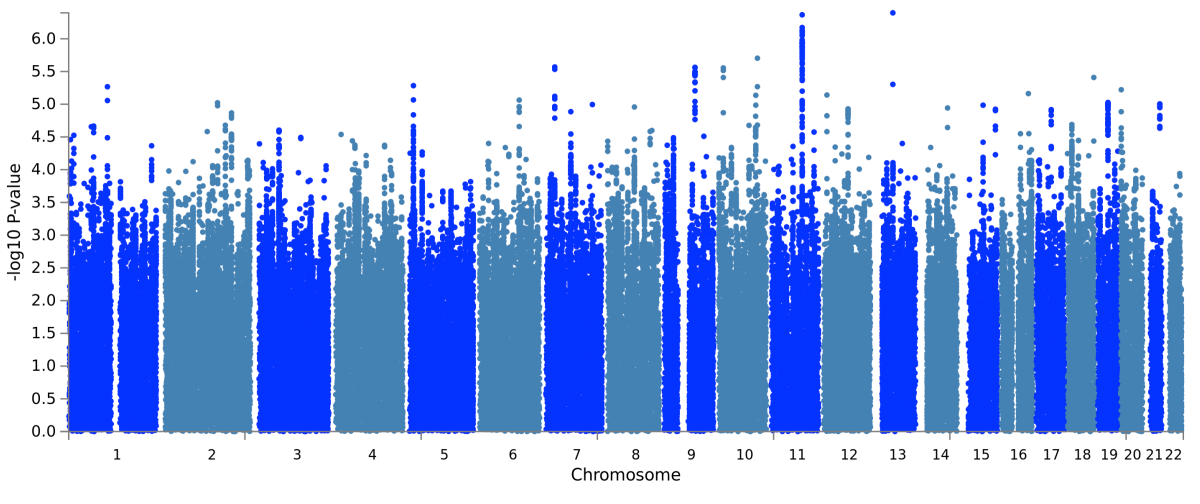


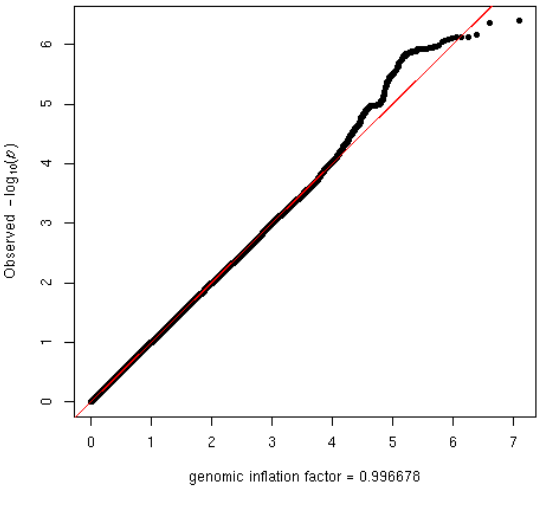
age-dependent linear



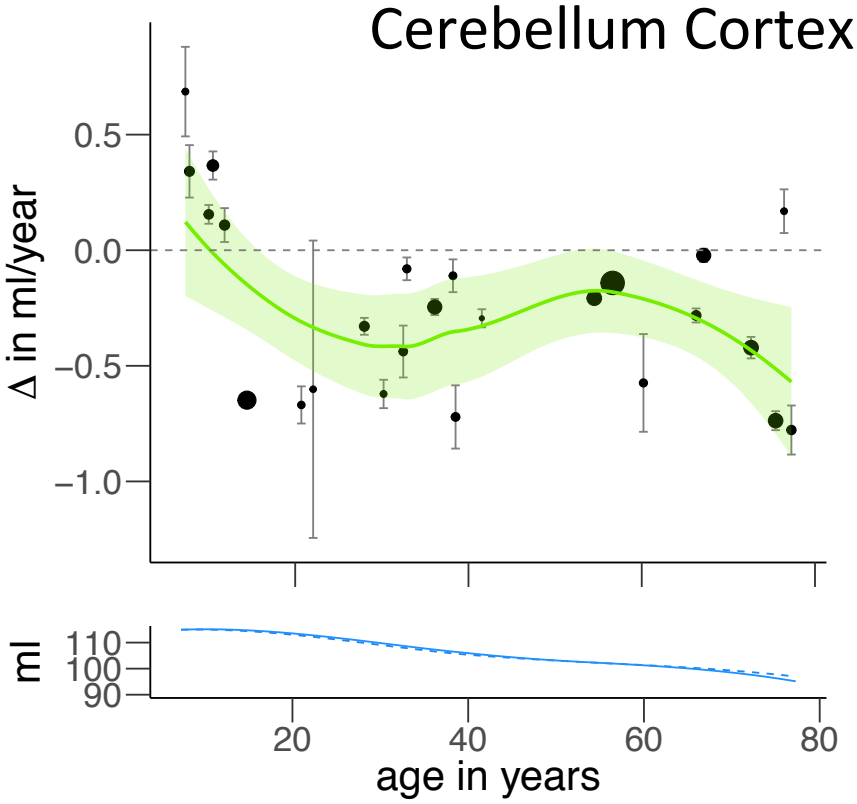


age-dependent quadratic

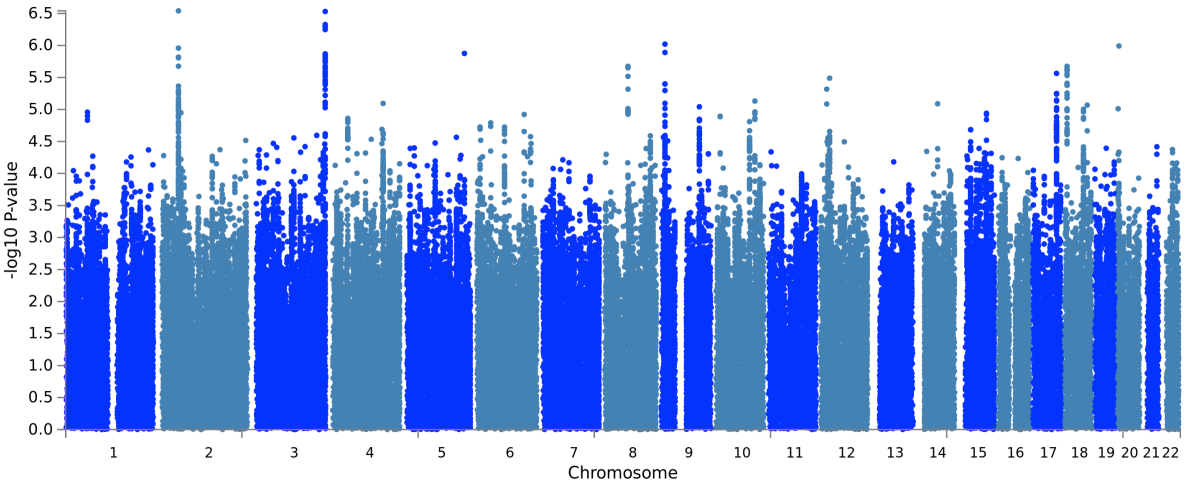


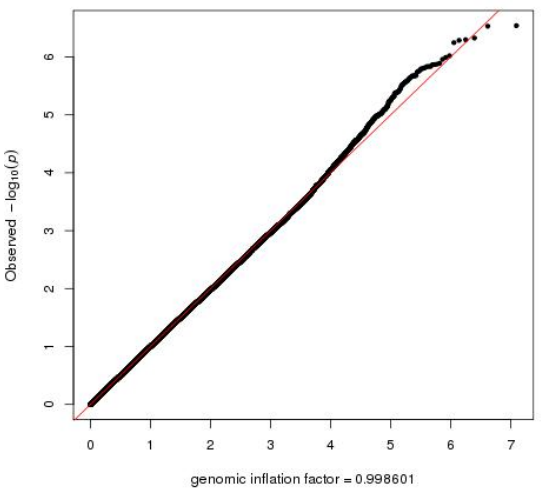


S3C

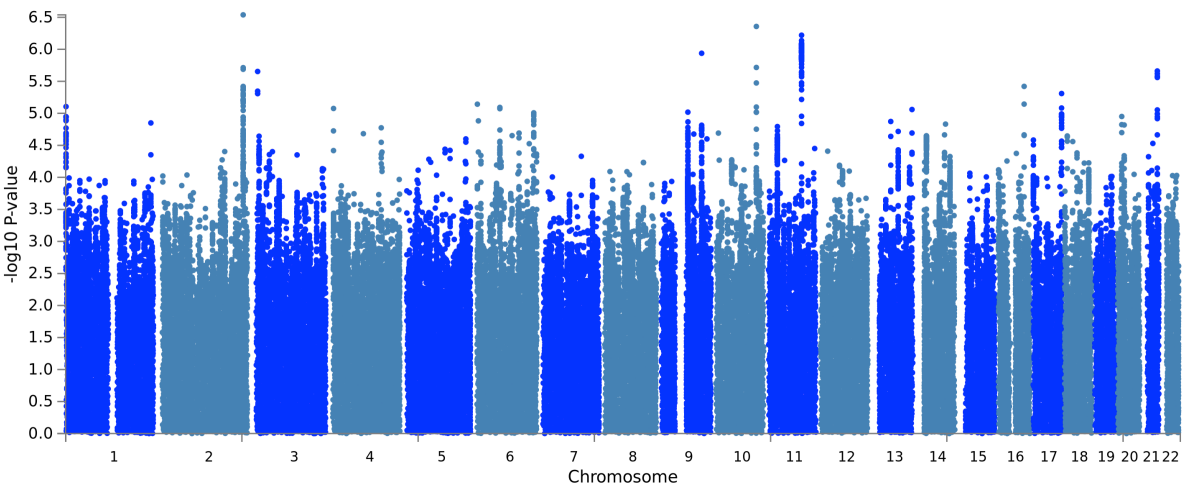


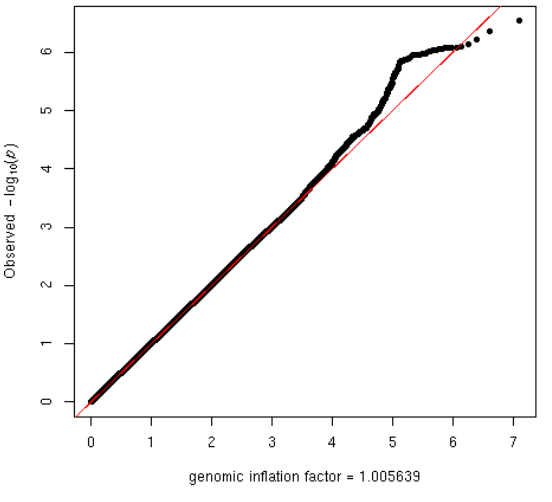
age-independent



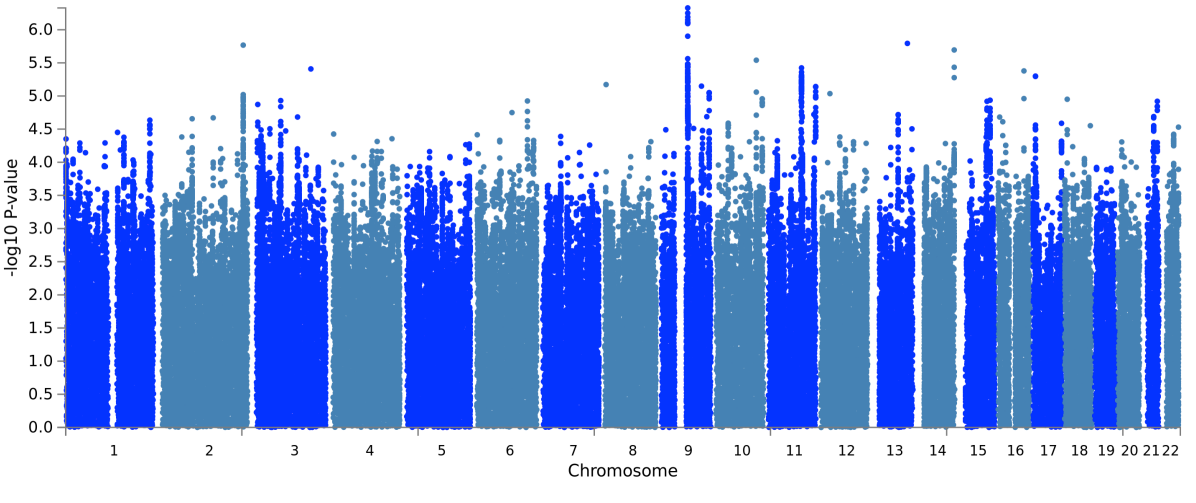


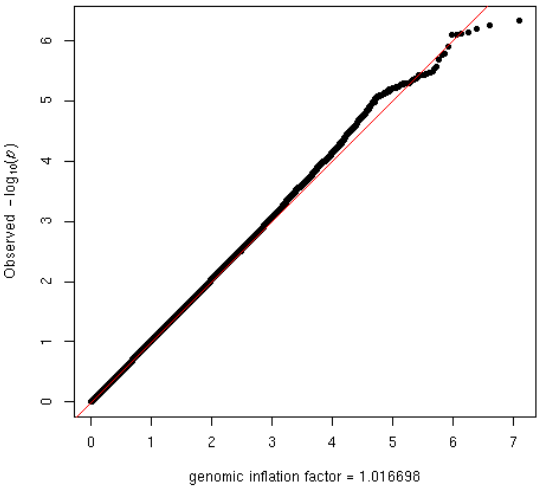
age-dependent linear





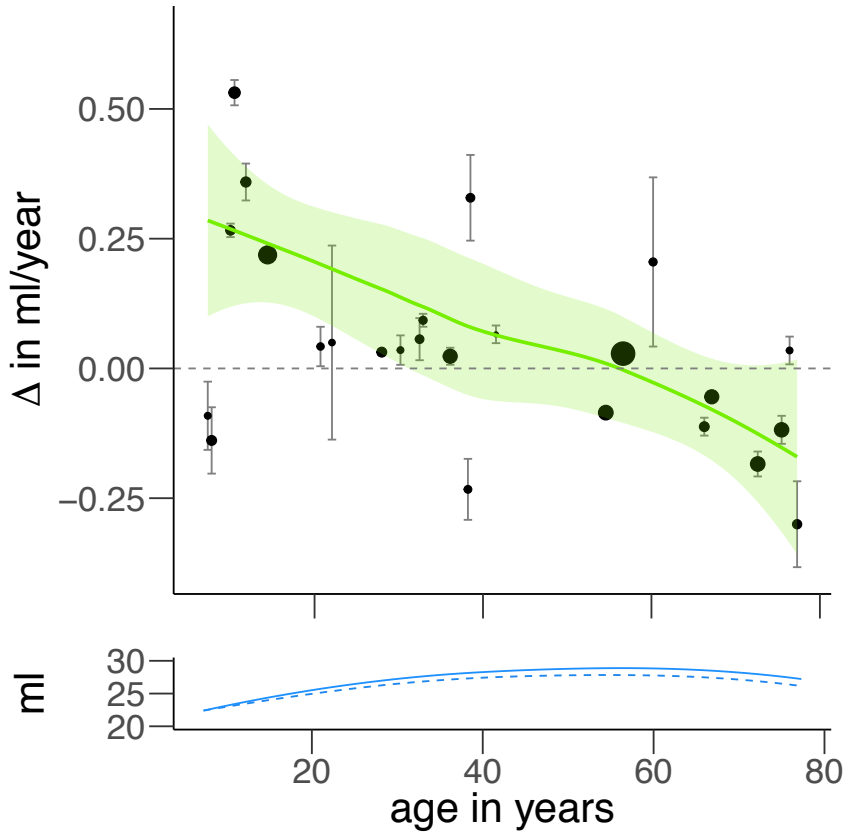
age-dependent quadratic

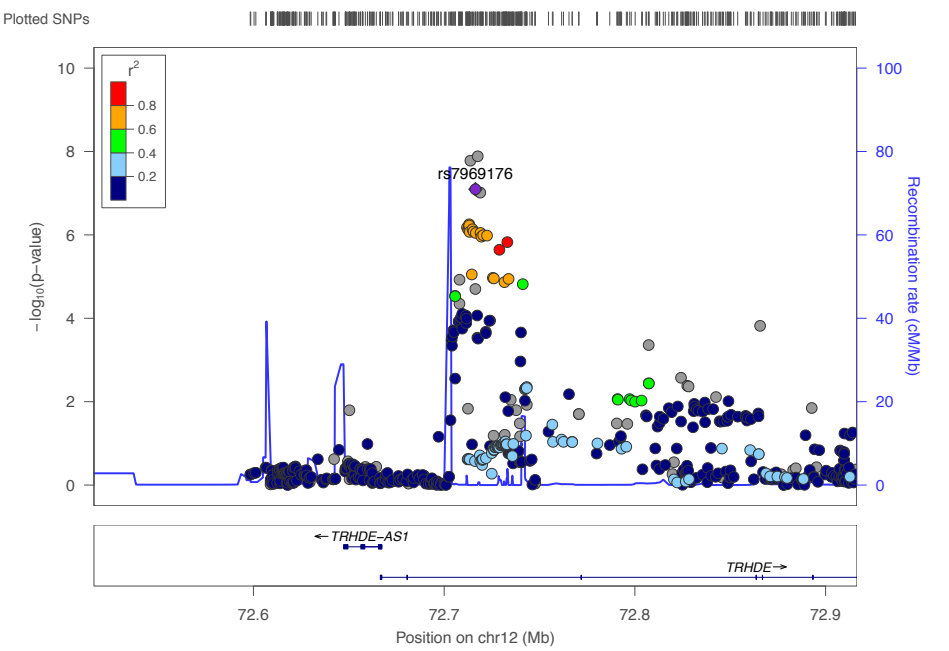




S3D

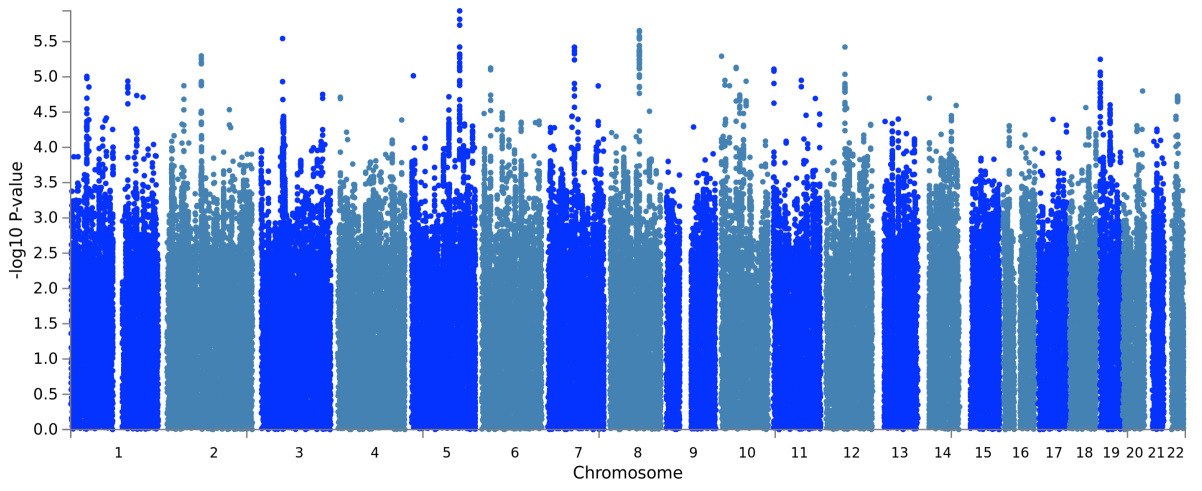
Cerebellum white matter annual change rate

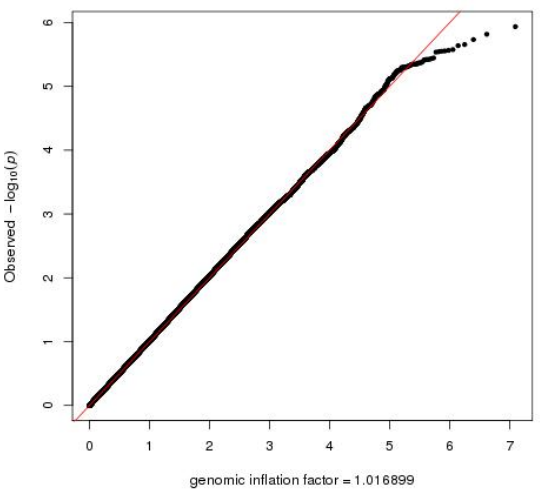




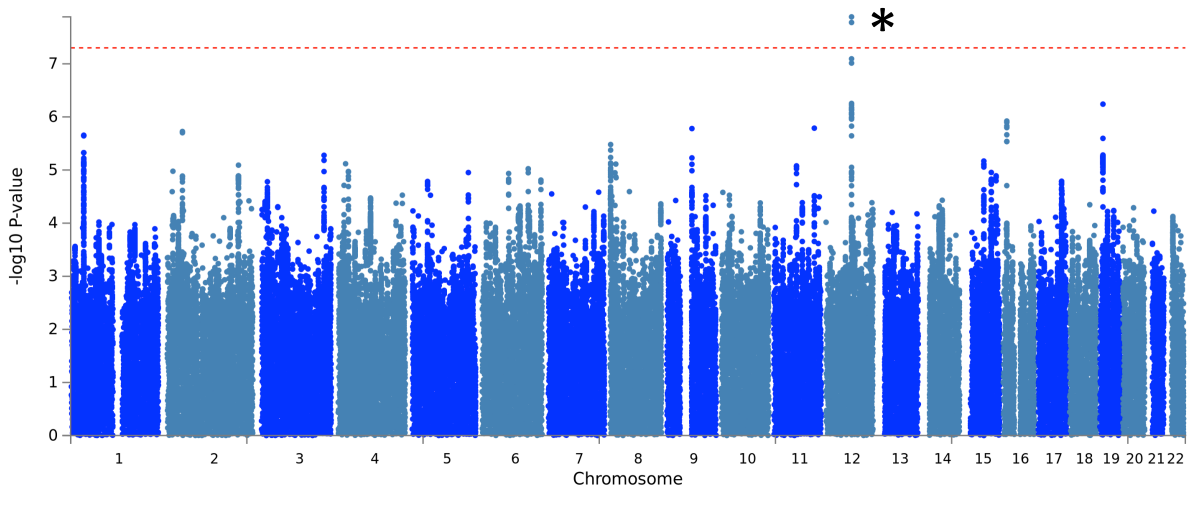
* locus plot of genome wide significant effect
no LD information present for top SNP rs10674957

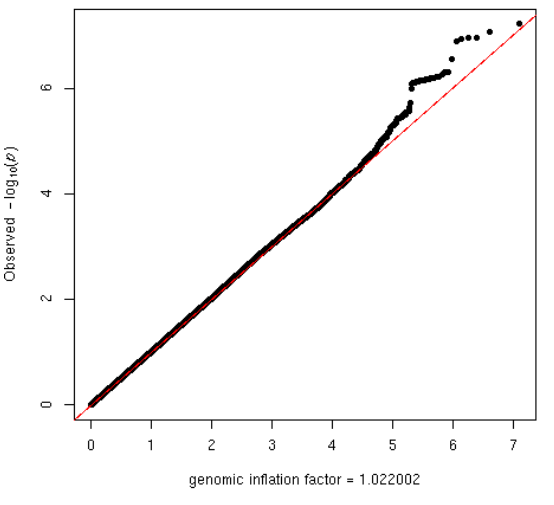
age-independent



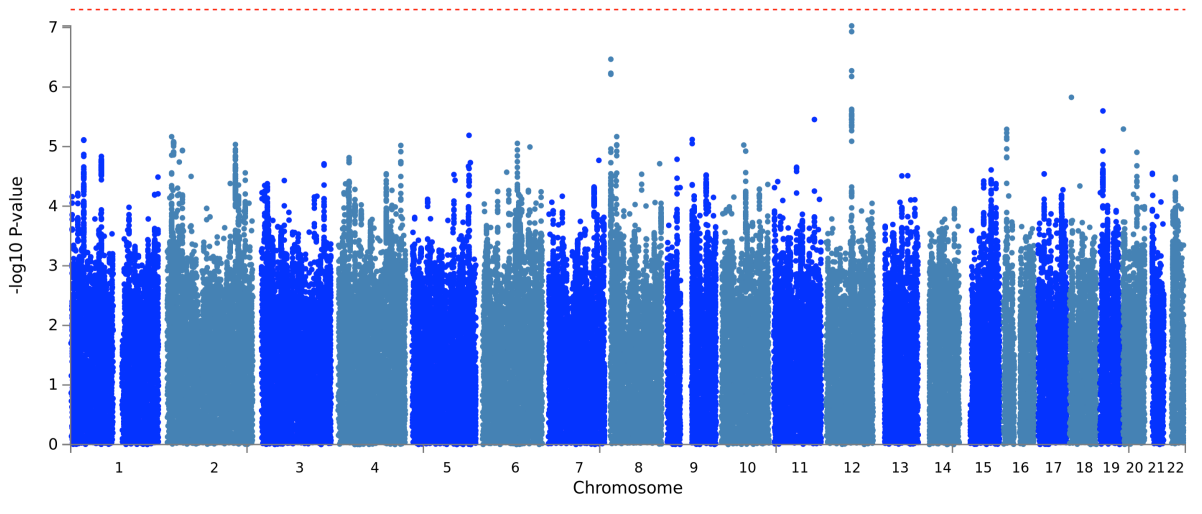


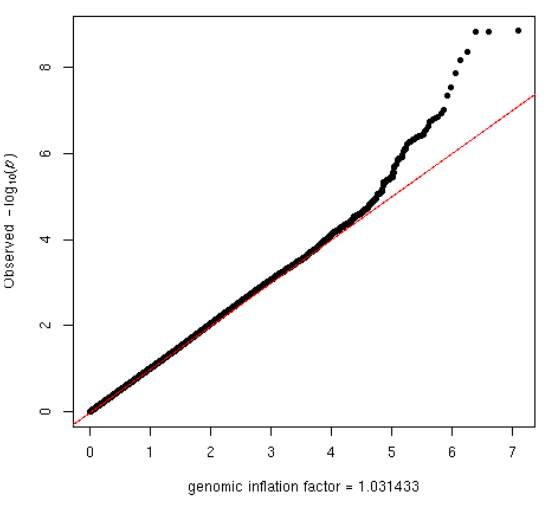
age-dependent linear





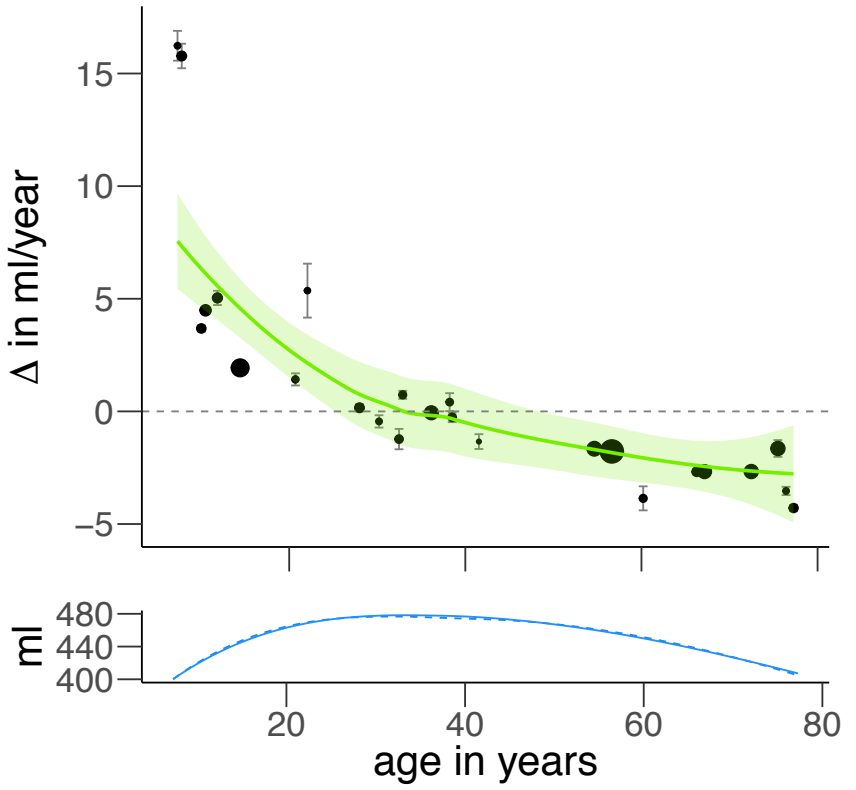
age-dependent quadratic

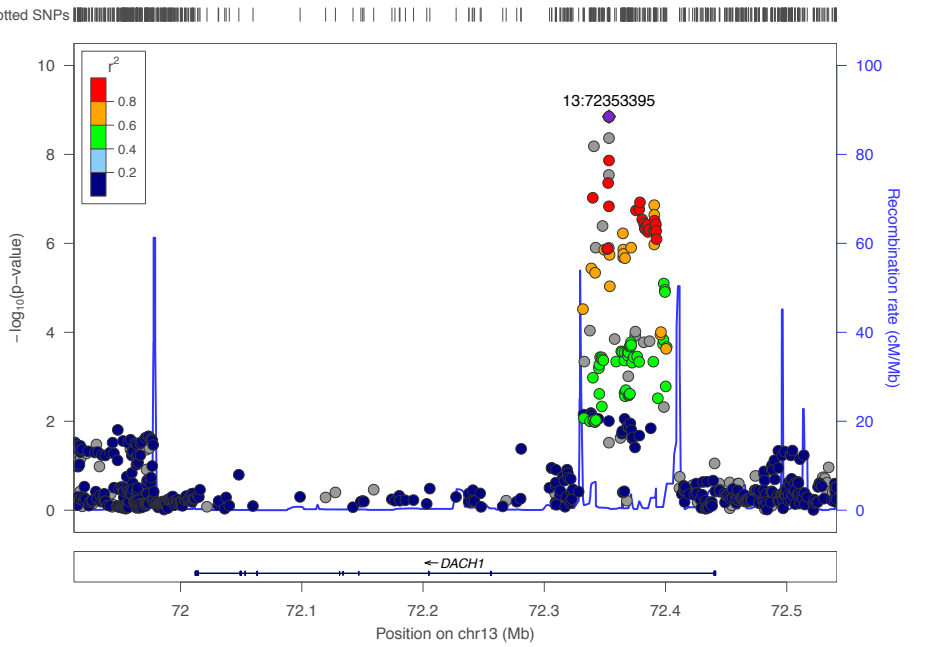




S3E

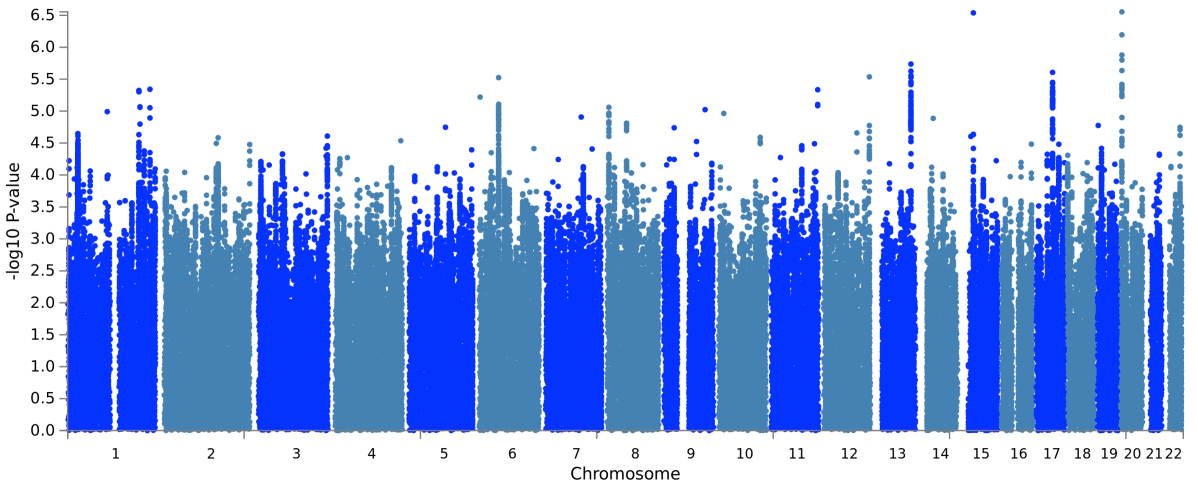
Cerebral white matter annual change rate

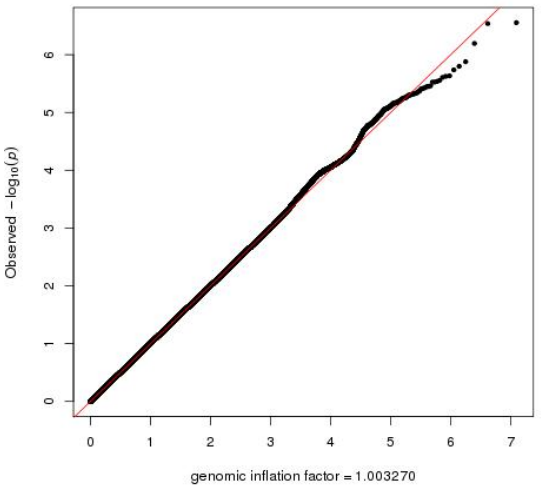




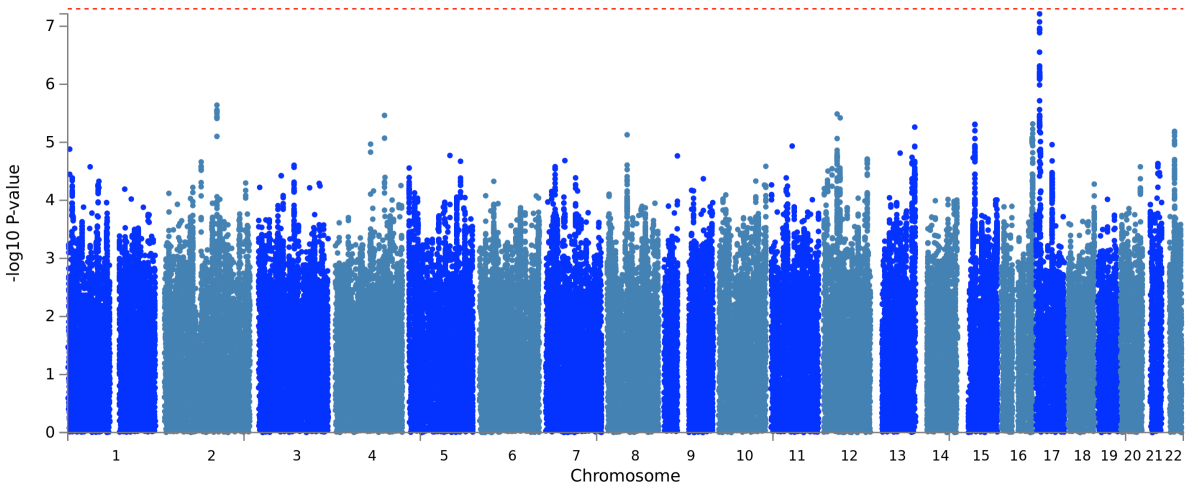
* locus plot of genome wide significant effect

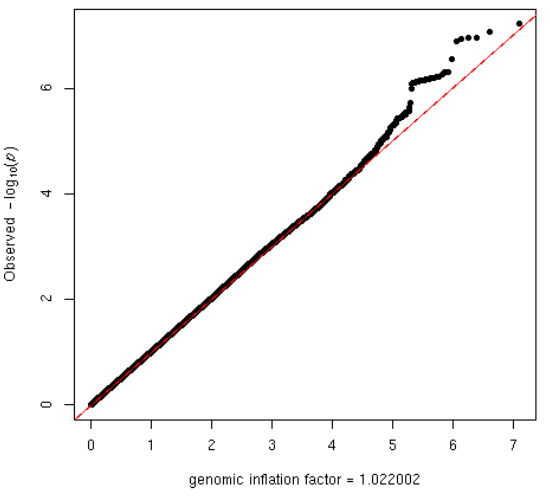
age-independent



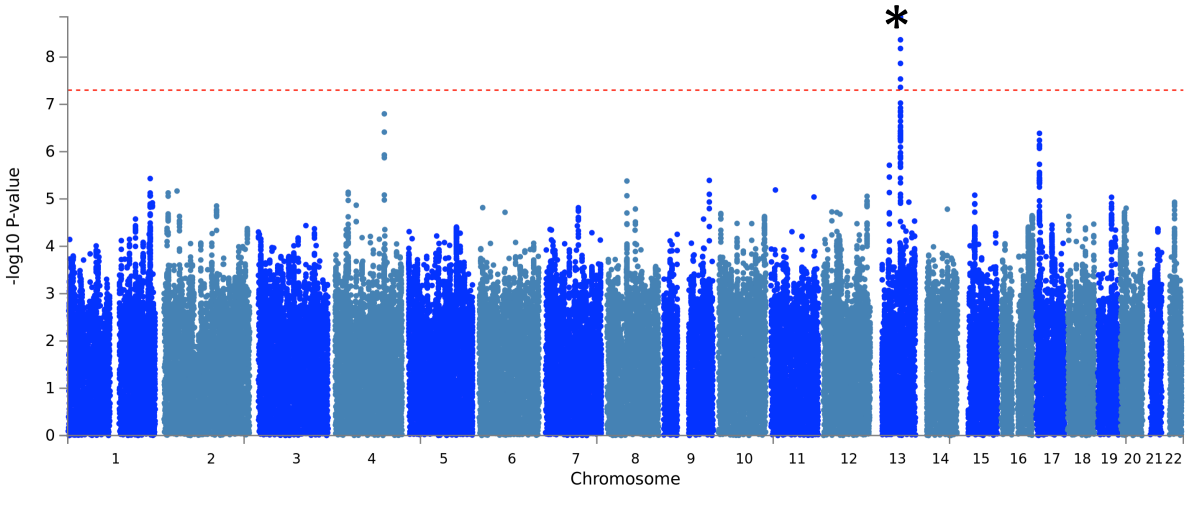


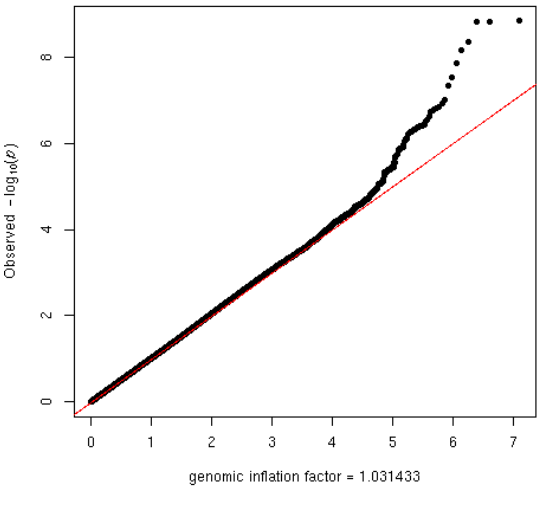
age-dependent linear





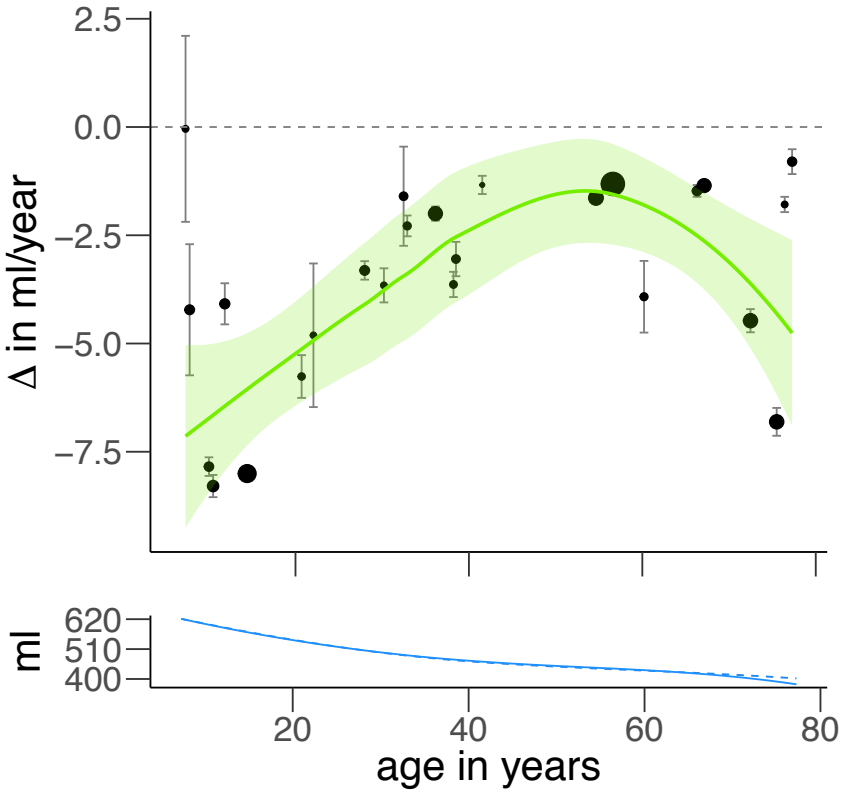
age-dependent quadratic



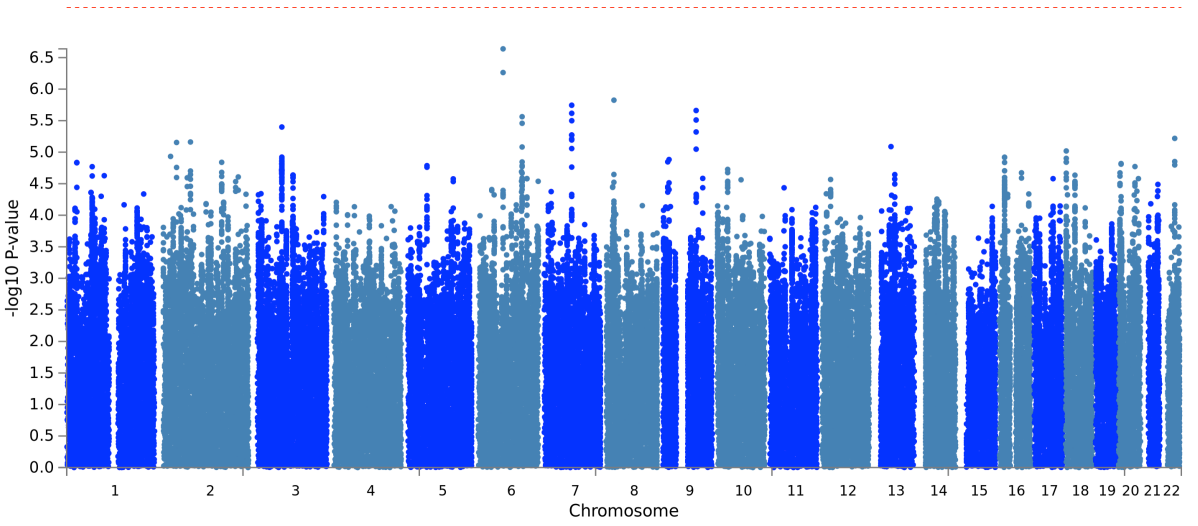


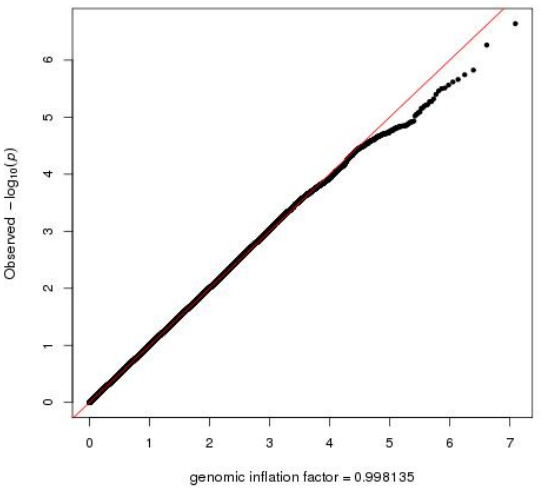
S3F

Cortex volume annual change rate

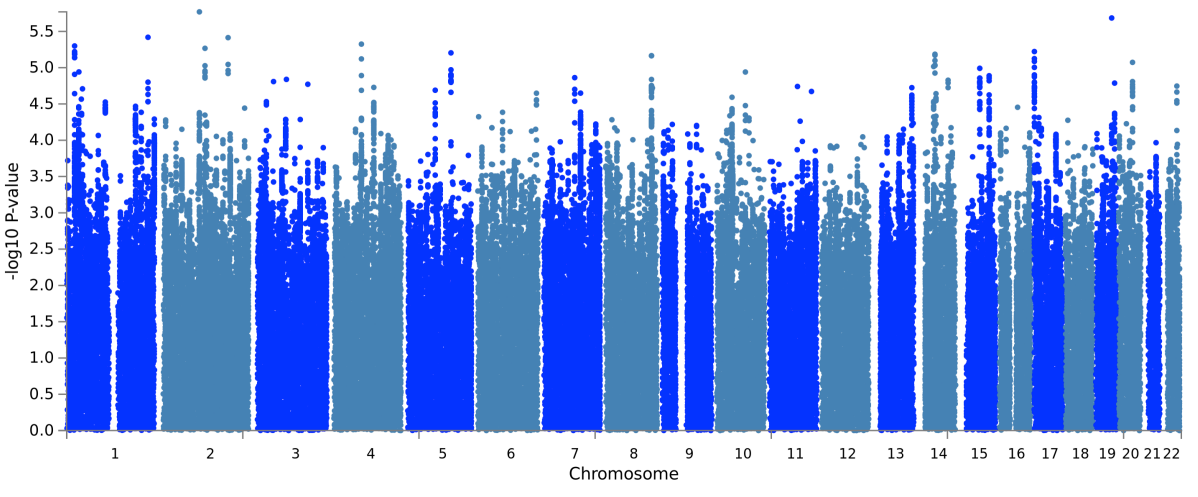


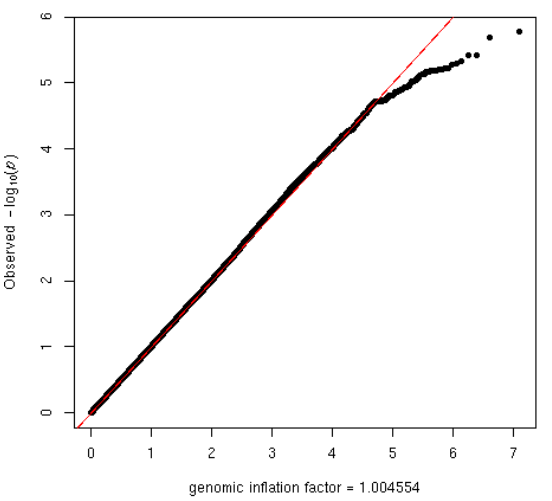
age-independent



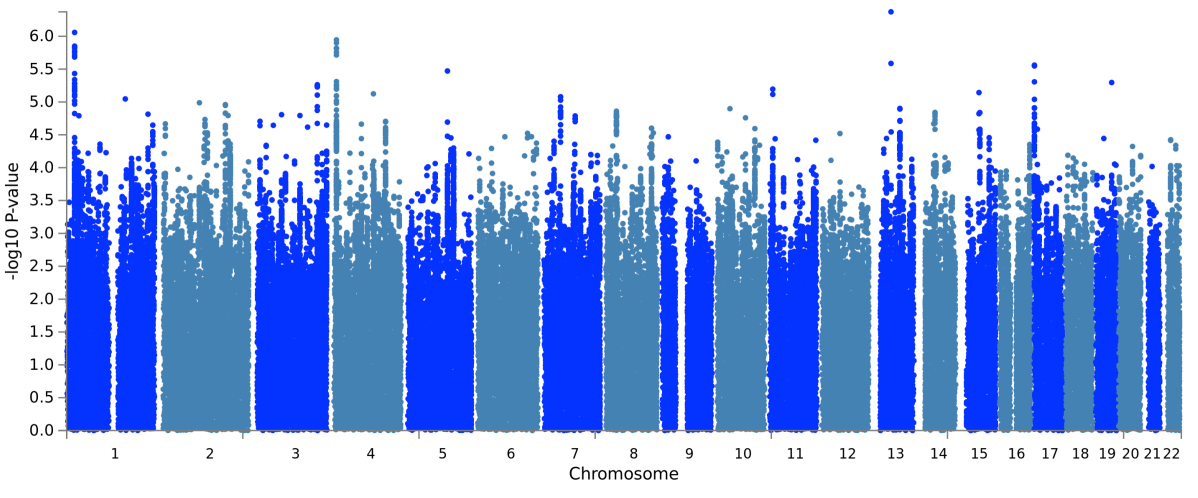


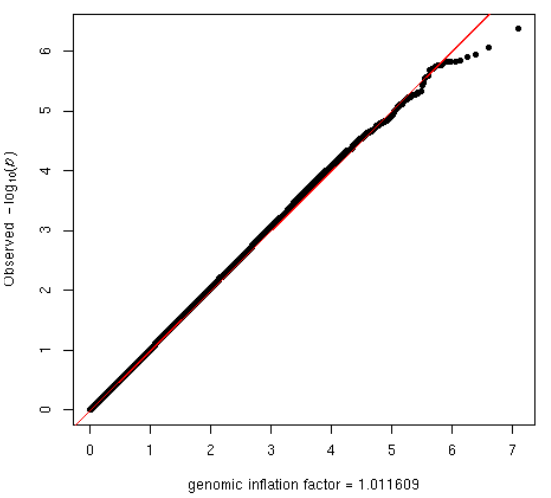
age-dependent linear





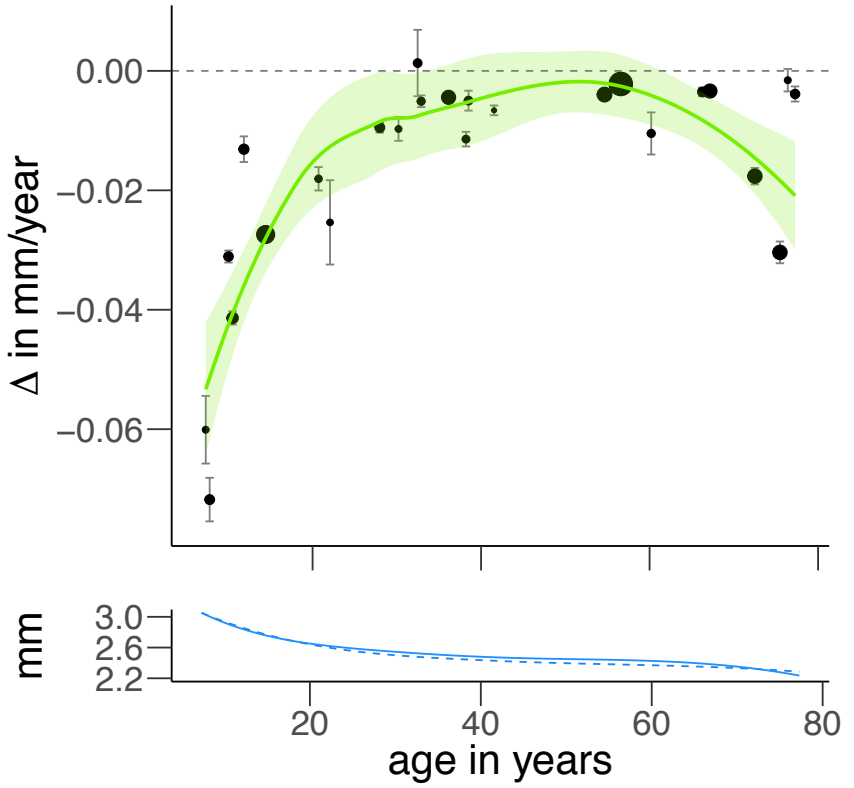
age-dependent quadratic



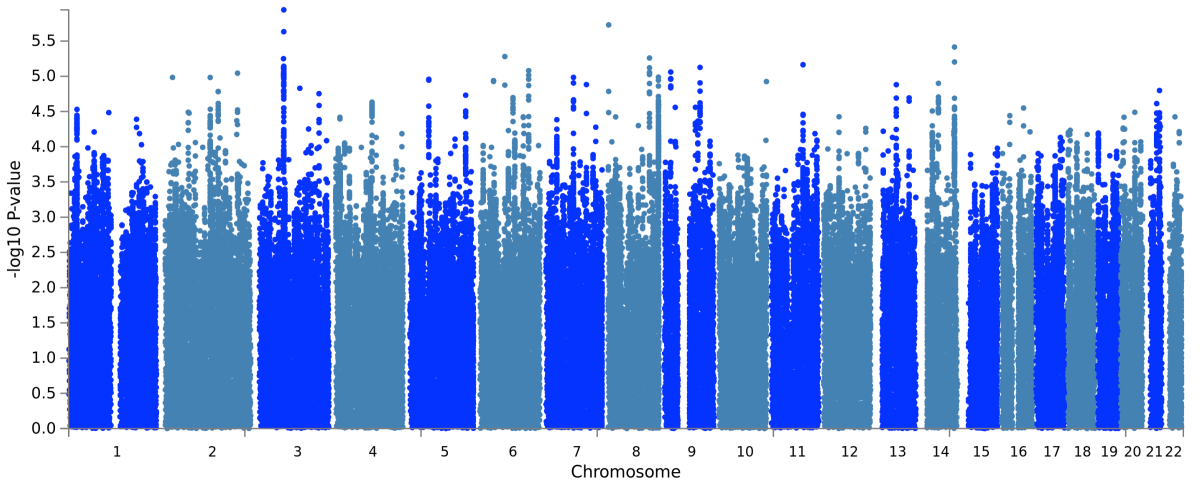


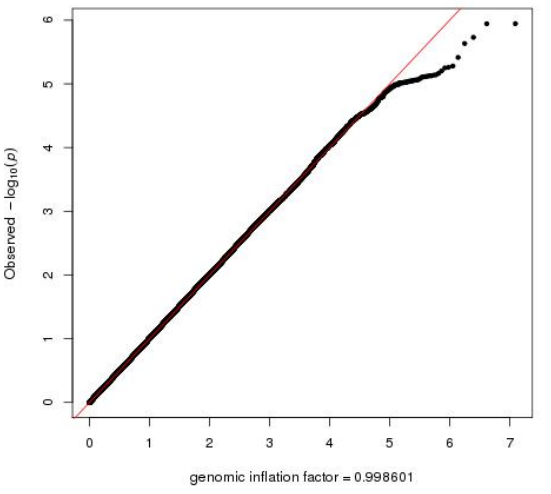
S3G

Cortical thickness annual change rate

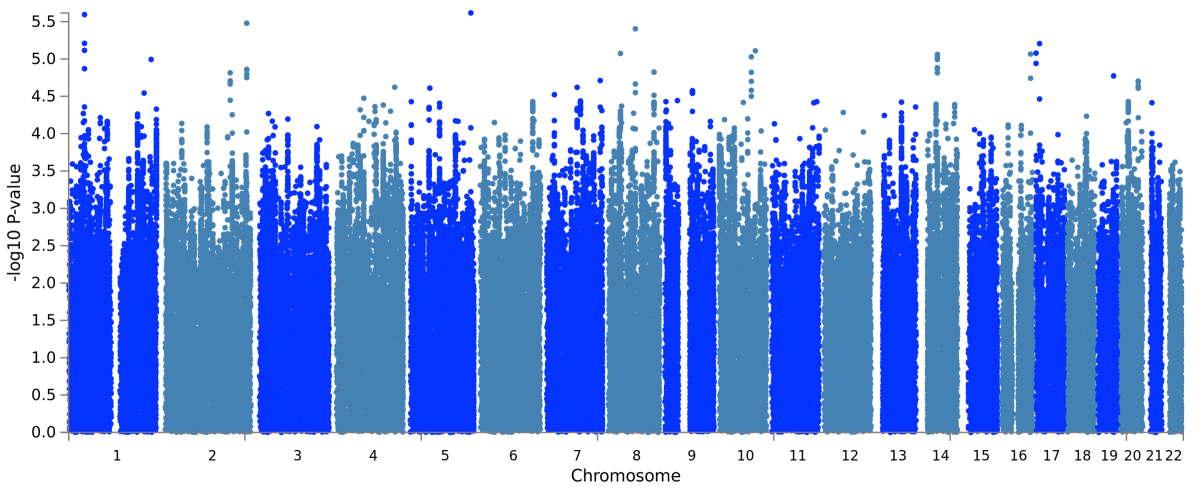


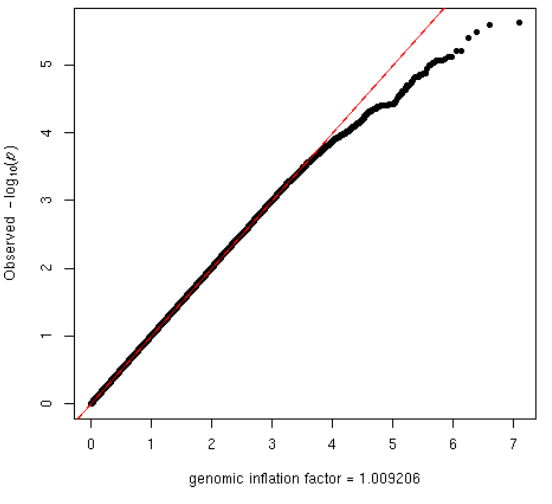
age-independent



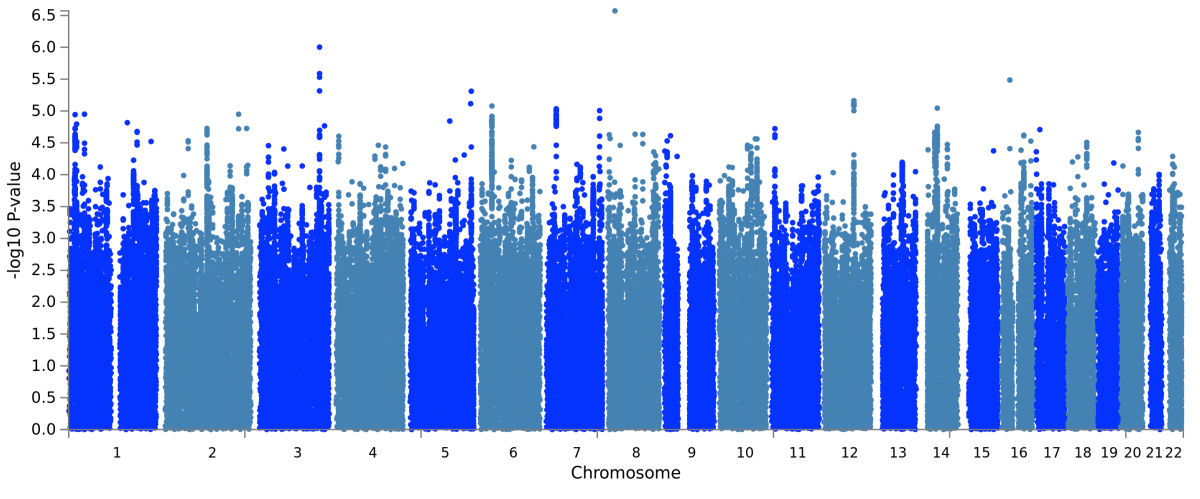


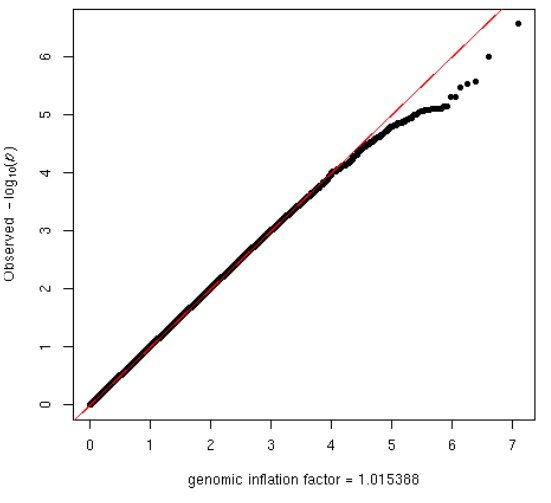
age-dependent linear





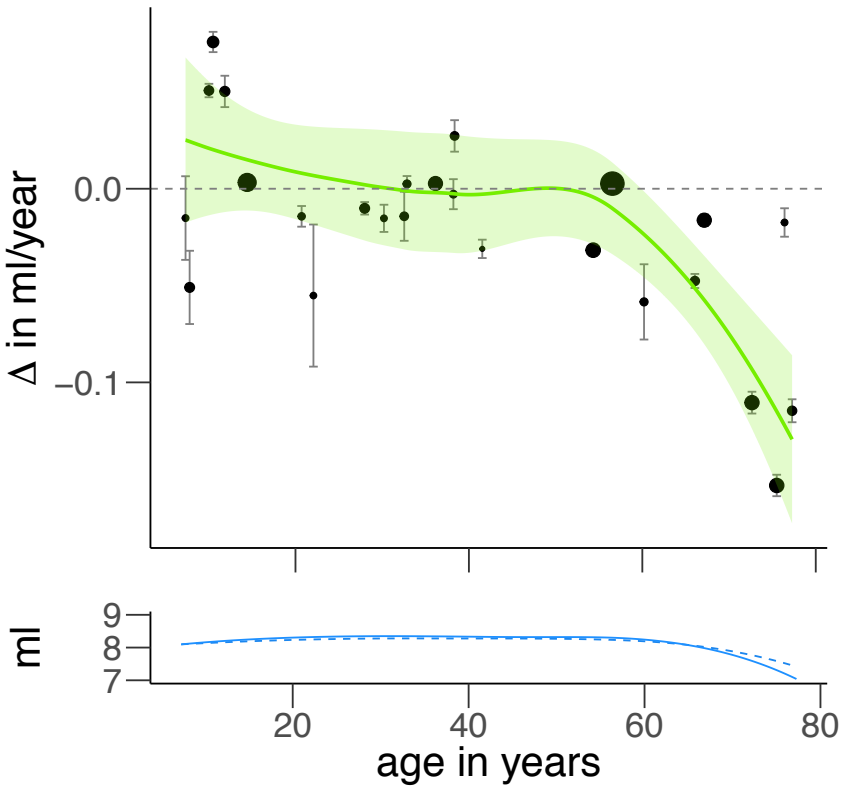
age-dependent quadratic



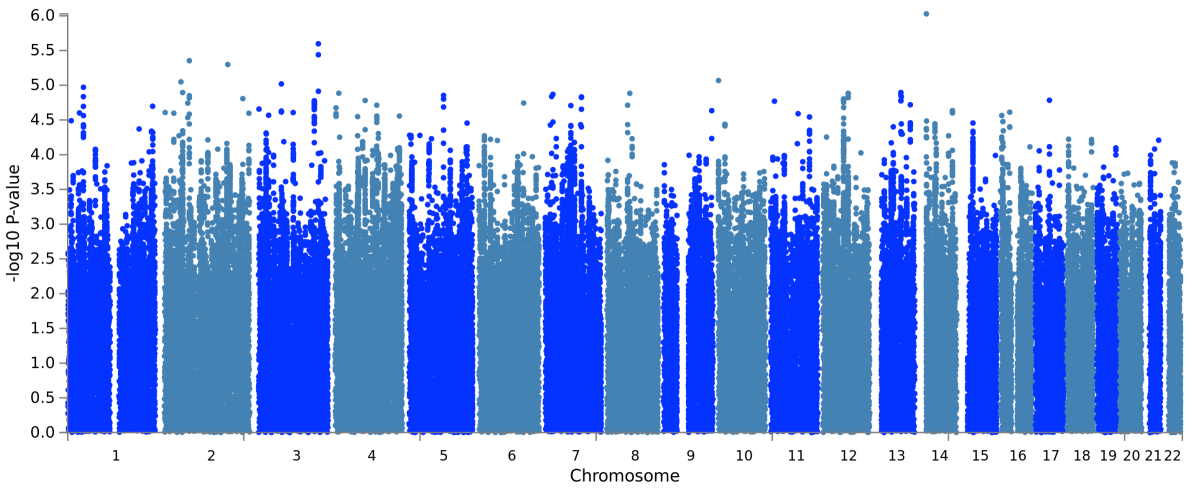


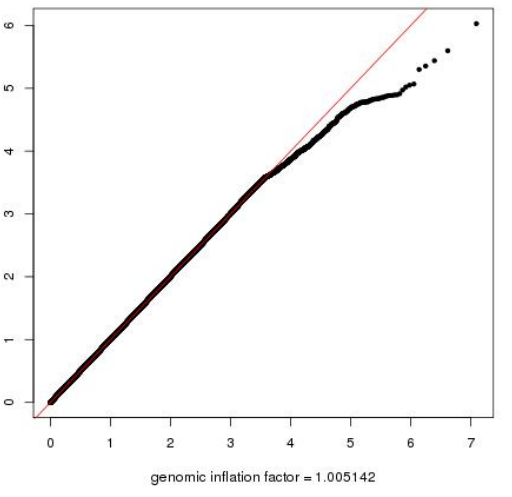
S3H

Hippocampus annual change rate

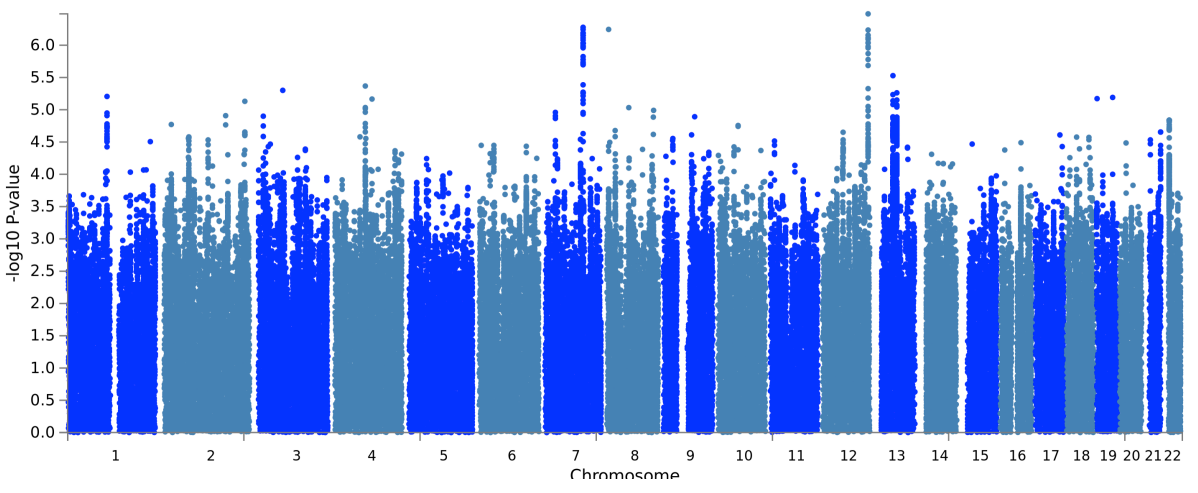


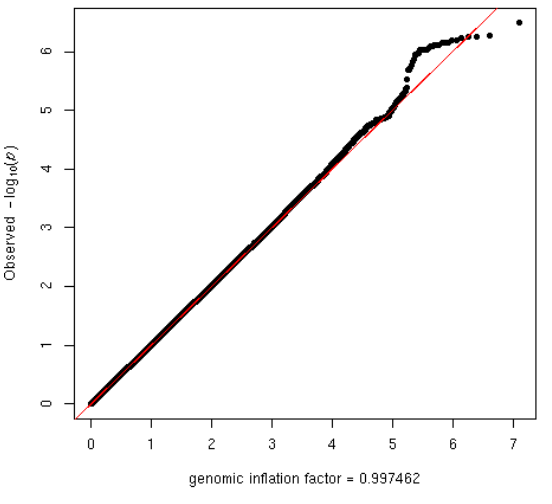
age-independent



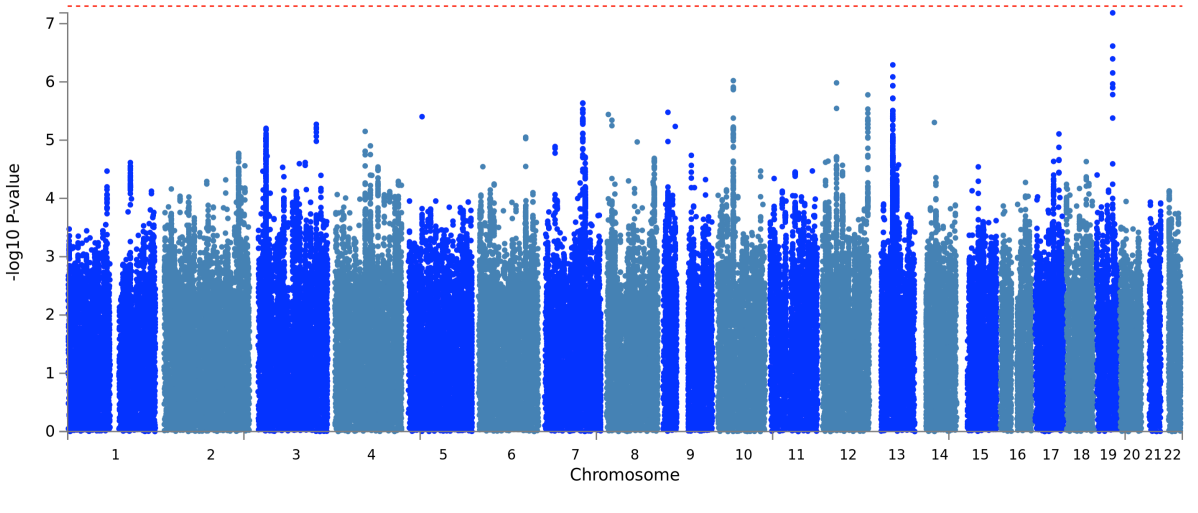


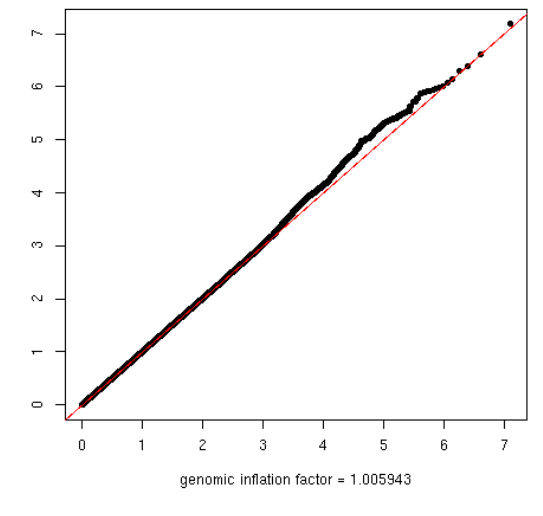
age-dependent linear



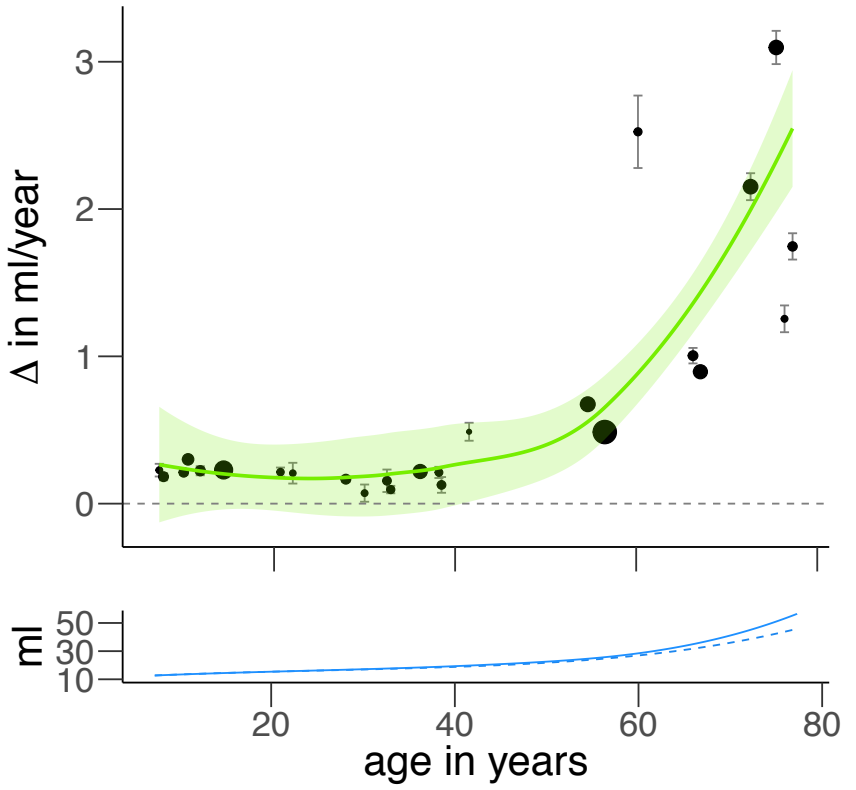


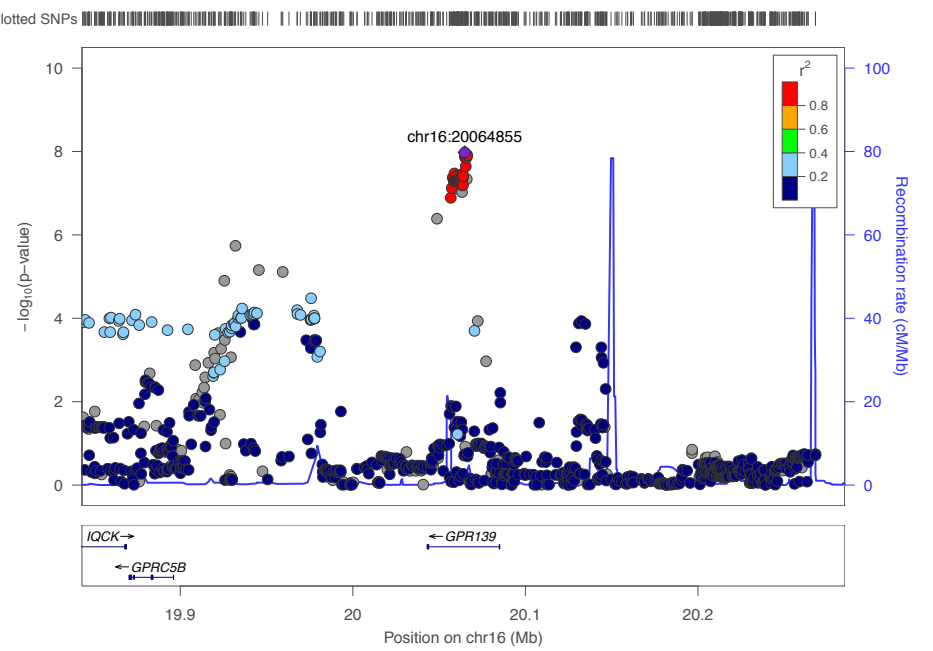
age-dependent quadratic





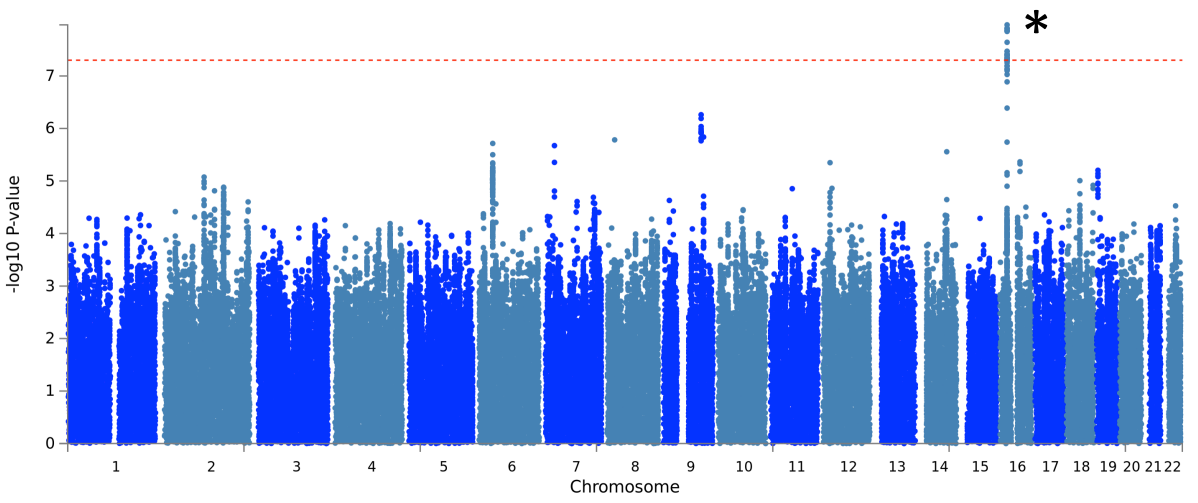
Lateral ventricles annual change rate

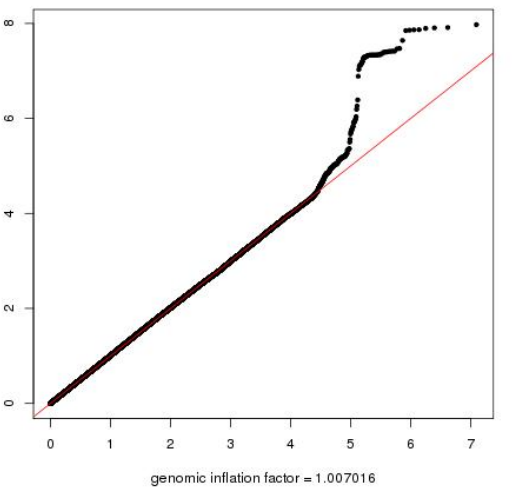




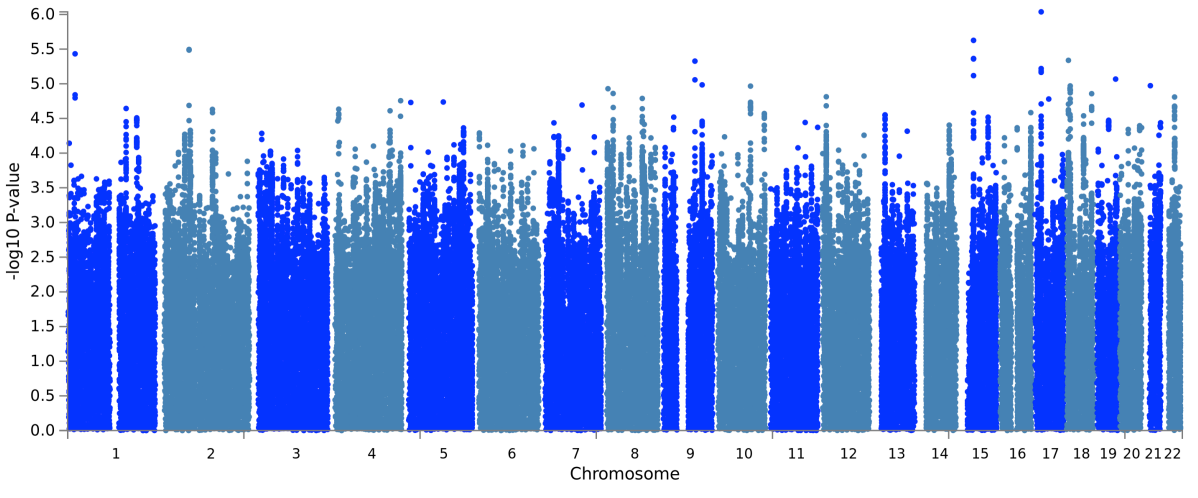
* locus plot of genome wide significant effect

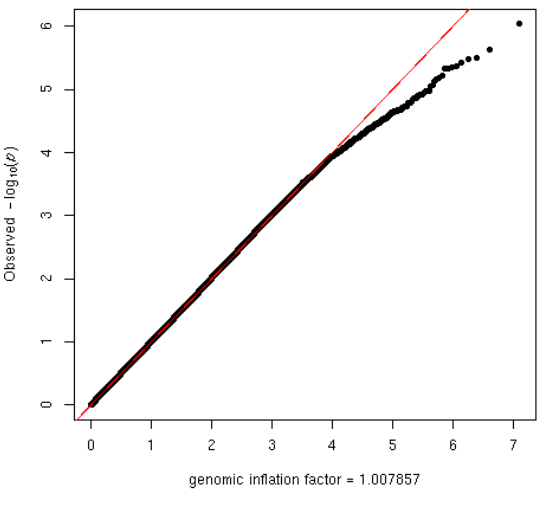
age-independent



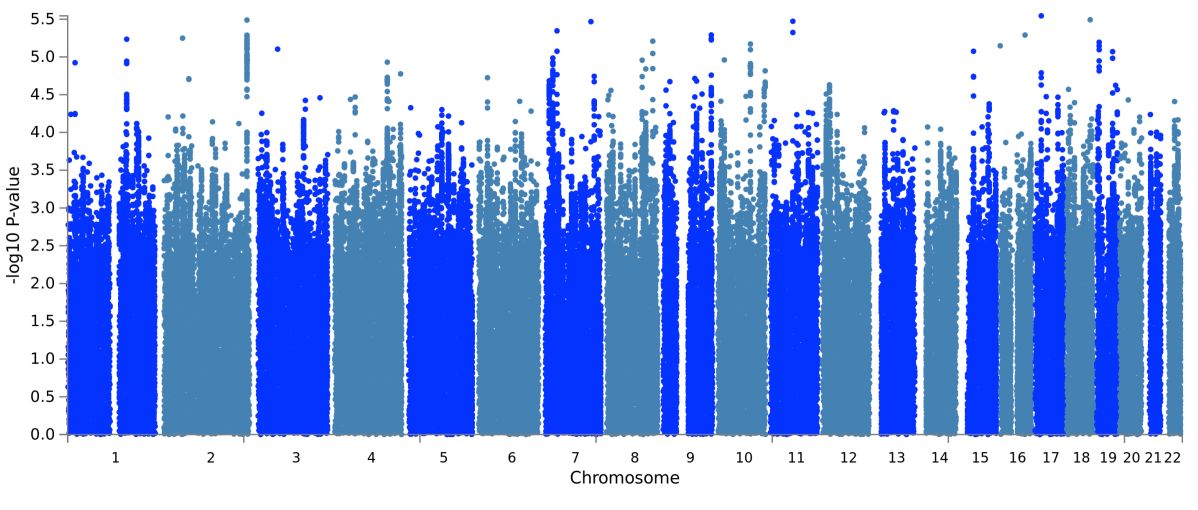


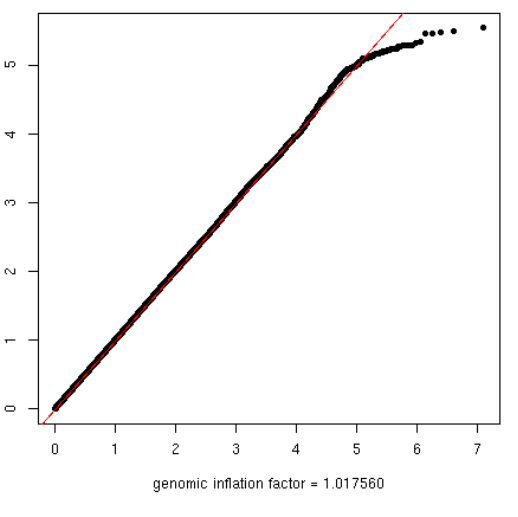
age-dependent linear





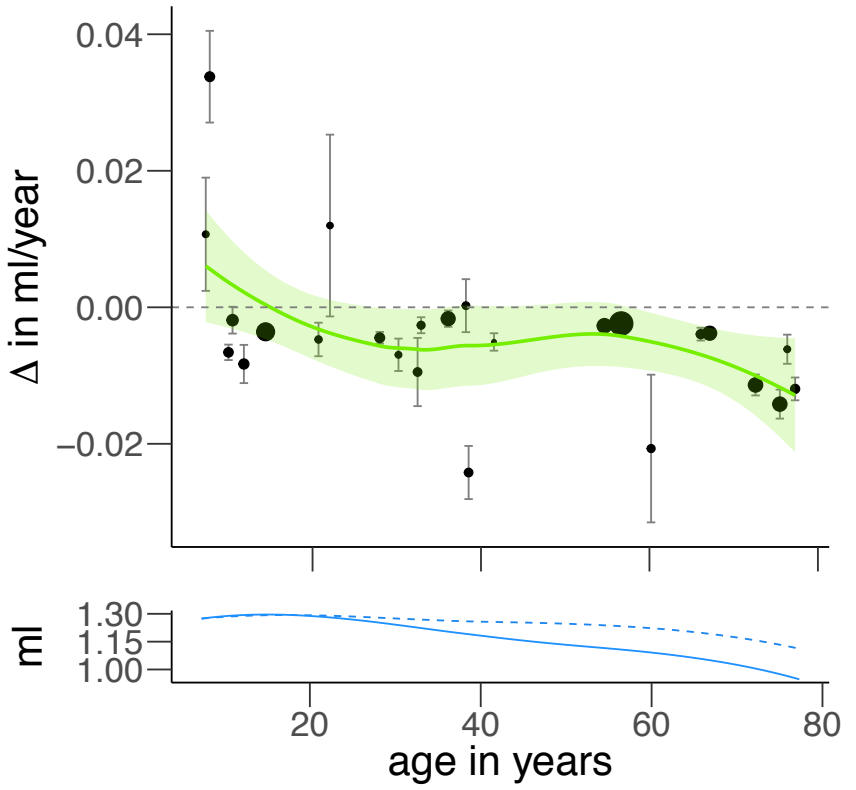
age-dependent quadratic

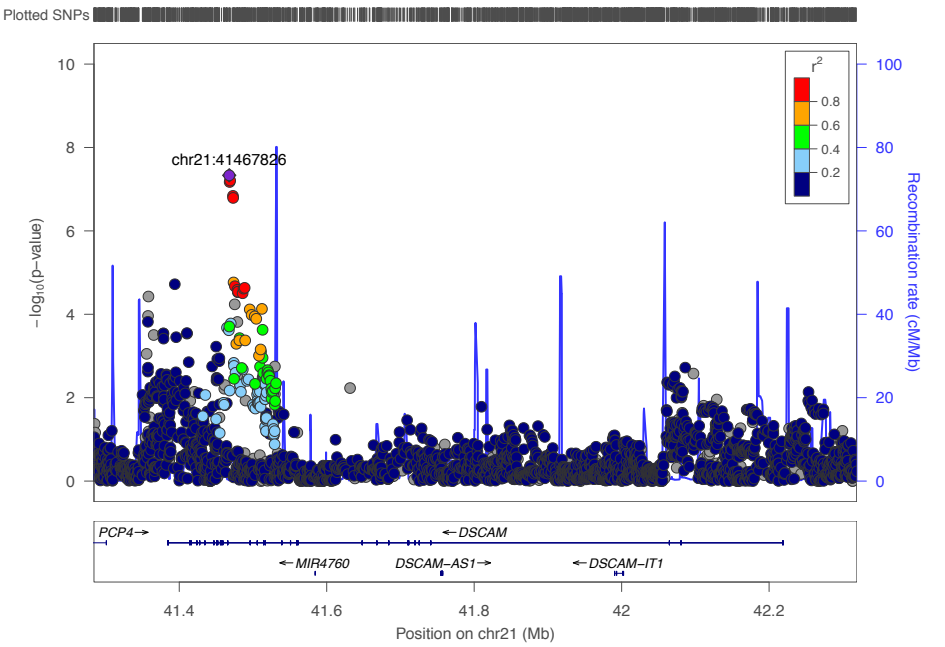




S3J

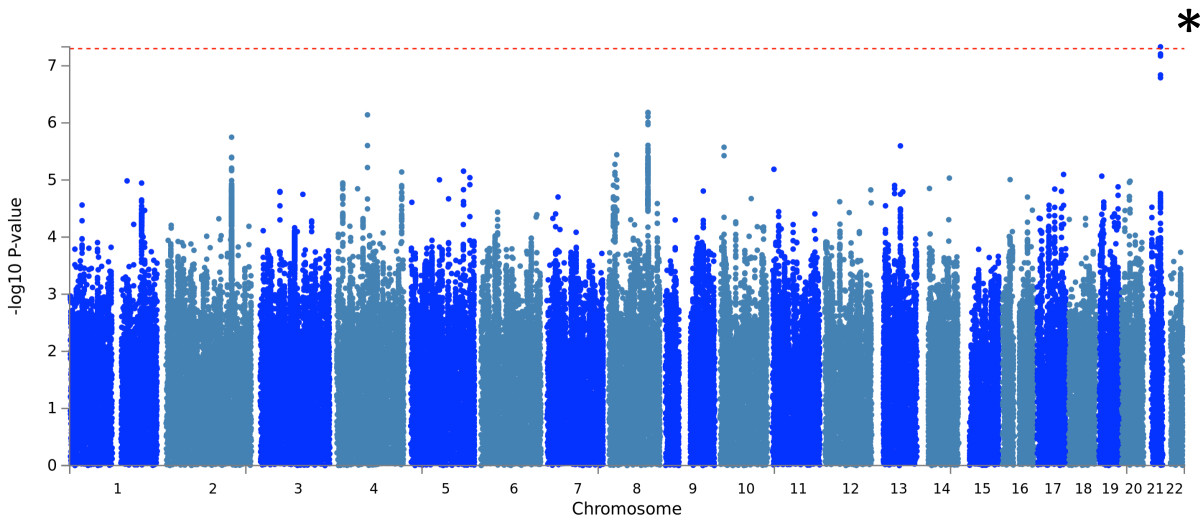
Nucleus accumbens annual change rate





* locus plot of genome wide significant effect

age-independent



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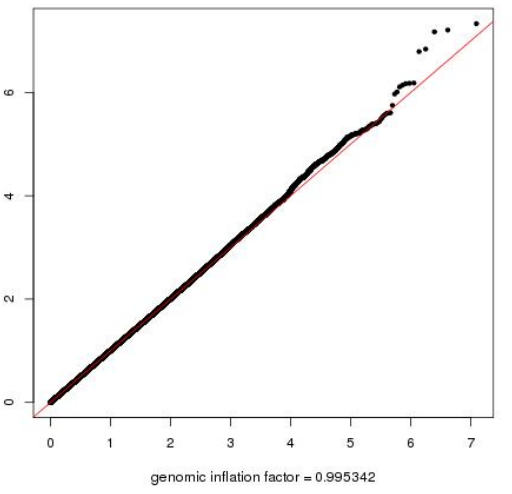
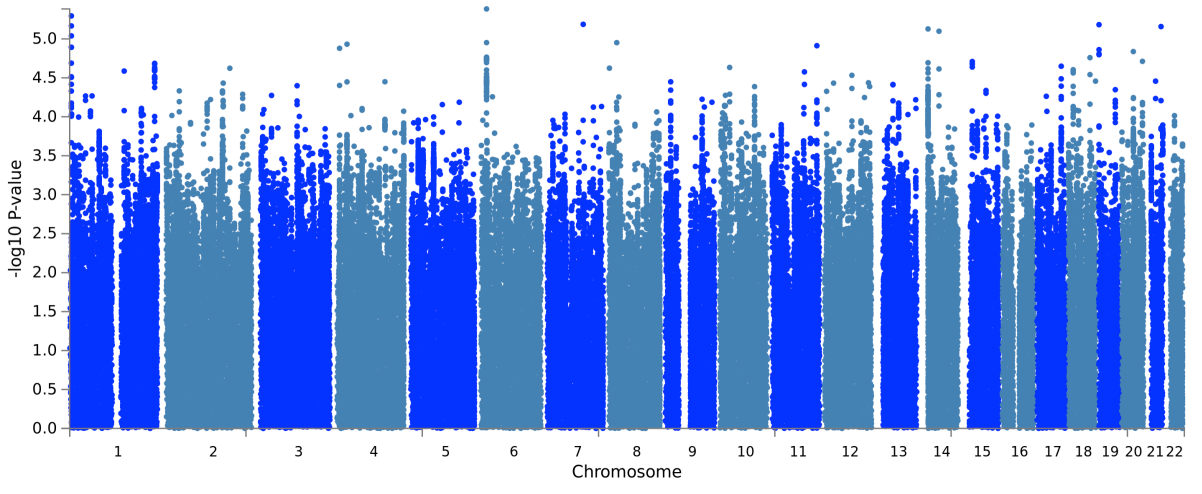
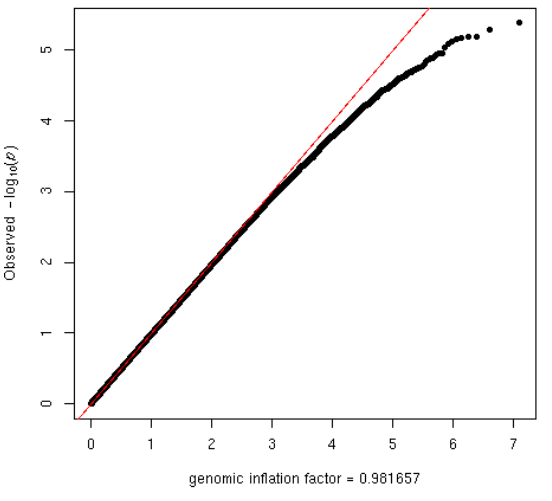
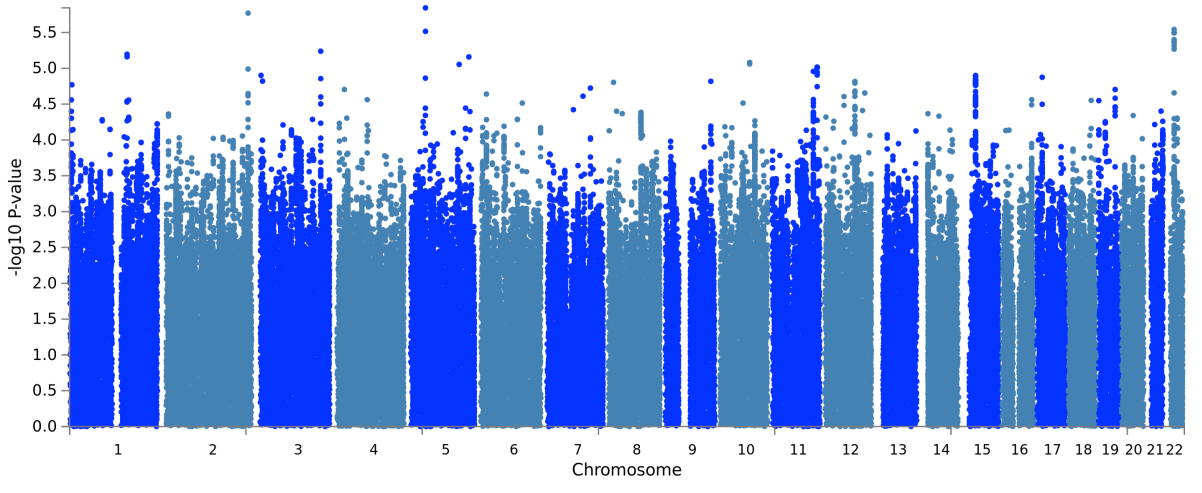


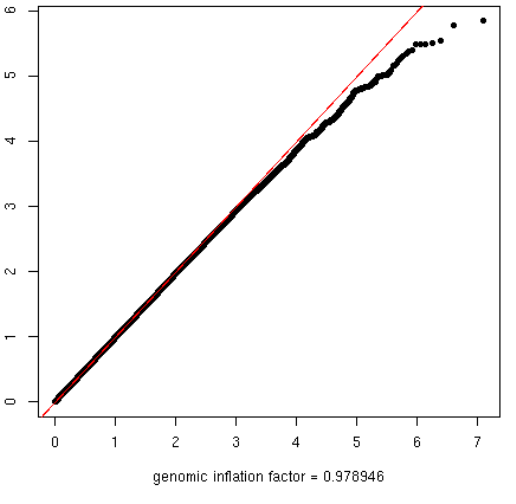
age-dependent linear





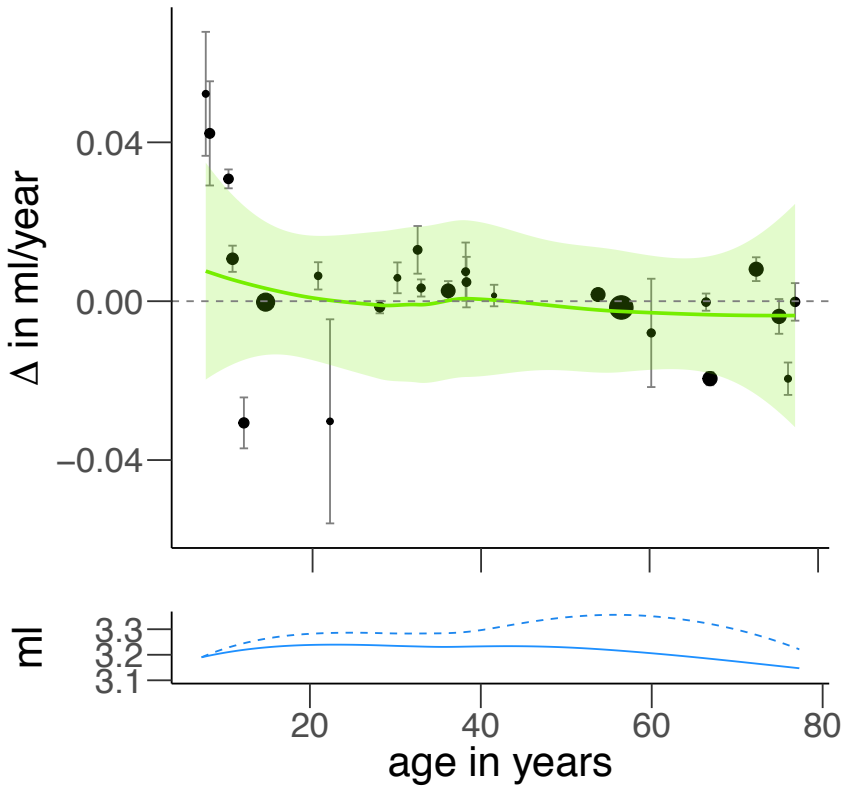
age-dependent quadratic



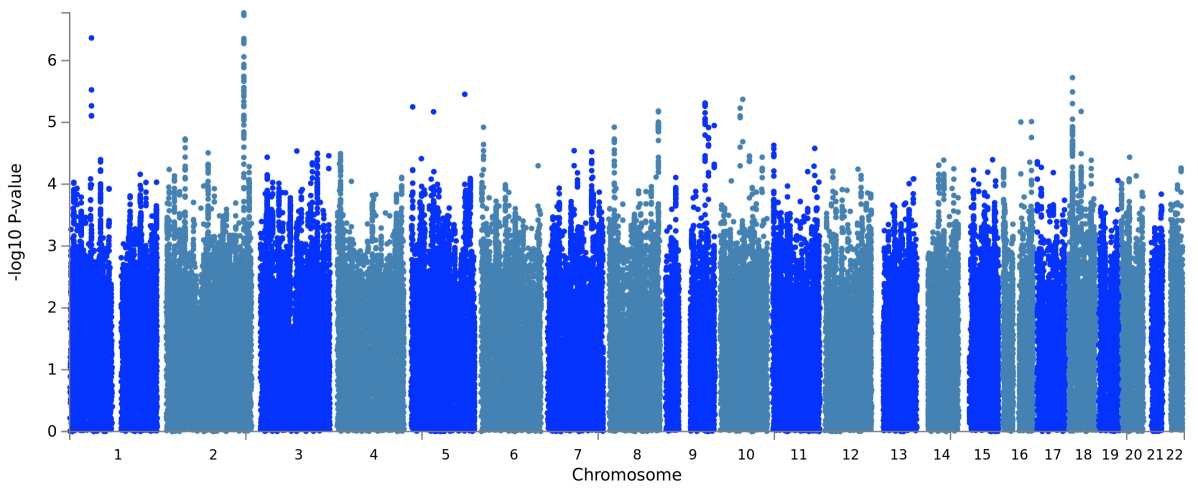


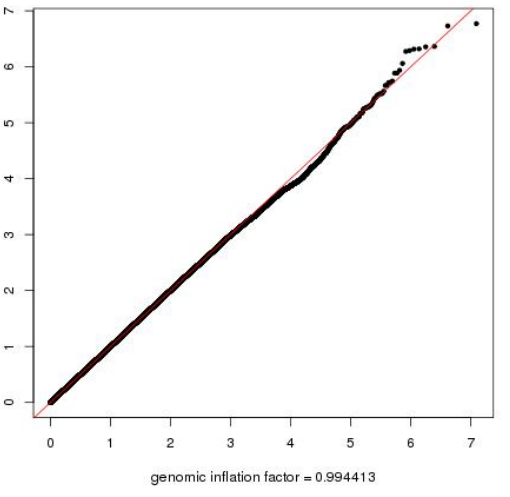
S3K

Pallidum annual change rate

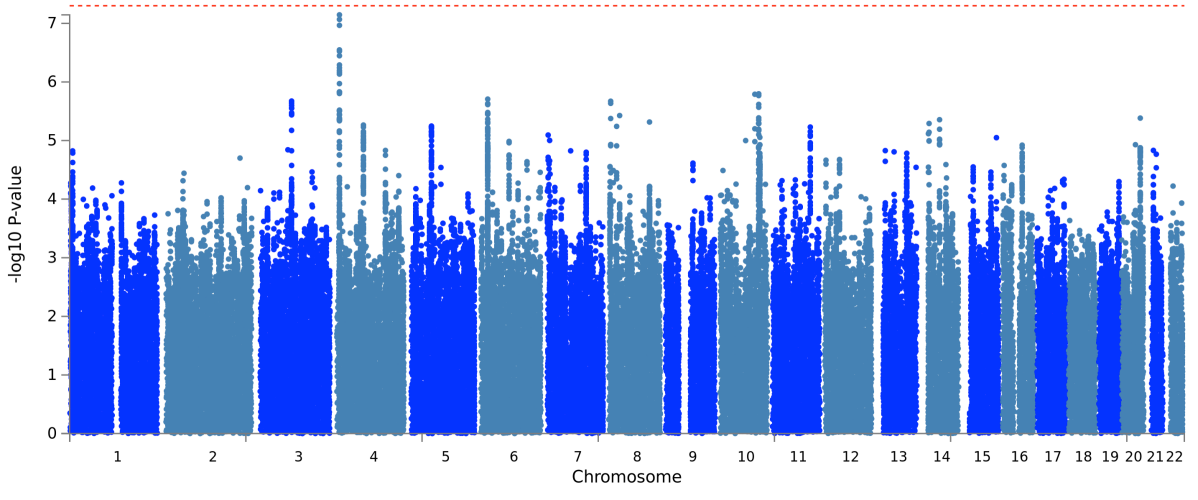


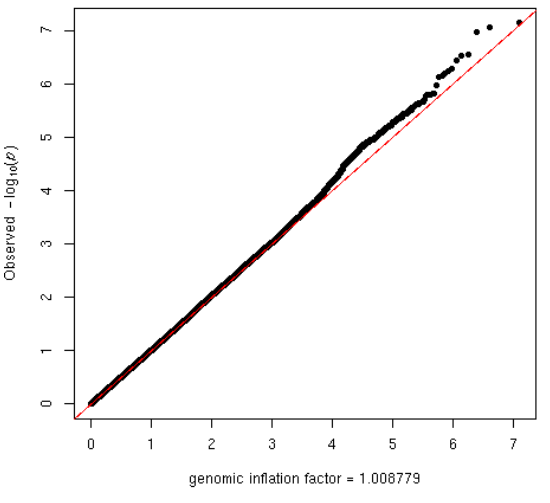
age-independent



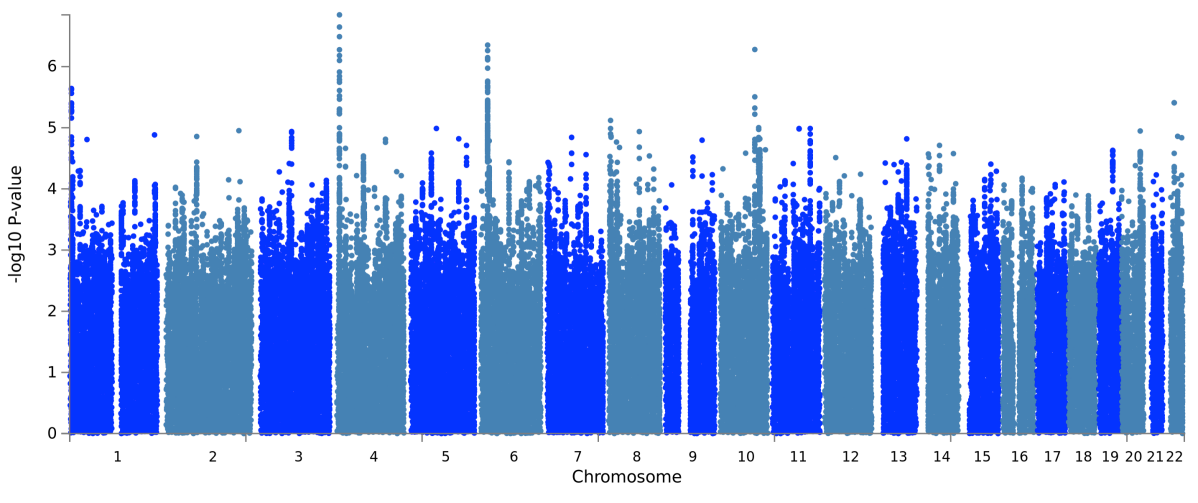


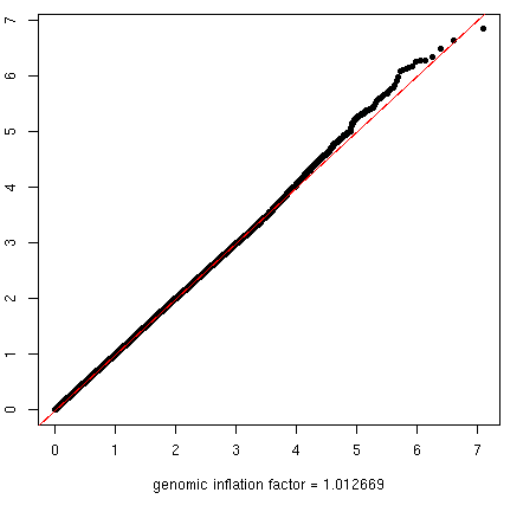
age-dependent linear





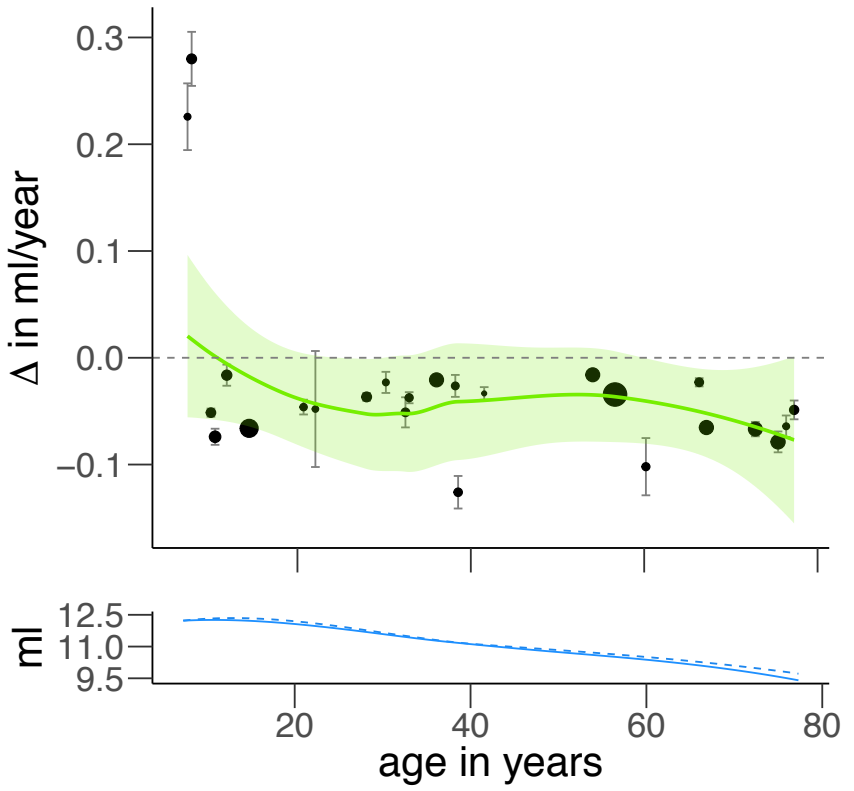
age-dependent quadratic



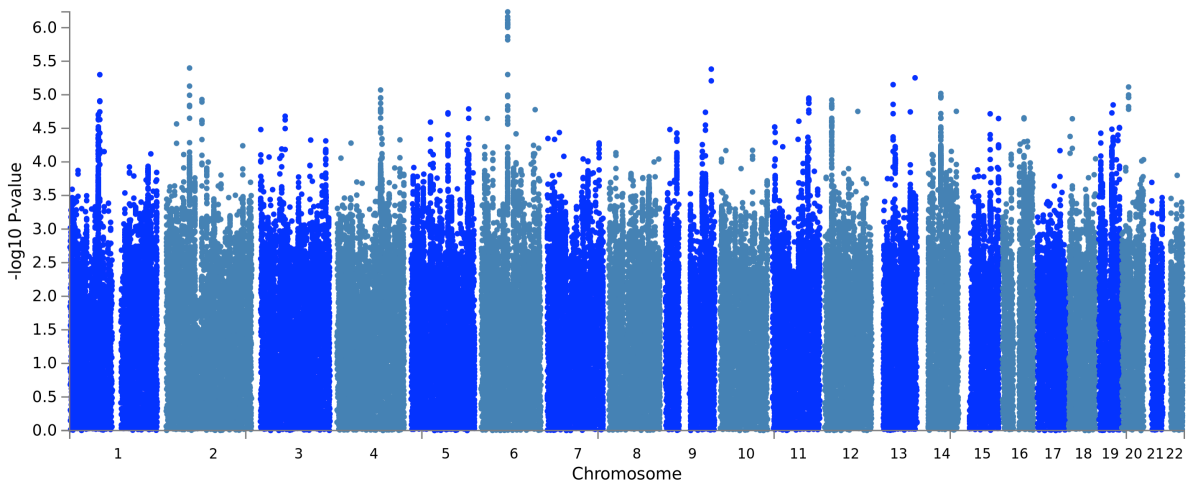


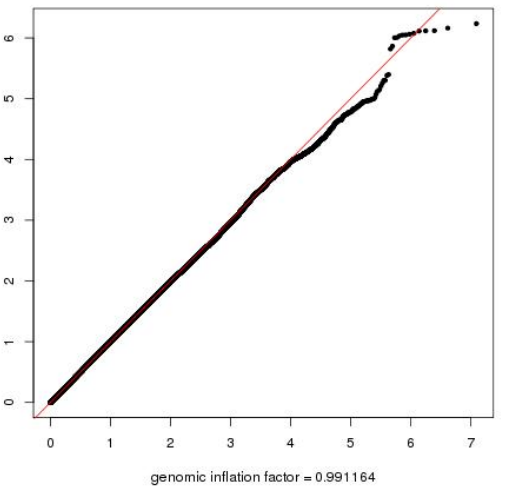
S3L

Putamen annual change rate

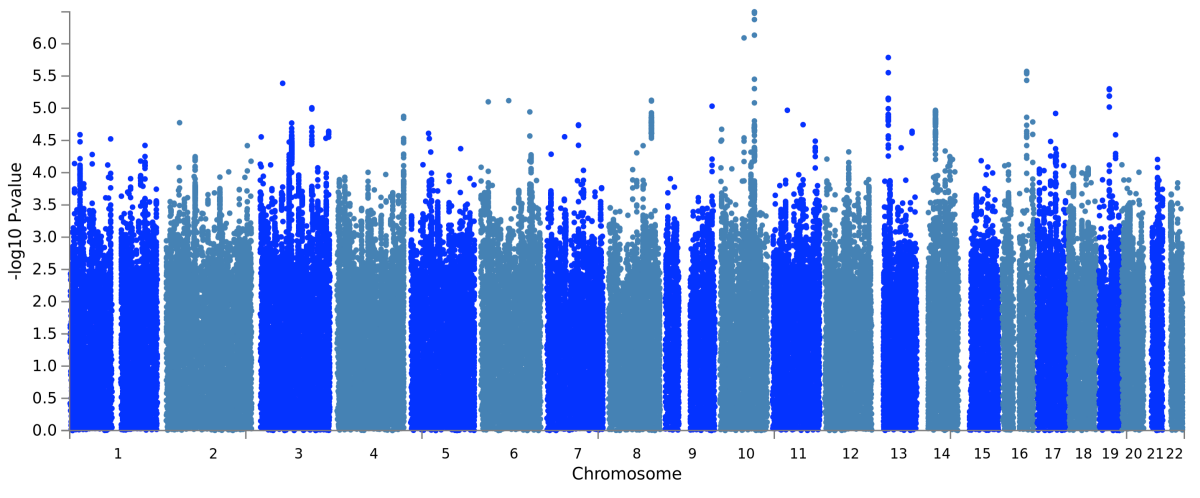


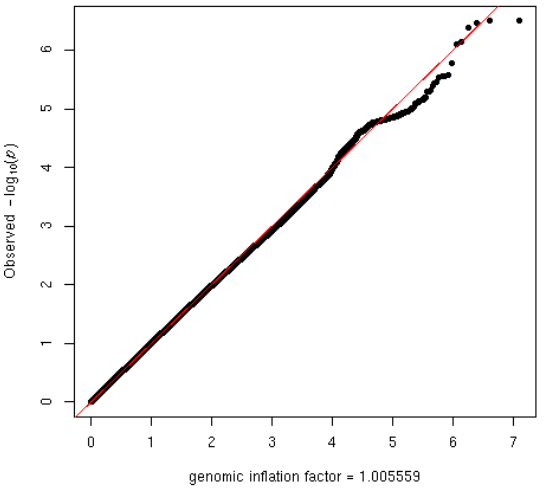
age-independent



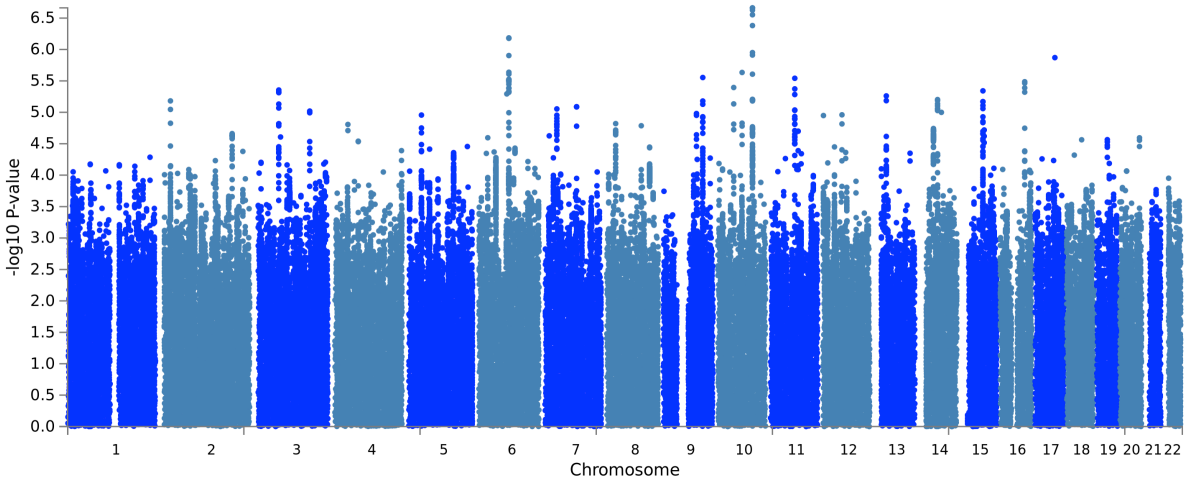


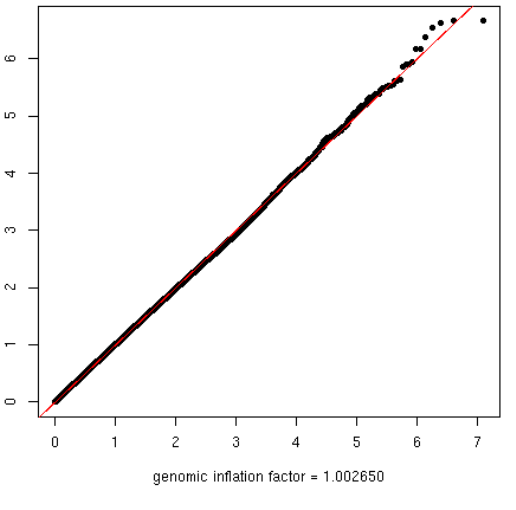
age-dependent linear





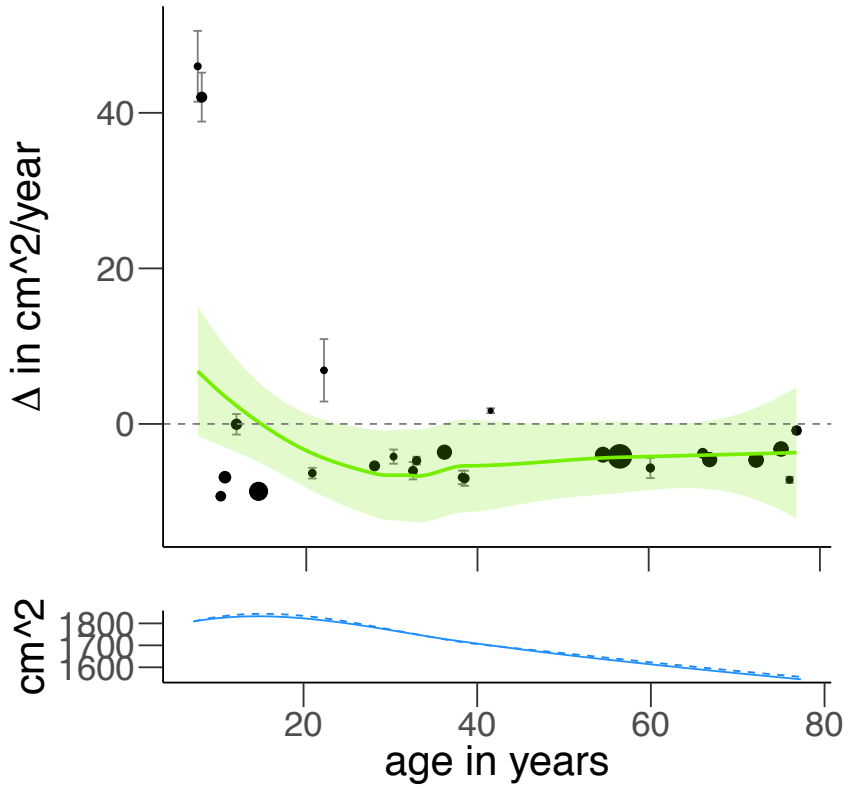
age-dependent quadratic

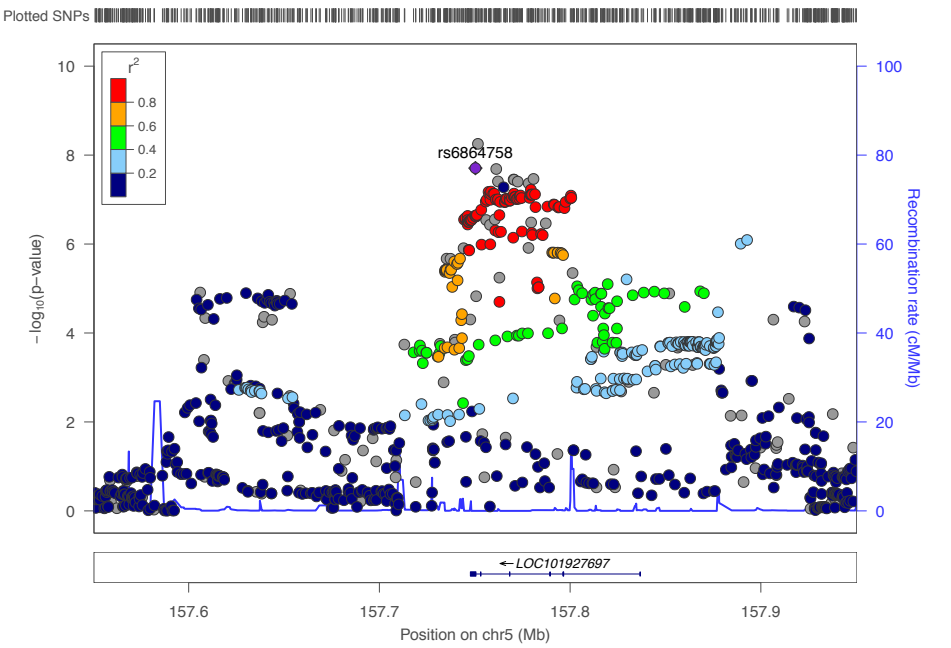




S3M

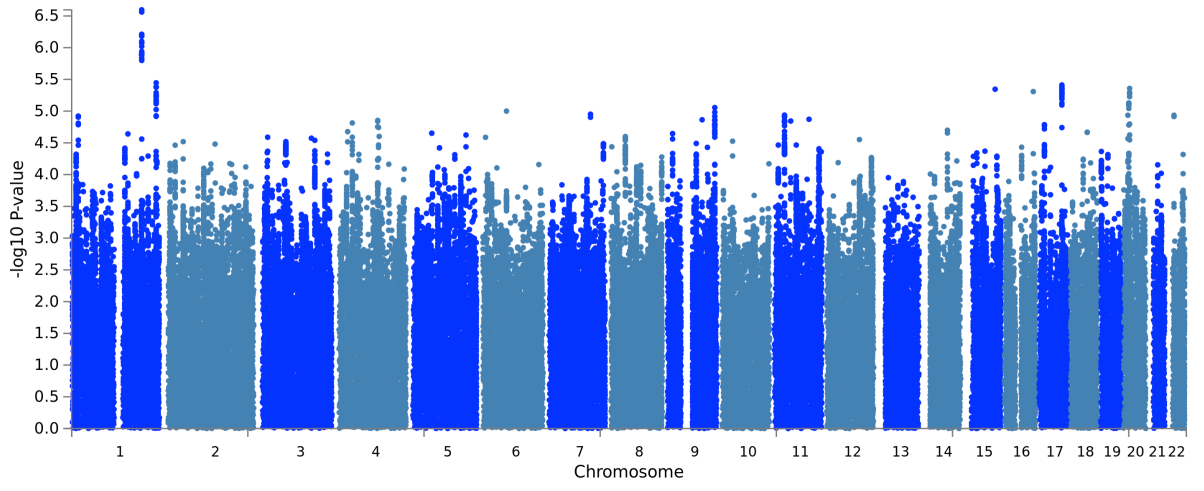
Surface area annual change rate

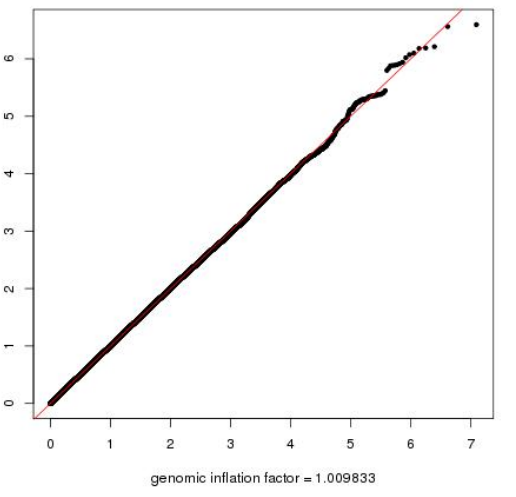




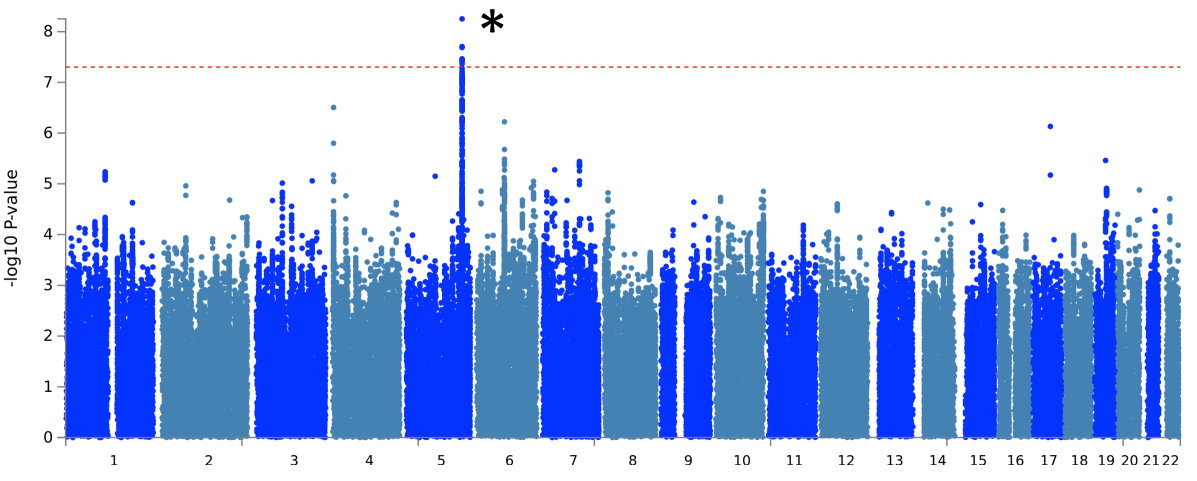
* locus plot of genome wide significant effect

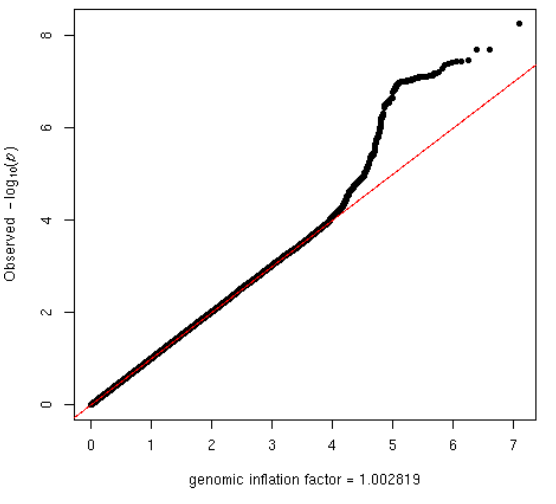
age-independent



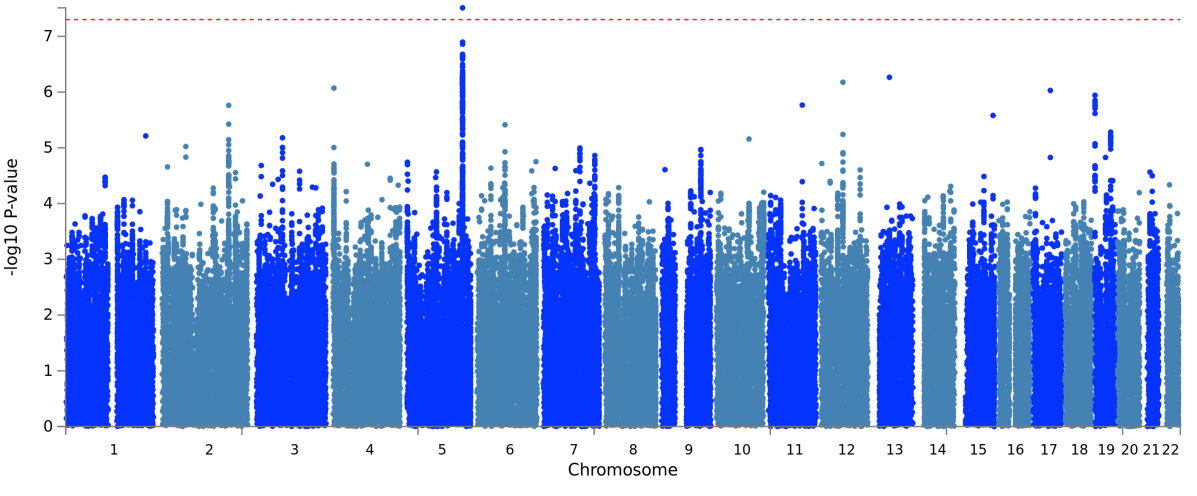


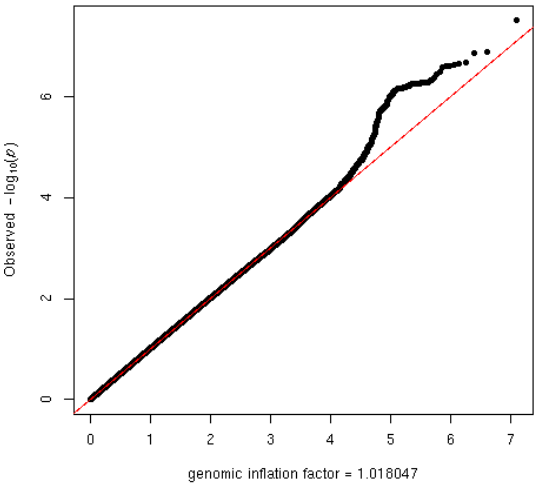
age-dependent linear





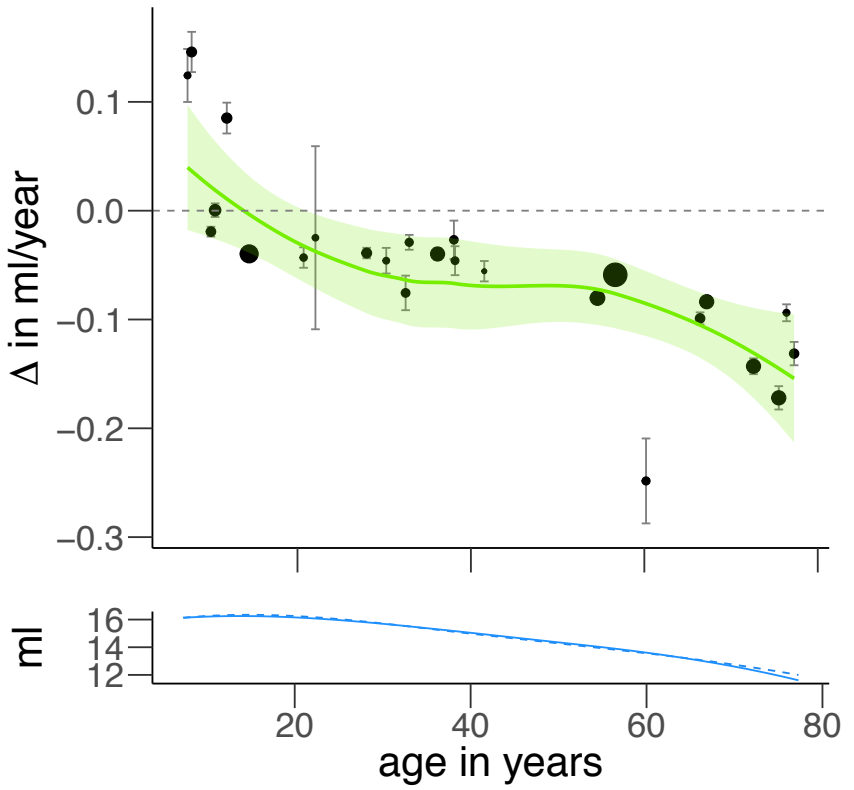
age-dependent quadratic



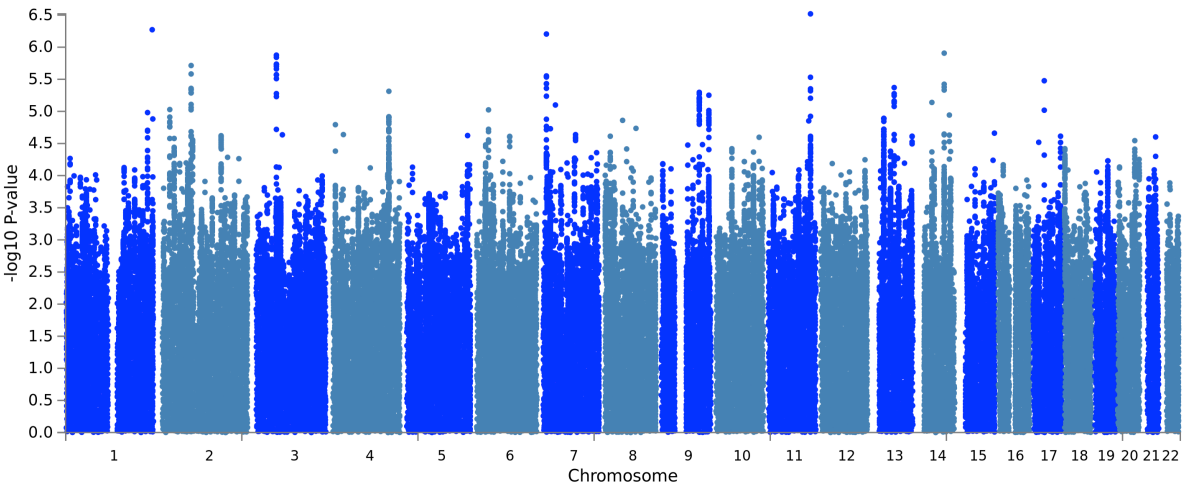


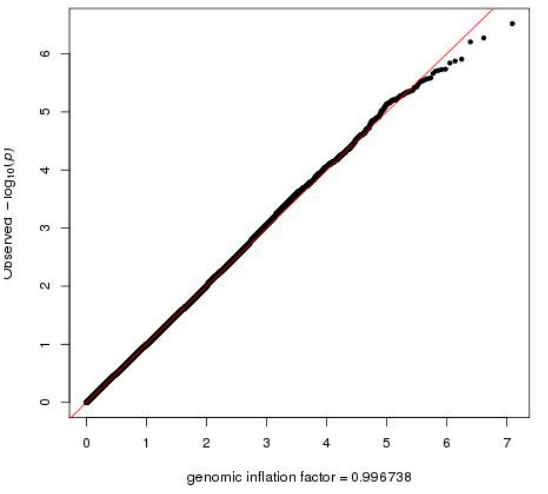
S3N

Thalamus annual change rate

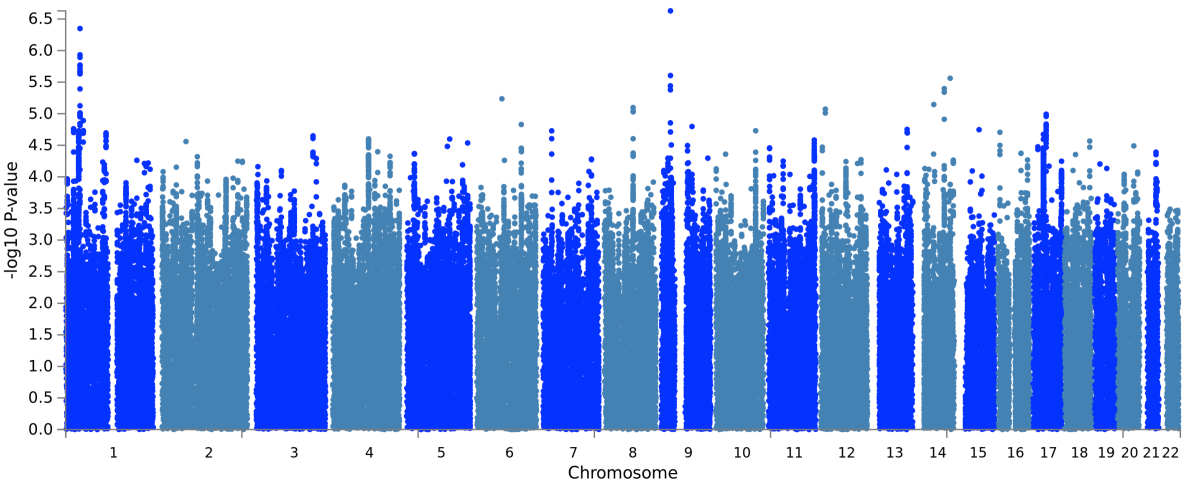


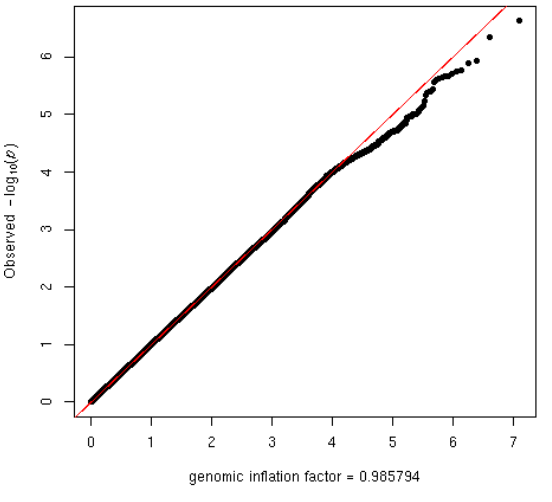
age-independent



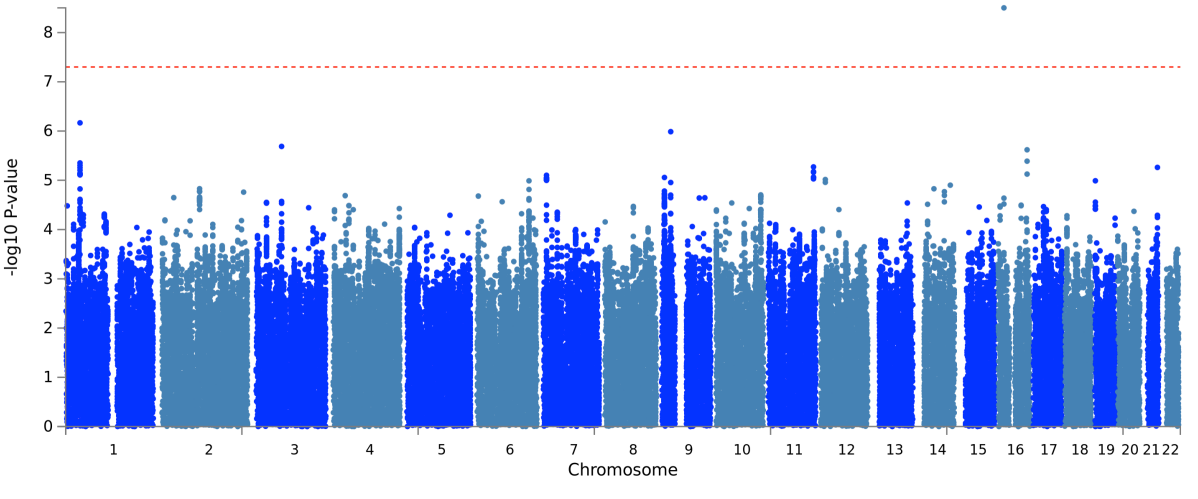


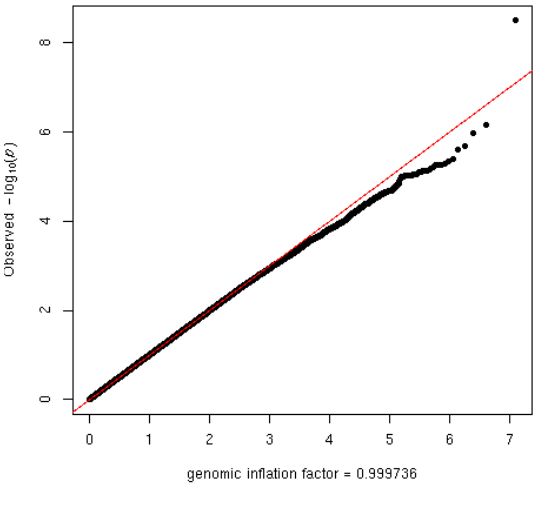
age-dependent linear



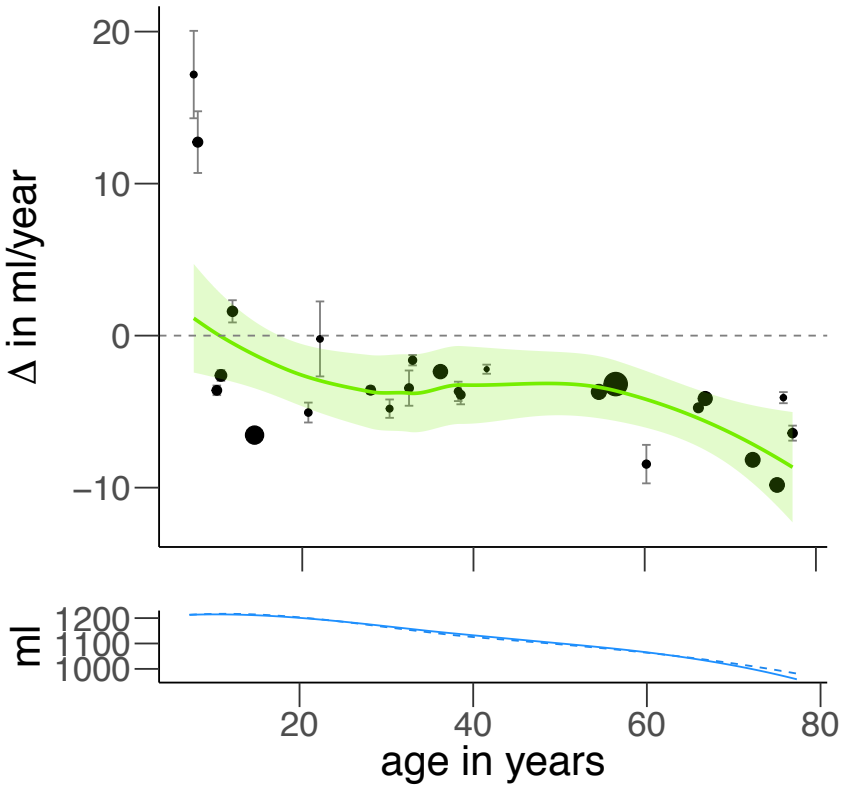


age-dependent quadratic

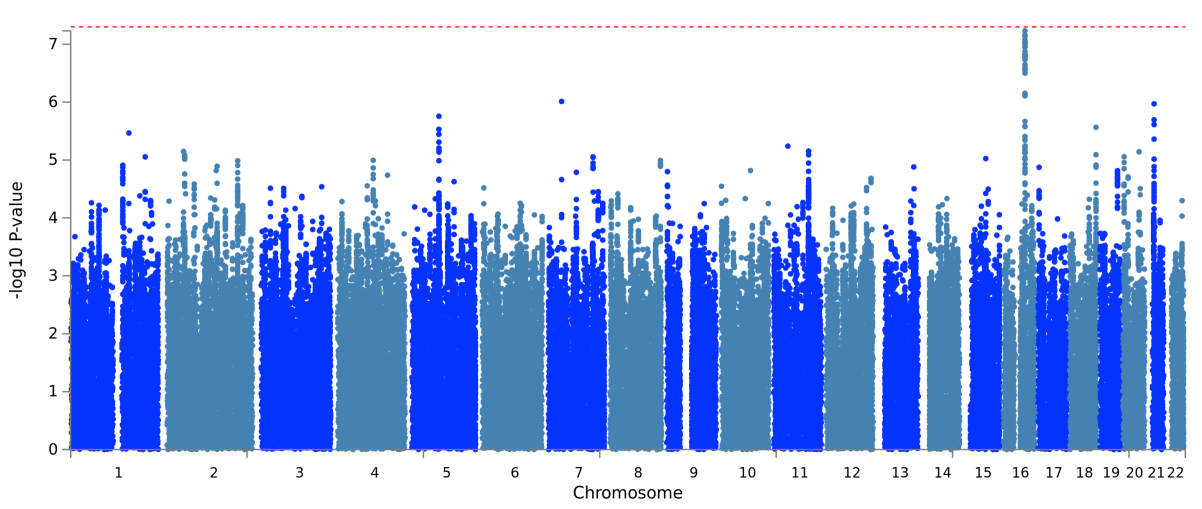


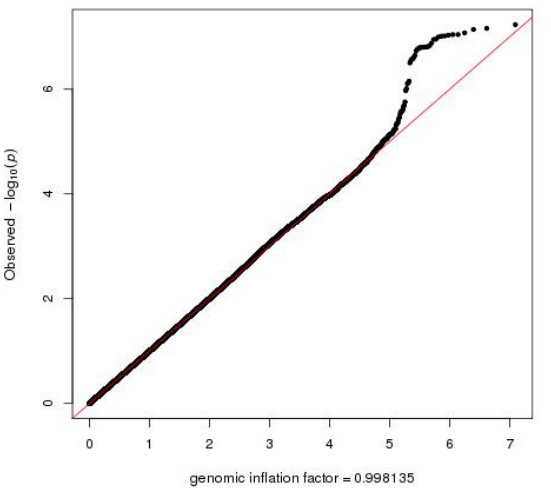


Total brain annual change rate

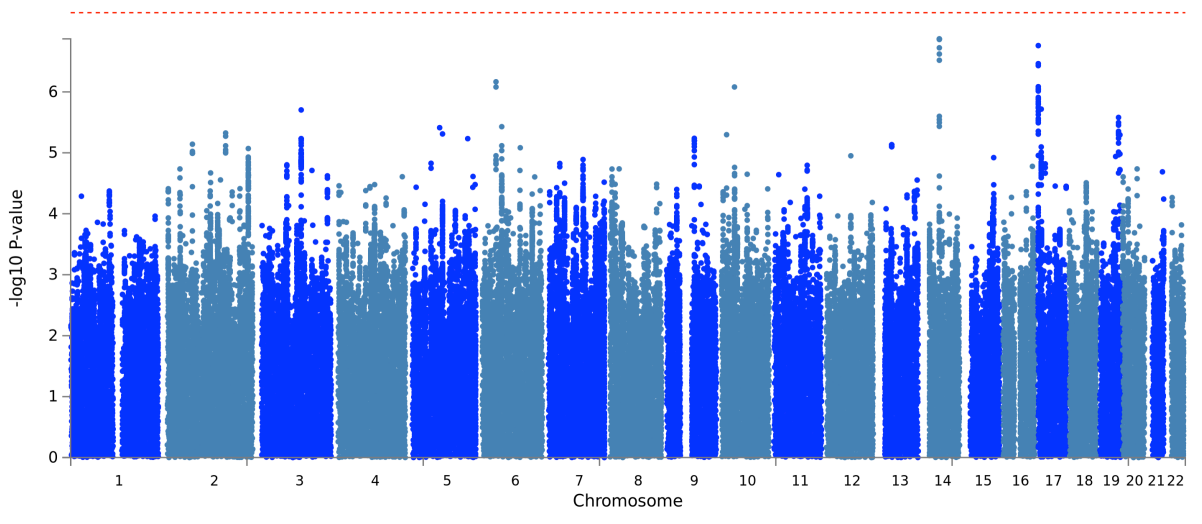


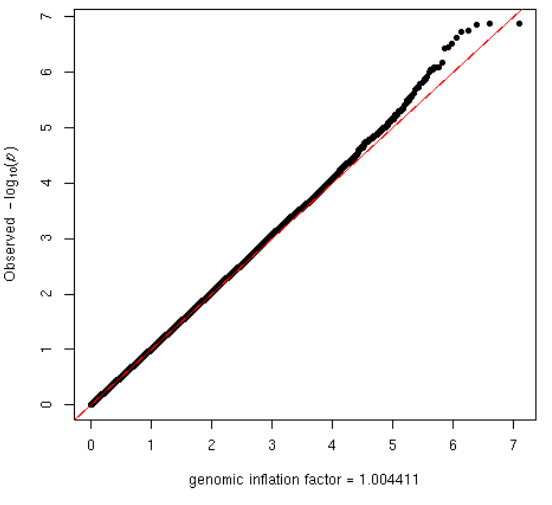
age-independent



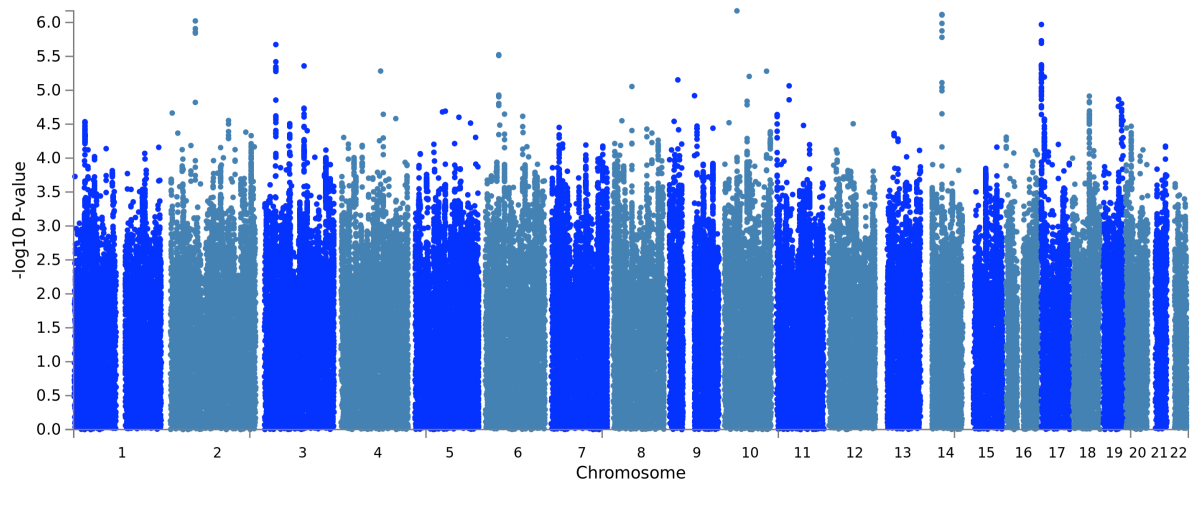


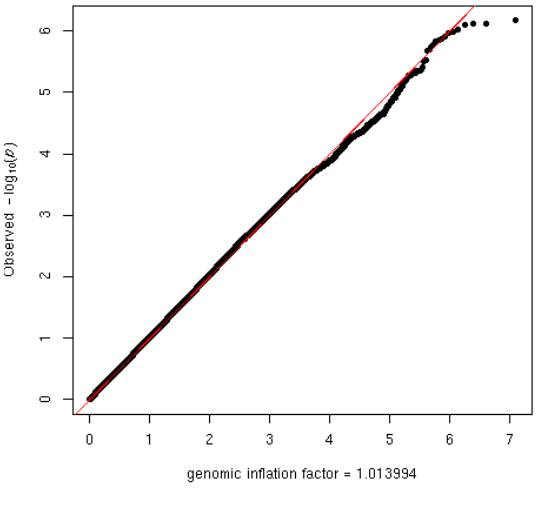
age-dependent linear



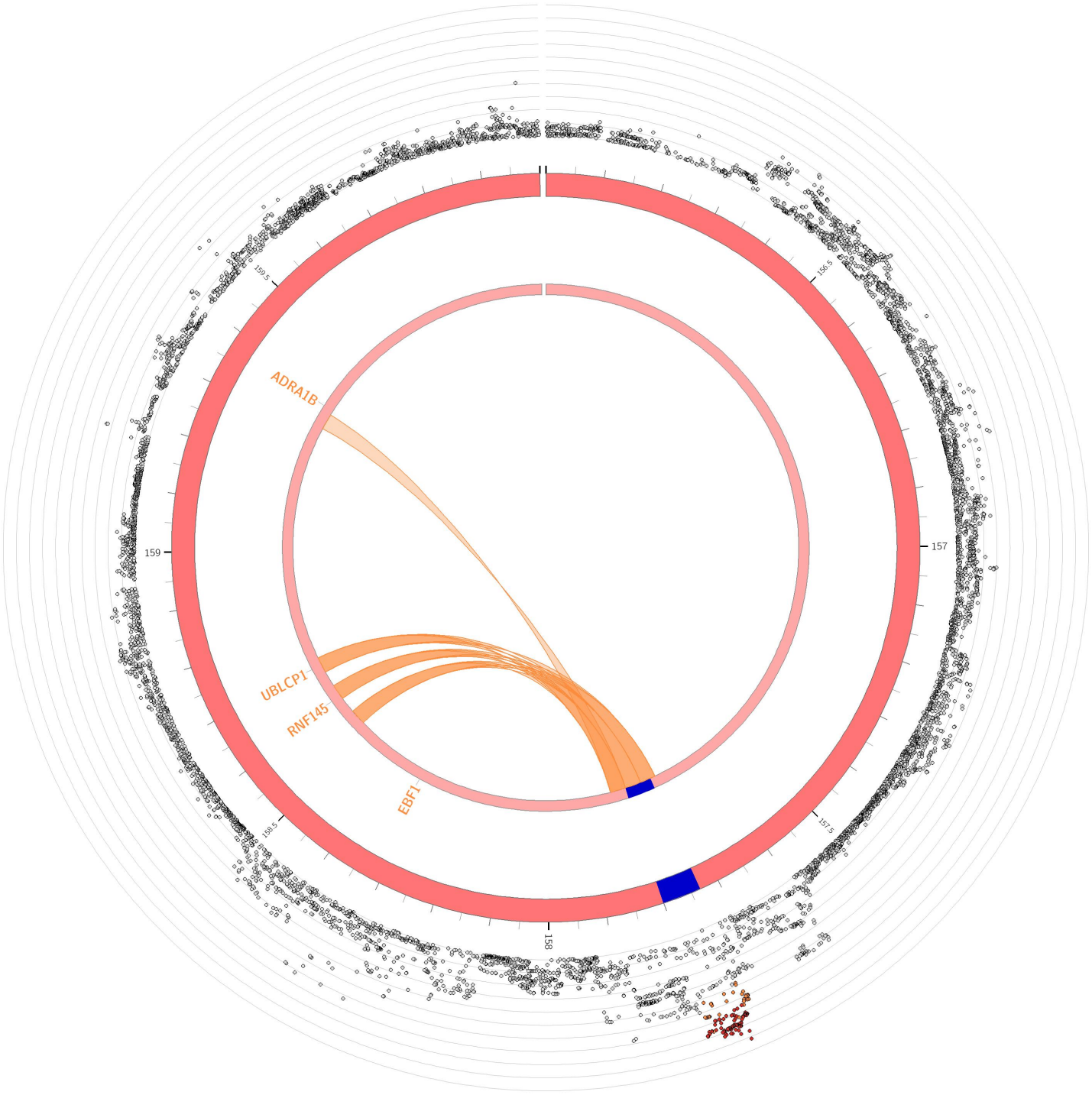


age-dependent quadratic

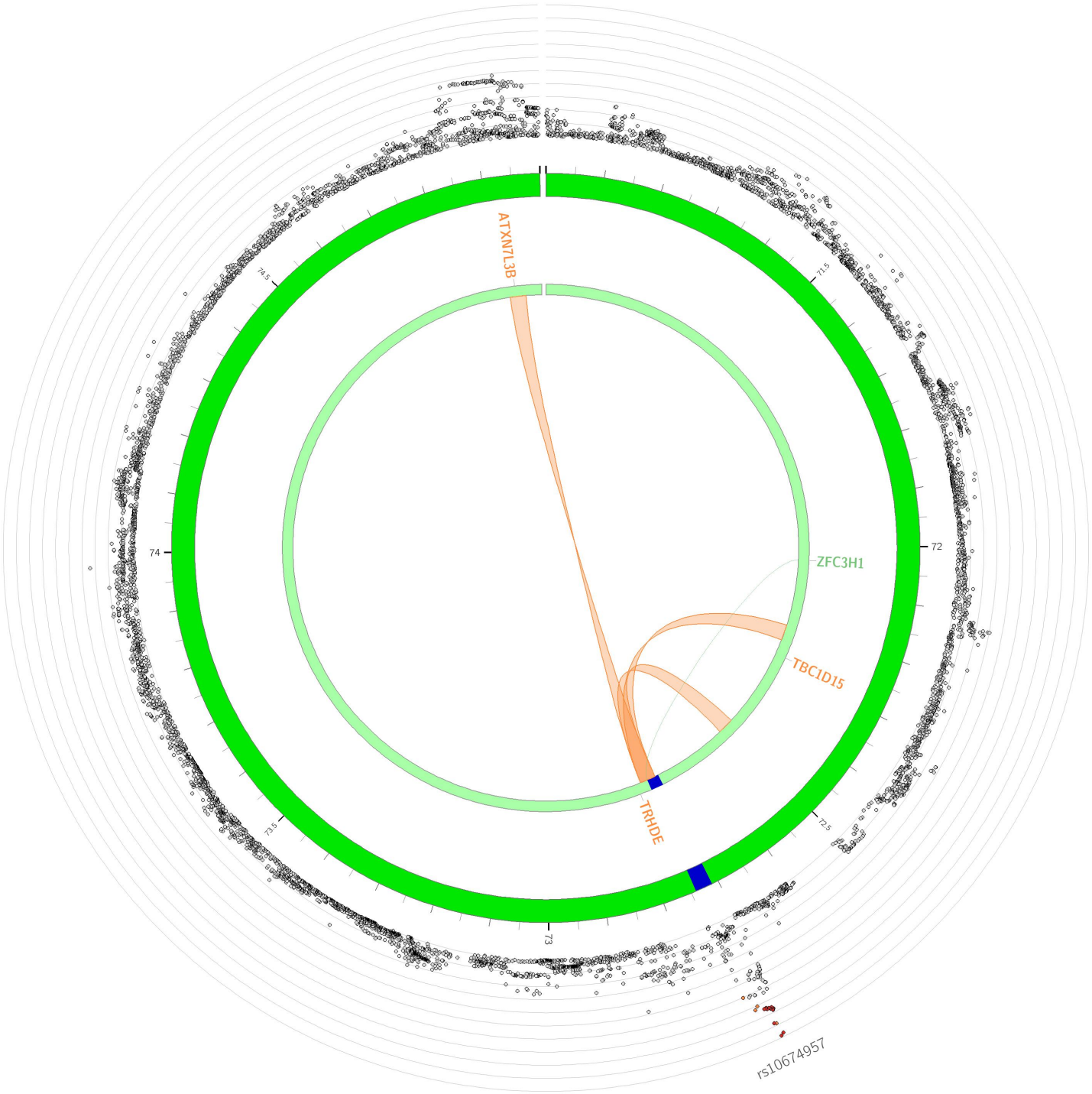




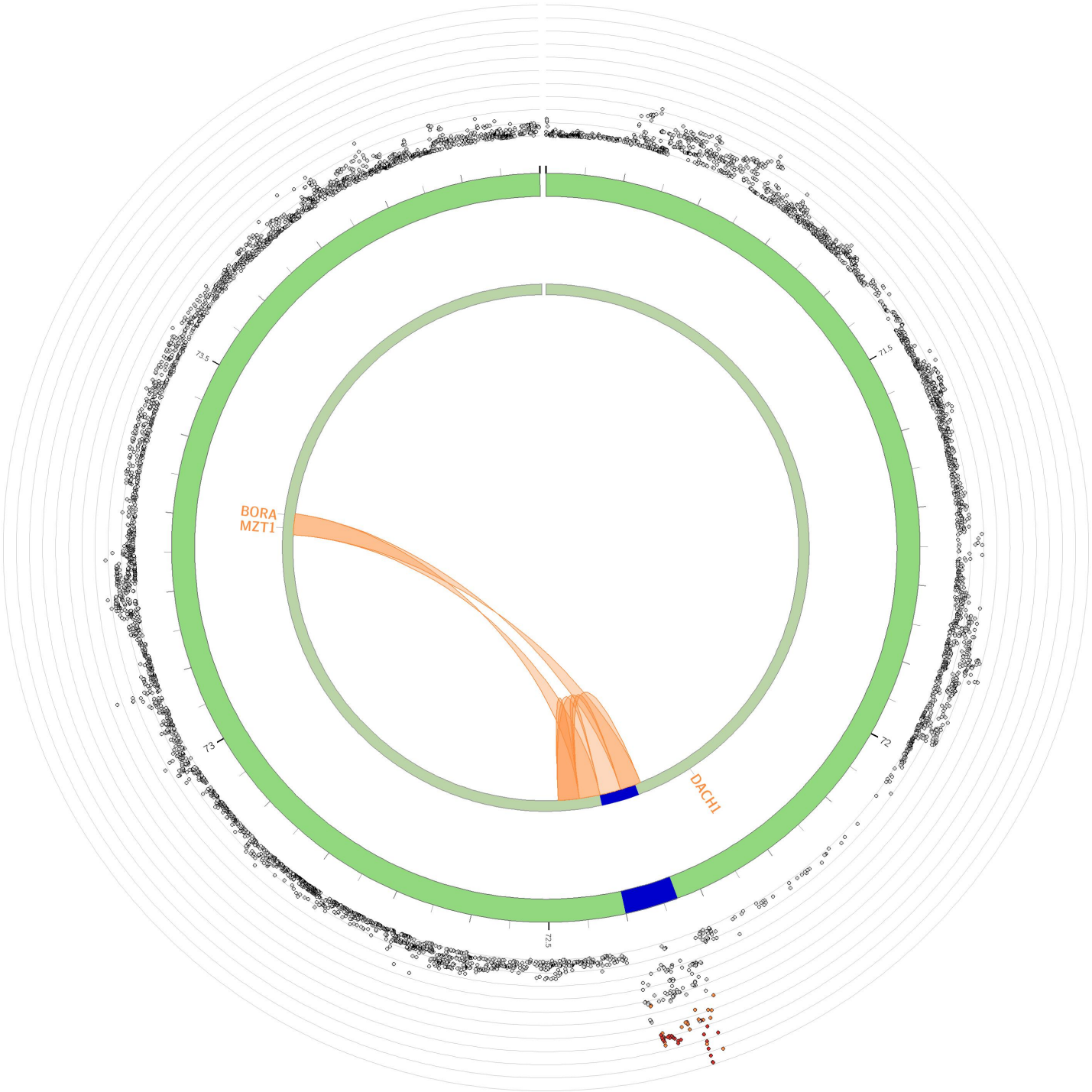
S4A chr 5: rs6864758



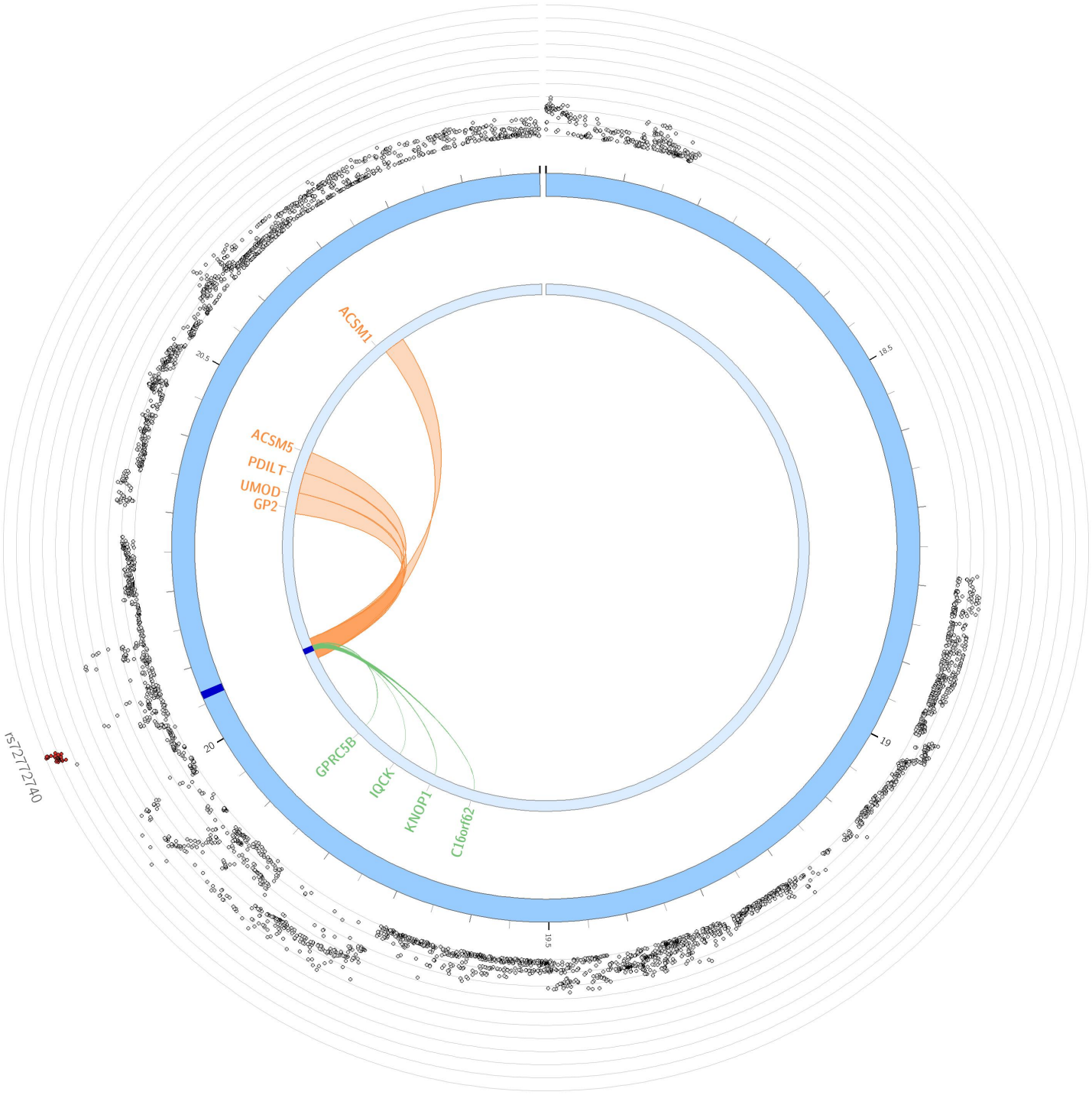
S4B chr 12: rs10674957 (*THRDE*)



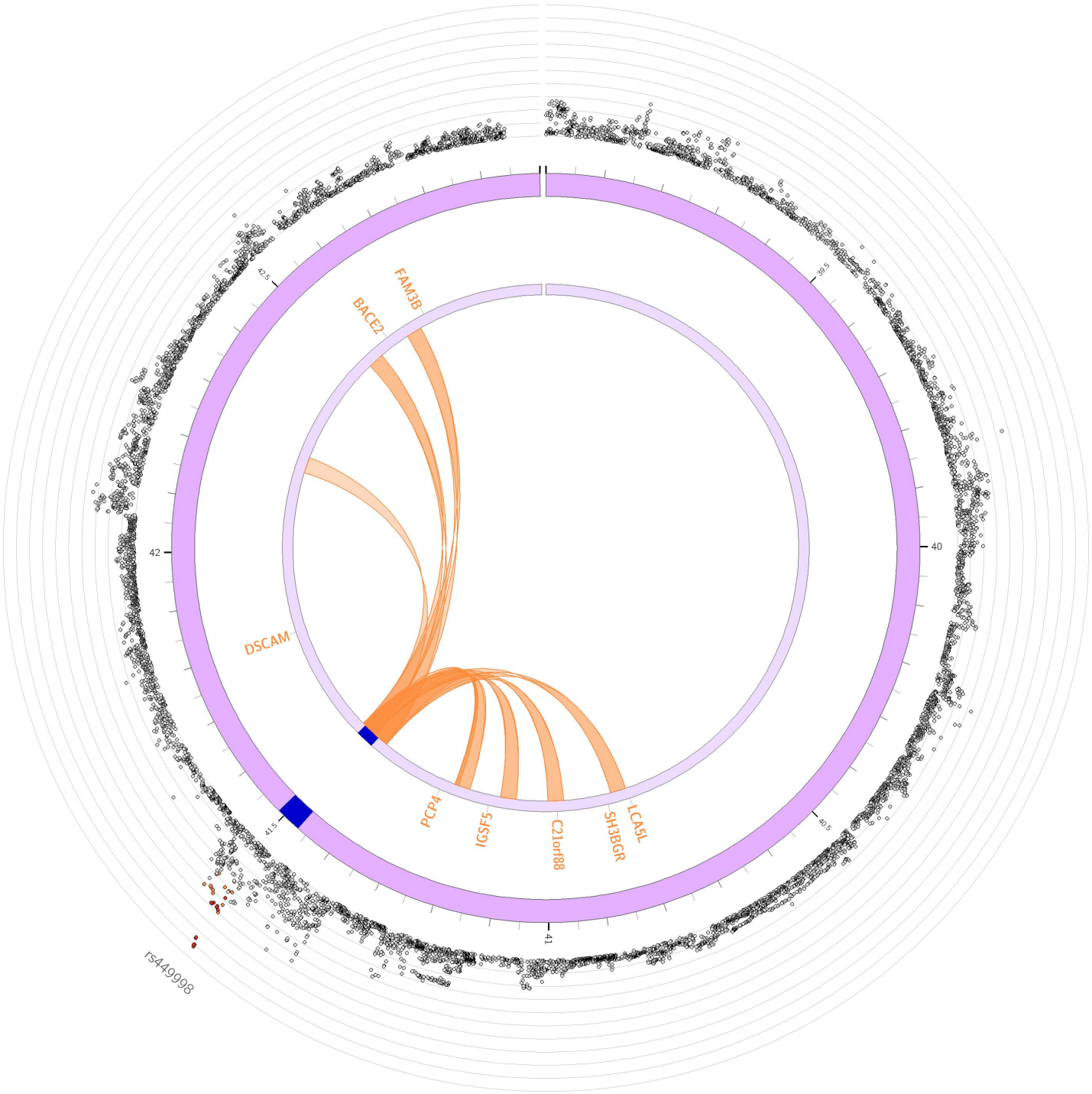
S4C chr 13: rs573983368 (*DACH1*)



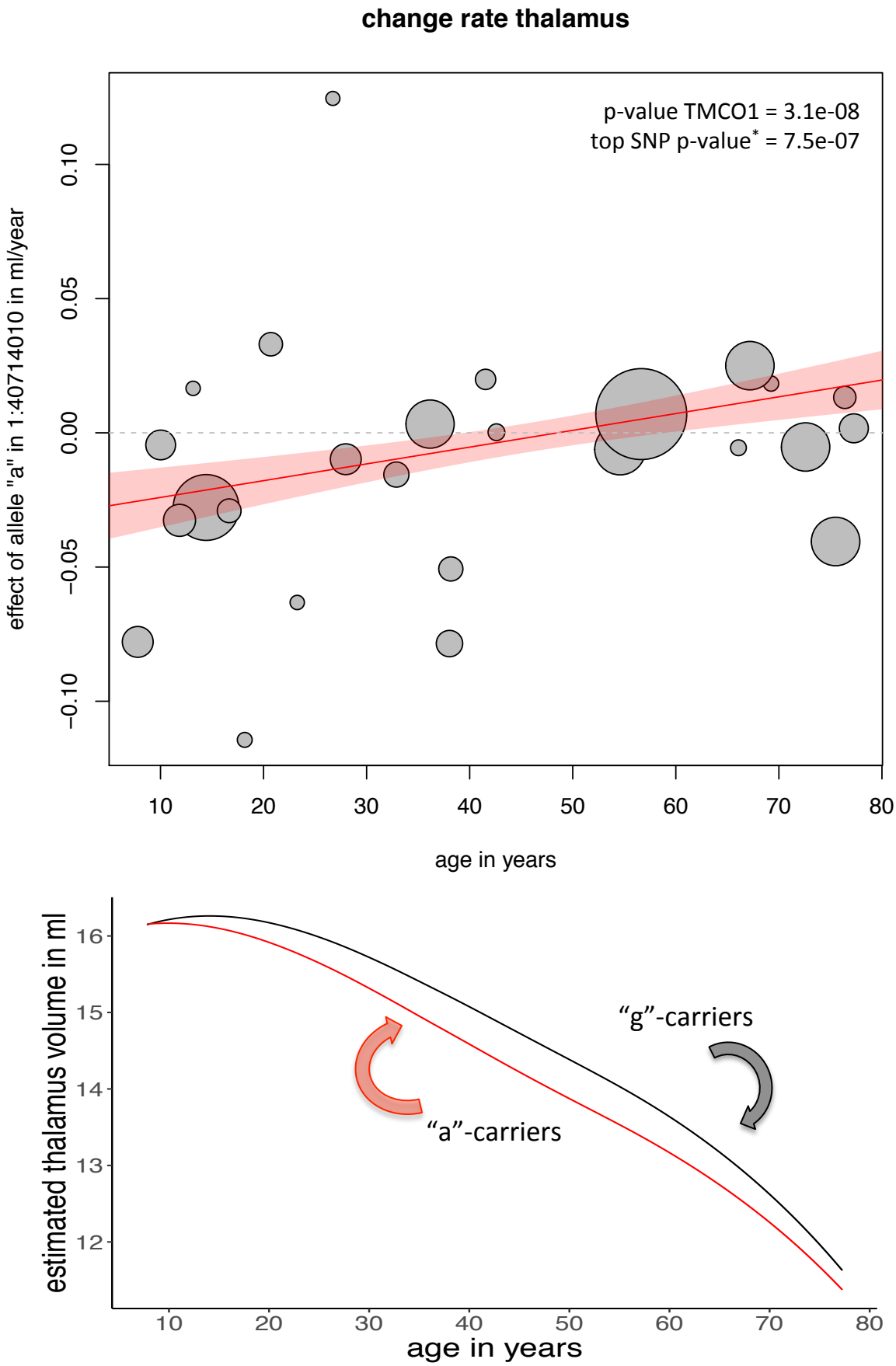
S4D chr 16: rs72772740 (*GPR139*)



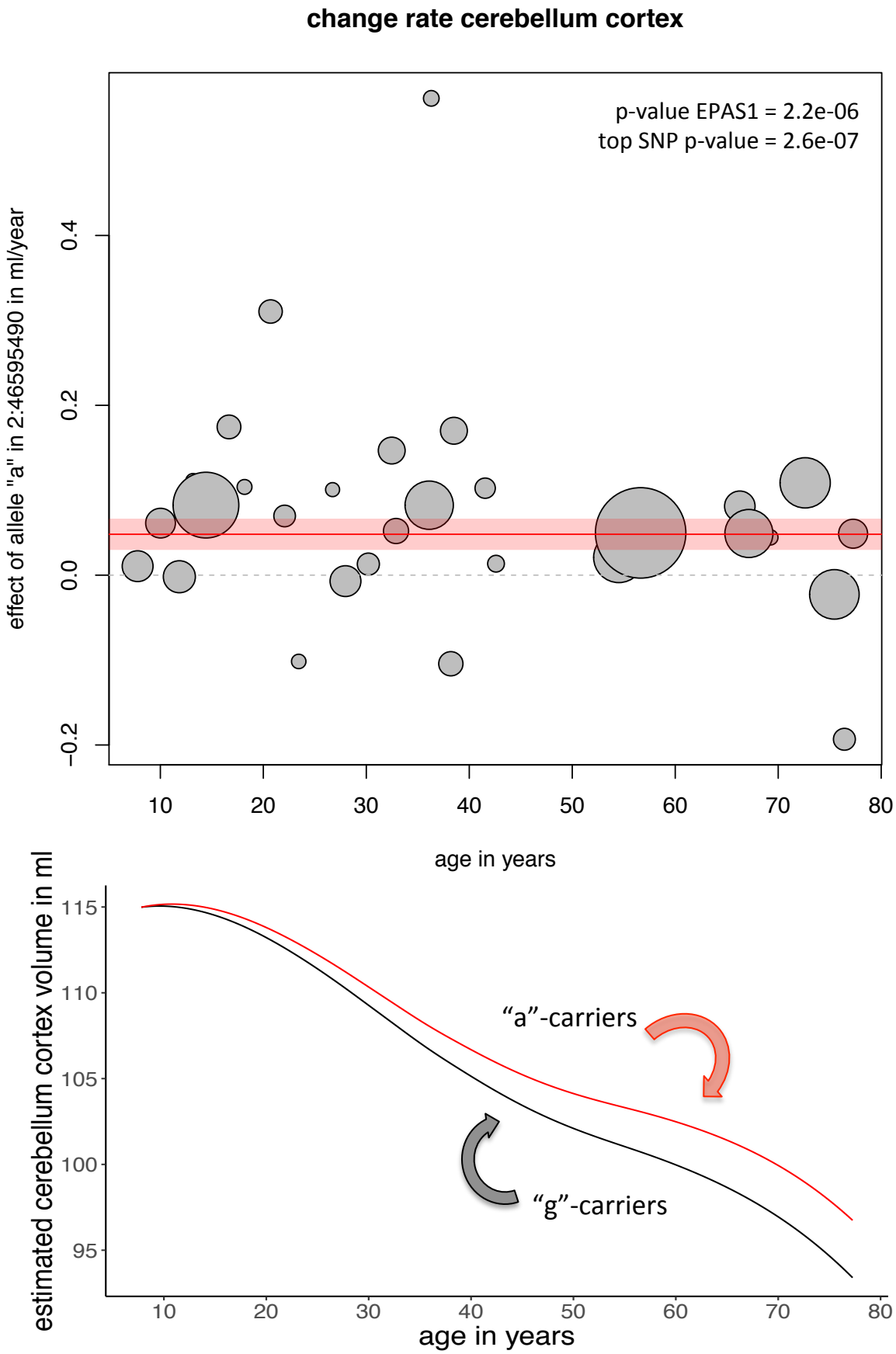
S4E chr 21: rs449998 (*DSACM*)



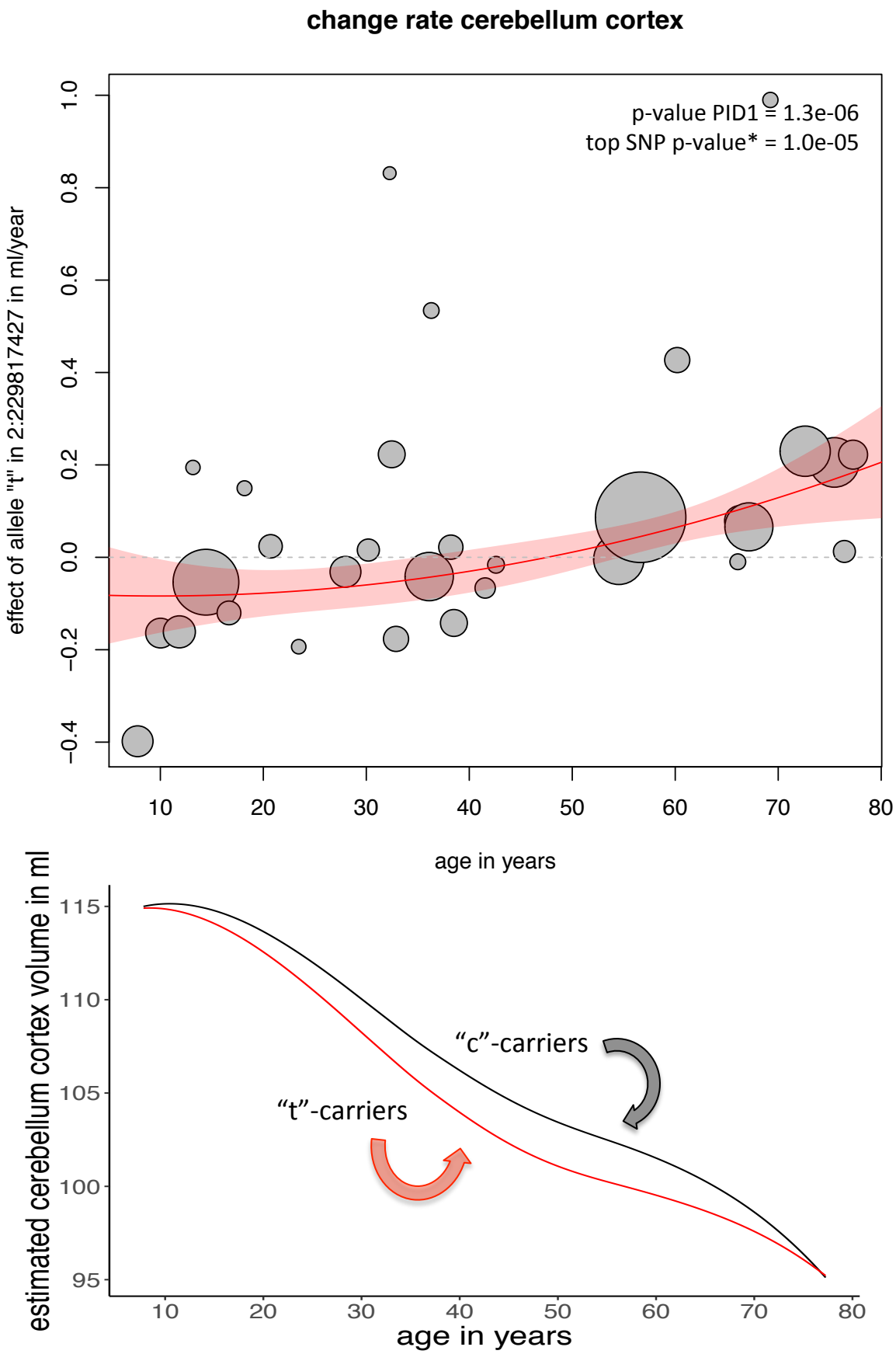
S5A


change rate thalamus
p-value TMCO1 = 3.1e-08
top SNP p-value* = 7.5e-07
effect of allele "a" in 1:40714010 in ml/year
0.10
0.05
0.00
−0.05
−0.10
10
20
30
40
50
60
70
80
age in years
estimated thalamus volume in ml
16
15
14
13
12
"g"-carriers
"a"-carriers
10
20
30
40
50
60
70
80
age in years

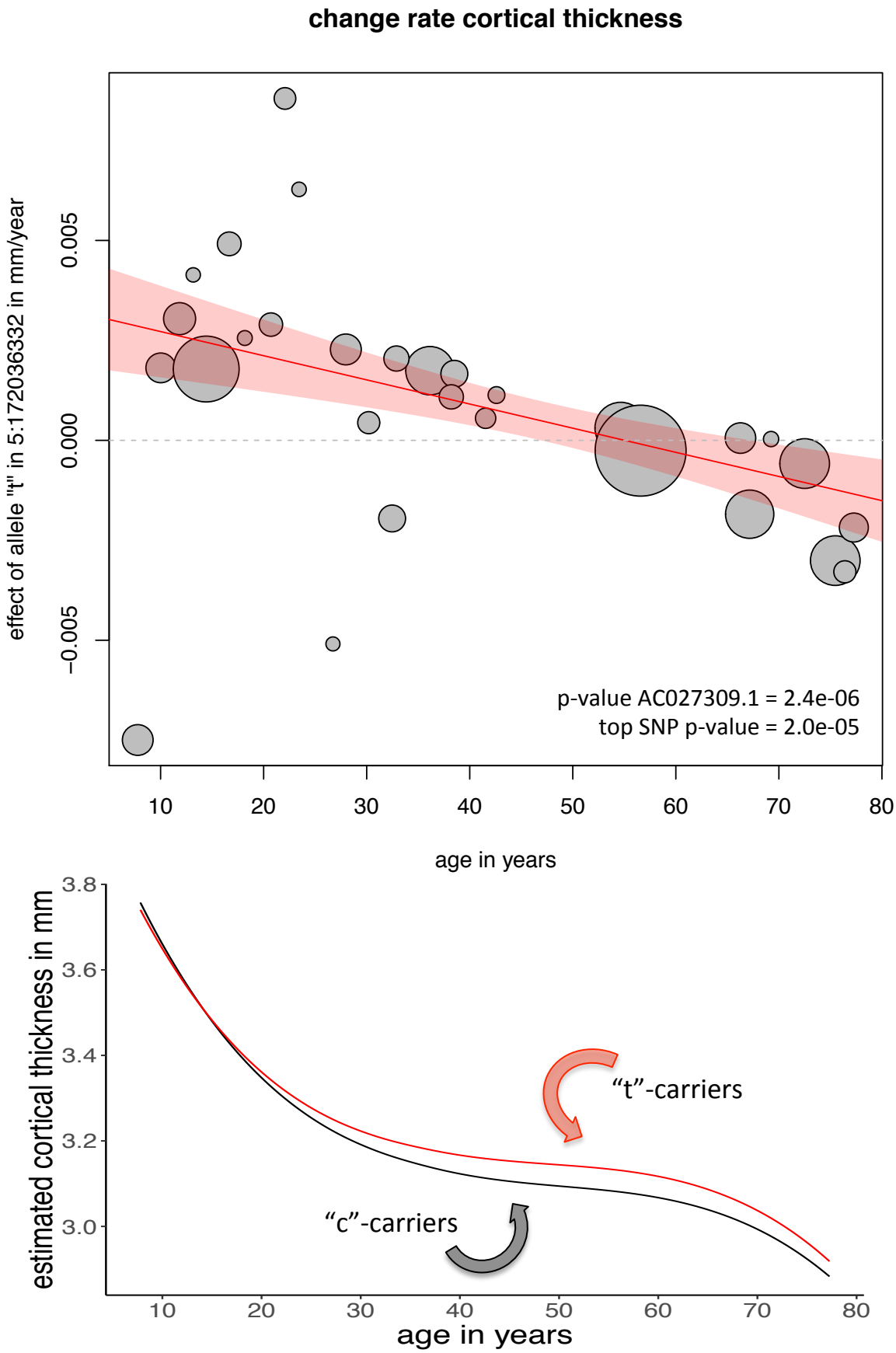
S5B


change rate cerebellum cortex
p-value EPAS1 = 2.2e-06
top SNP p-value = 2.6e-07
effect of allele "a" in 2:46595490 in ml/year
0.4
0.2
0.0
−0.2
10
20
30
40
50
60
70
80
age in years
estimated cerebellum cortex volume in ml
115
110
105
100
95
"a"-carriers
"g"-carriers
10
20
30
40
50
60
70
80
age in years

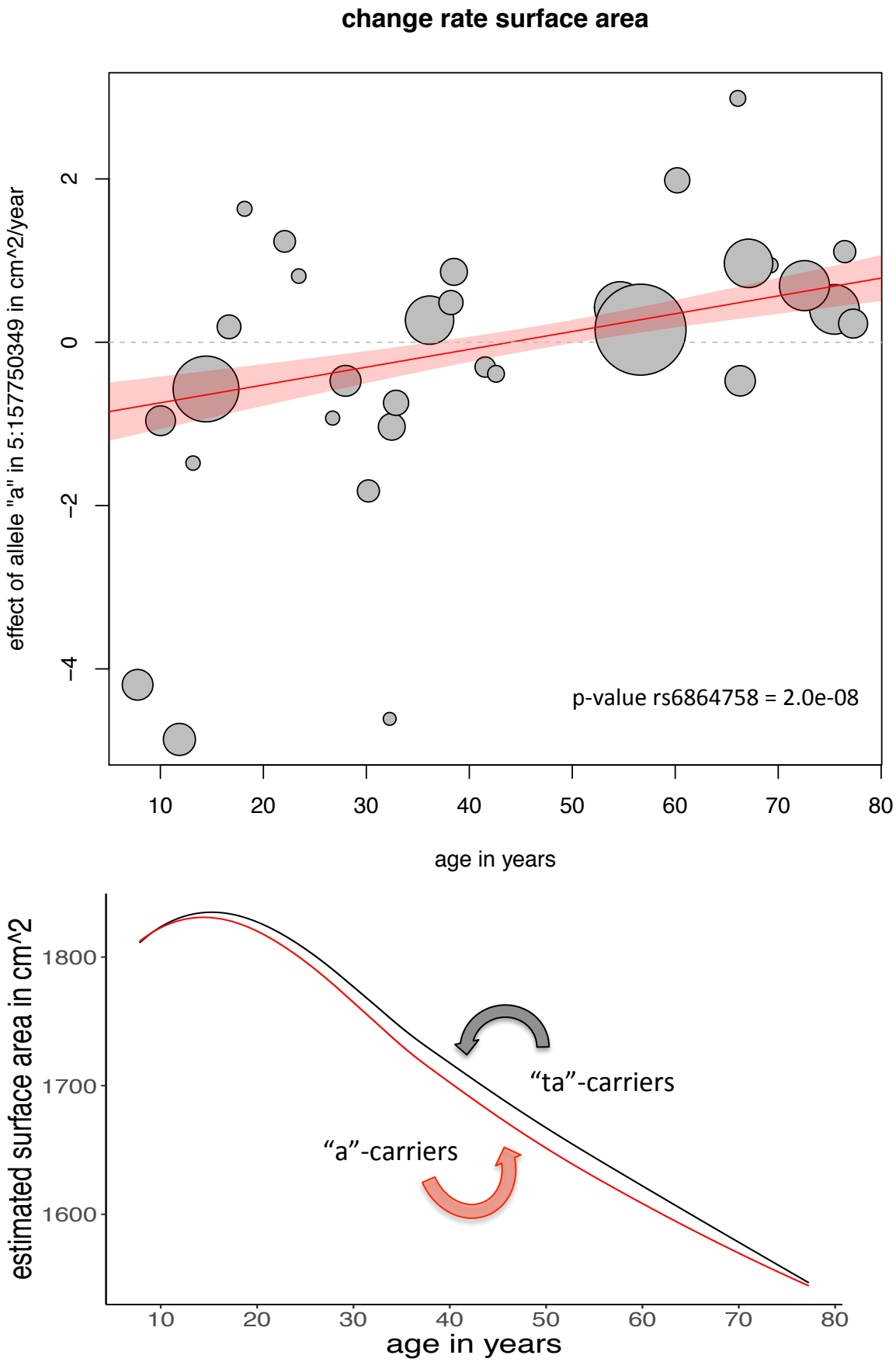
S5C


change rate cerebellum cortex
p-value PID1 = 1.3e-06
top SNP p-value* = 1.0e-05
effect of allele "t" in 2:229817427 in ml/year
1.0
0.8
0.6
0.4
0.2
0.0
−0.2
−0.4
10
20
30
40
50
60
70
80
age in years
estimated cerebellum cortex volume in ml
115
110
105
100
95
"c"-carriers
"t"-carriers
10
20
30
40
50
60
70
80
age in years

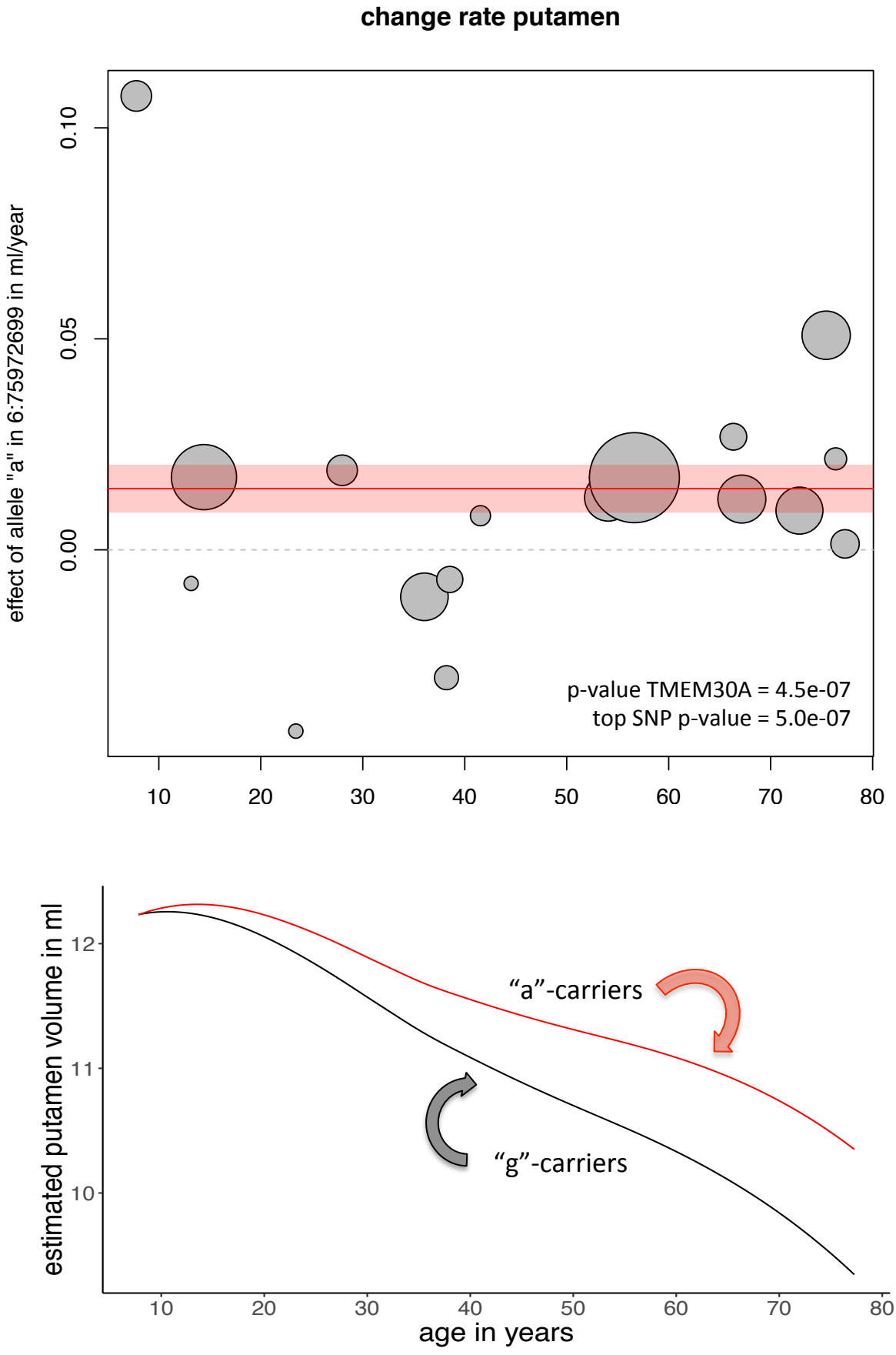
S5D


change rate cortical thickness
effect of allele "t" in 5:172036332 in mm/year
0.005
0.000
−0.005
p-value AC027309.1 = 2.4e-06
top SNP p-value = 2.0e-05
10
20
30
40
50
60
70
80
age in years
estimated cortical thickness in mm
3.8
3.6
3.4
3.2
3.0
“t”-carriers
“c”-carriers
10
20
30
40
50
60
70
80
age in years

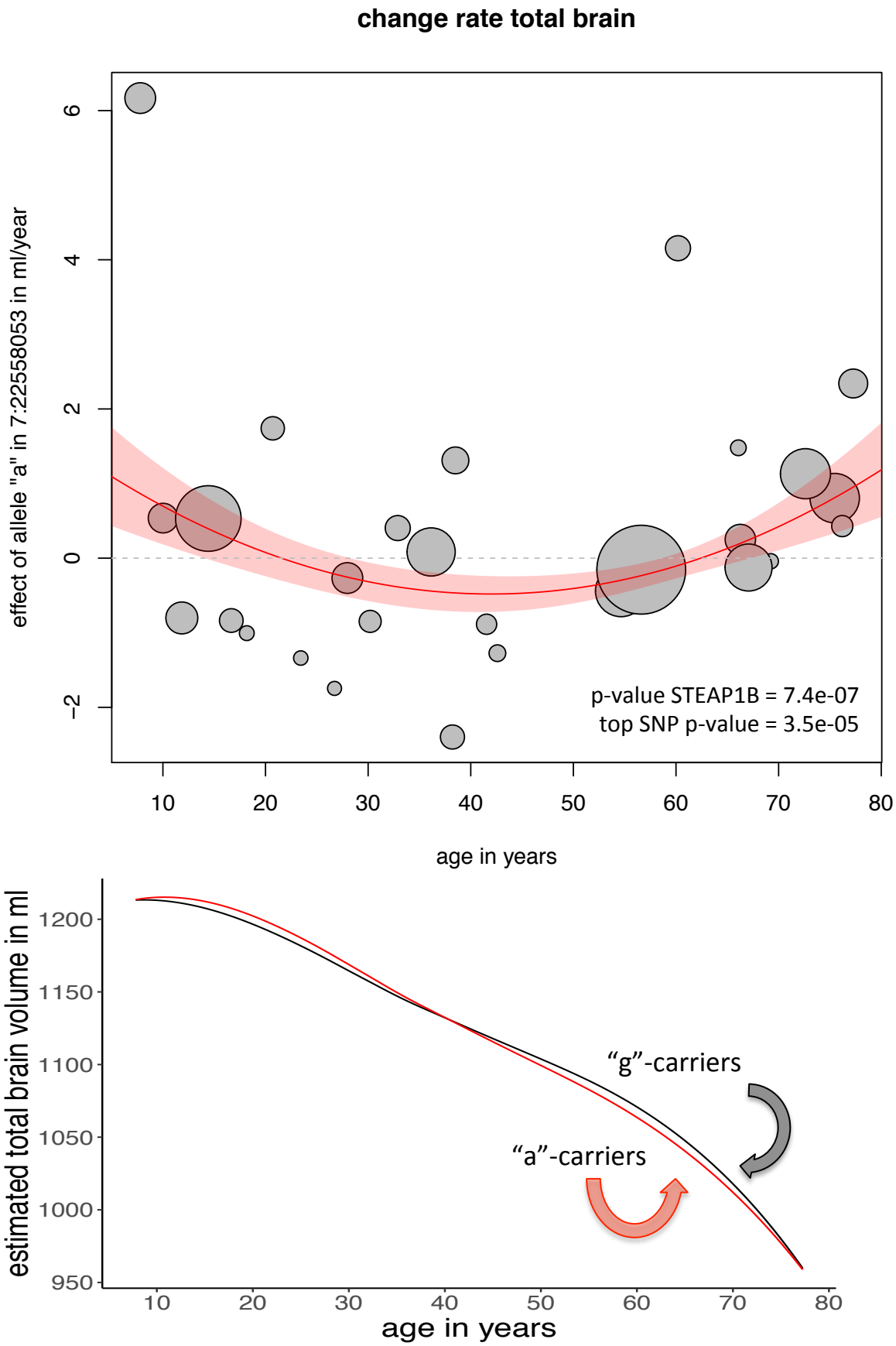
S5E


change rate surface area
effect of allele "a" in 5:157750349 in cm^2/year
2
0
−2
−4
p-value rs6864758 = 2.0e-08
10
20
30
40
50
60
70
80
age in years
estimated surface area in cm^2
1800
1700
1600
“ta”-carriers
“a”-carriers
10
20
30
40
50
60
70
80
age in years

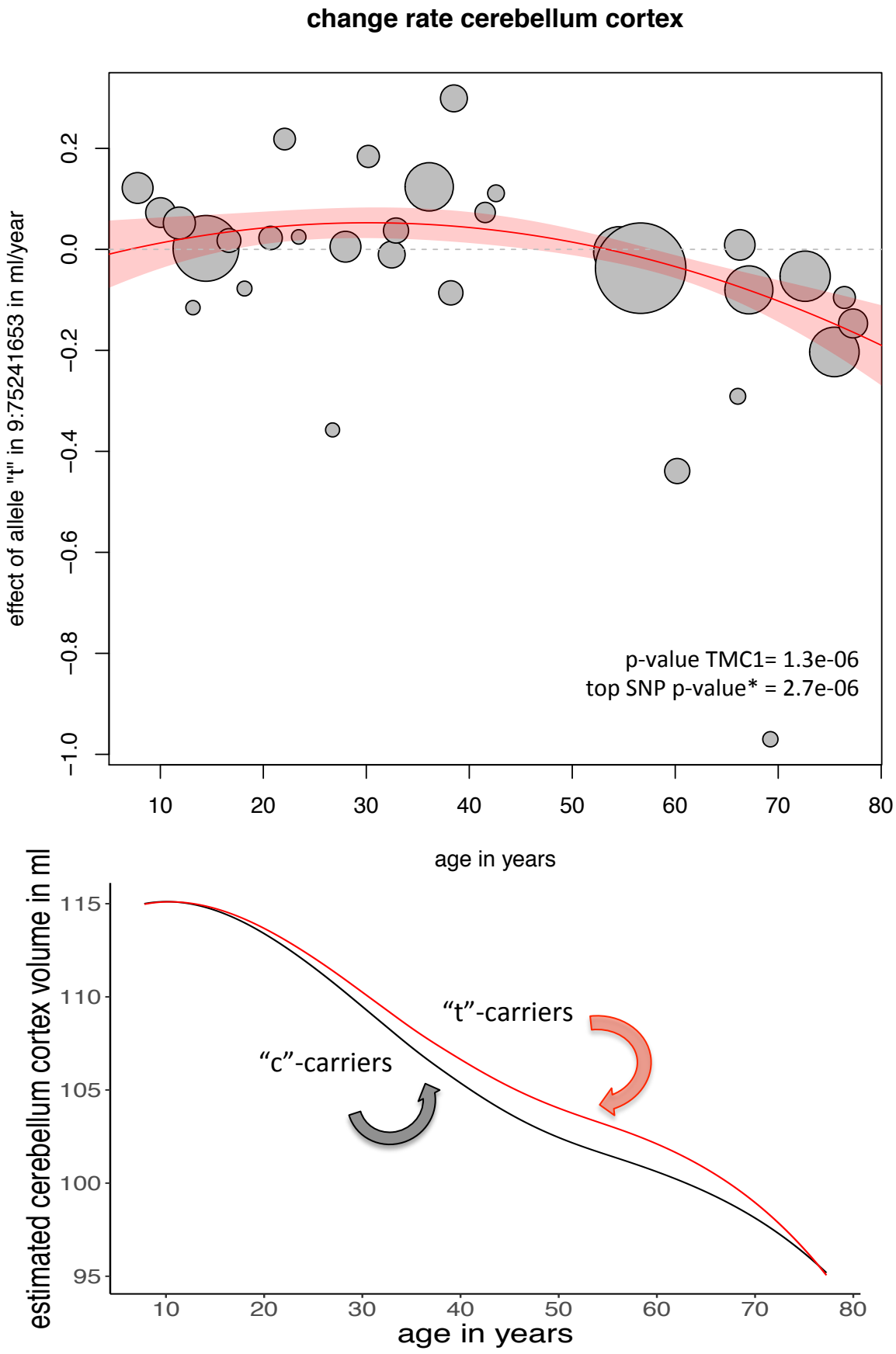
S5F


change rate putamen
effect of allele "a" in 6:75972699 in ml/year
0.10
0.05
0.00
p-value TMEM30A = 4.5e-07
top SNP p-value = 5.0e-07
10
20
30
40
50
60
70
80
estimated putamen volume in ml
12
11
10
"a"-carriers
"g"-carriers
age in years

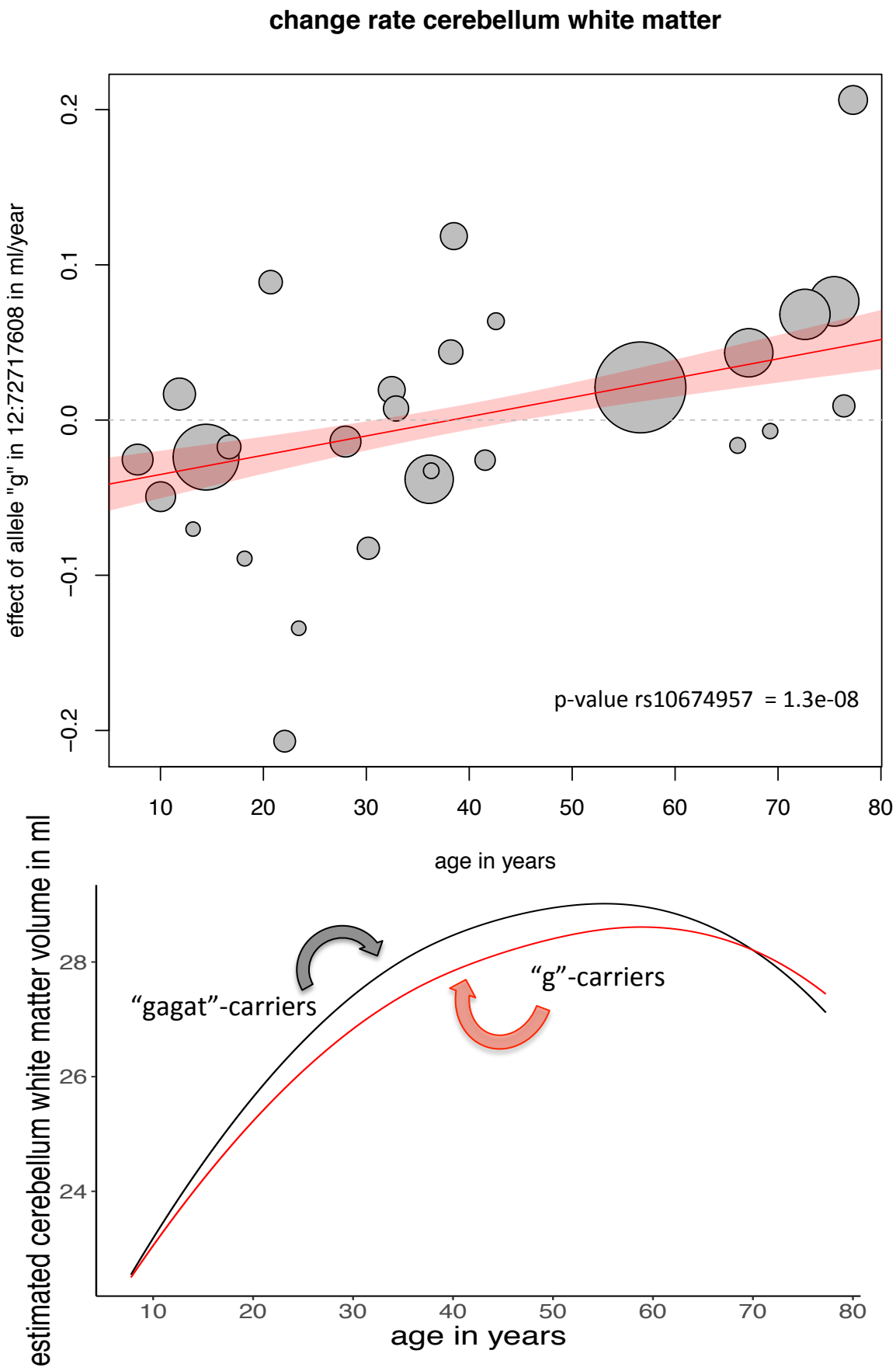
S5G


change rate total brain
effect of allele "a" in 7:22558053 in ml/year
6
4
2
0
−2
p-value STEAP1B = 7.4e-07
top SNP p-value = 3.5e-05
10
20
30
40
50
60
70
80
age in years
estimated total brain volume in ml
1200
1150
1100
1050
1000
950
"g"-carriers
"a"-carriers
10
20
30
40
50
60
70
80
age in years

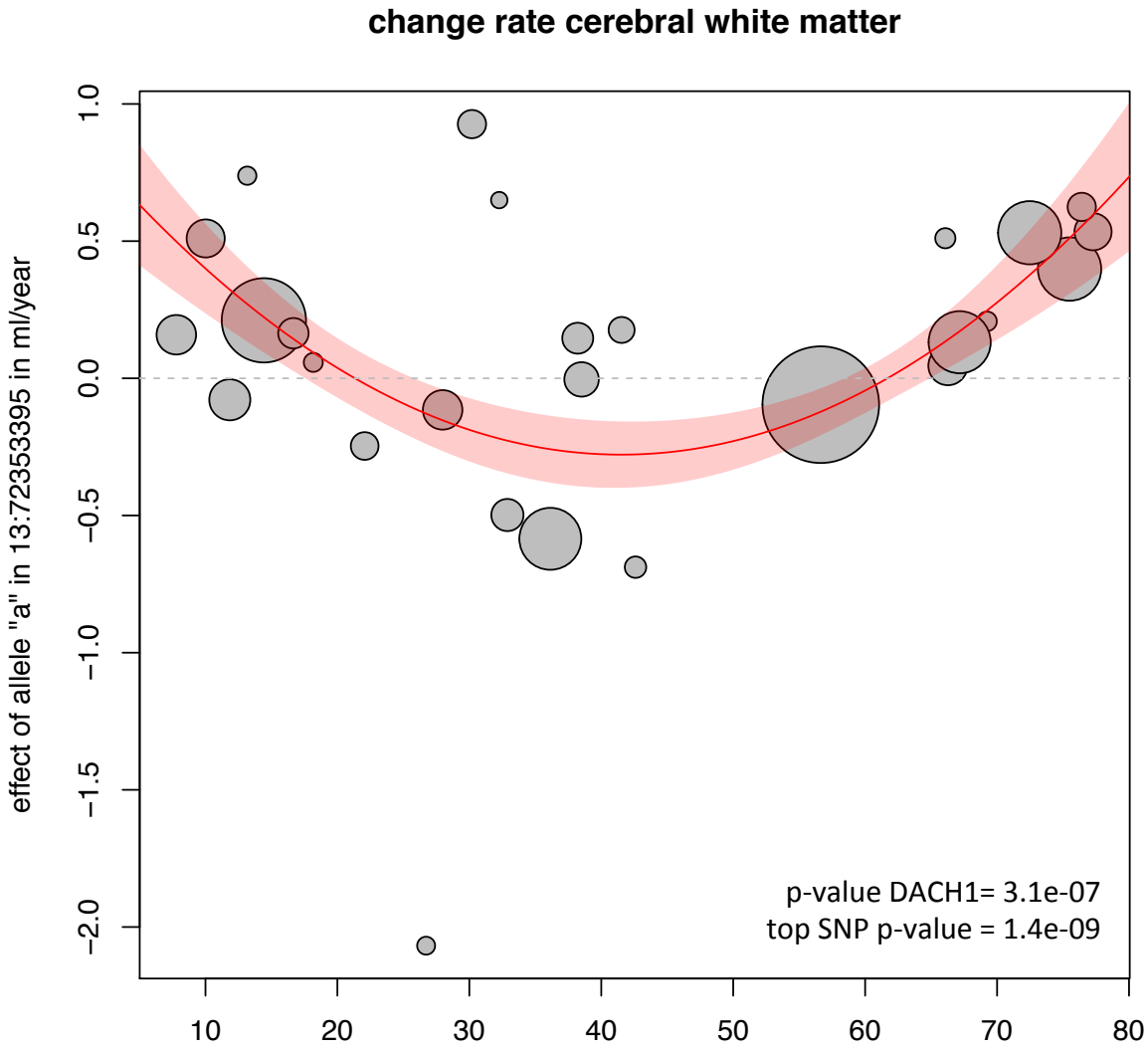
S5H

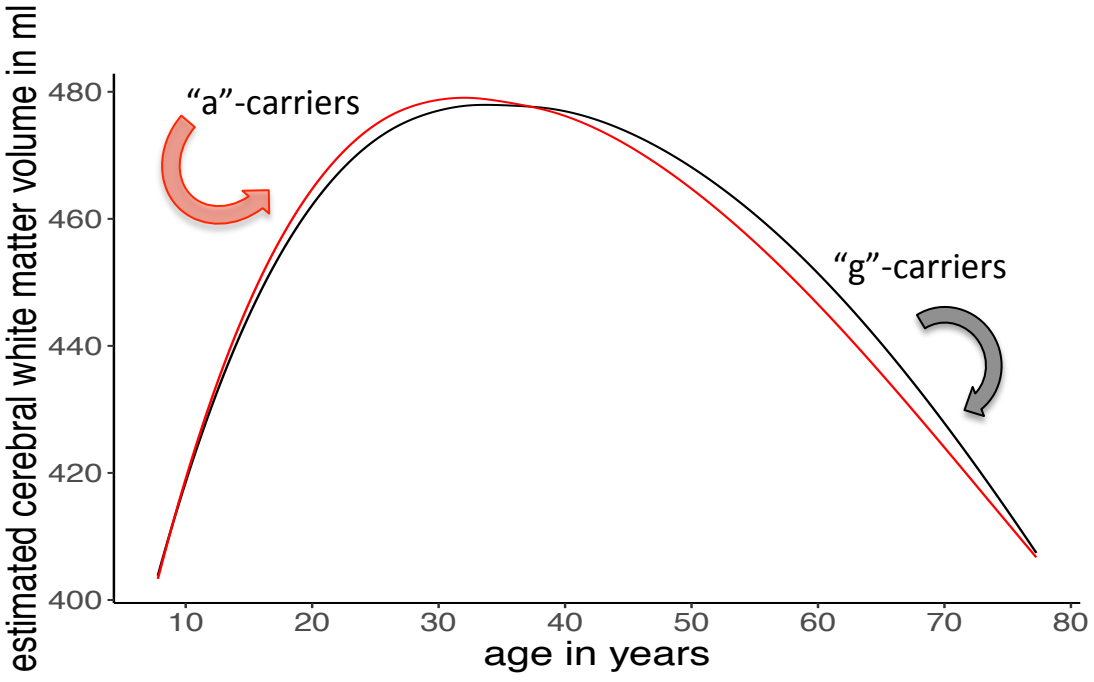

change rate cerebellum cortex
effect of allele "t" in 9:75241653 in ml/year
0.2
0.0
−0.2
−0.4
−0.6
−0.8
−1.0
10
20
30
40
50
60
70
80
age in years
p-value TMC1= 1.3e-06
top SNP p-value* = 2.7e-06
estimated cerebellum cortex volume in ml
115
110
105
100
95
“t”-carriers
“c”-carriers
10
20
30
40
50
60
70
80
age in years

S5I

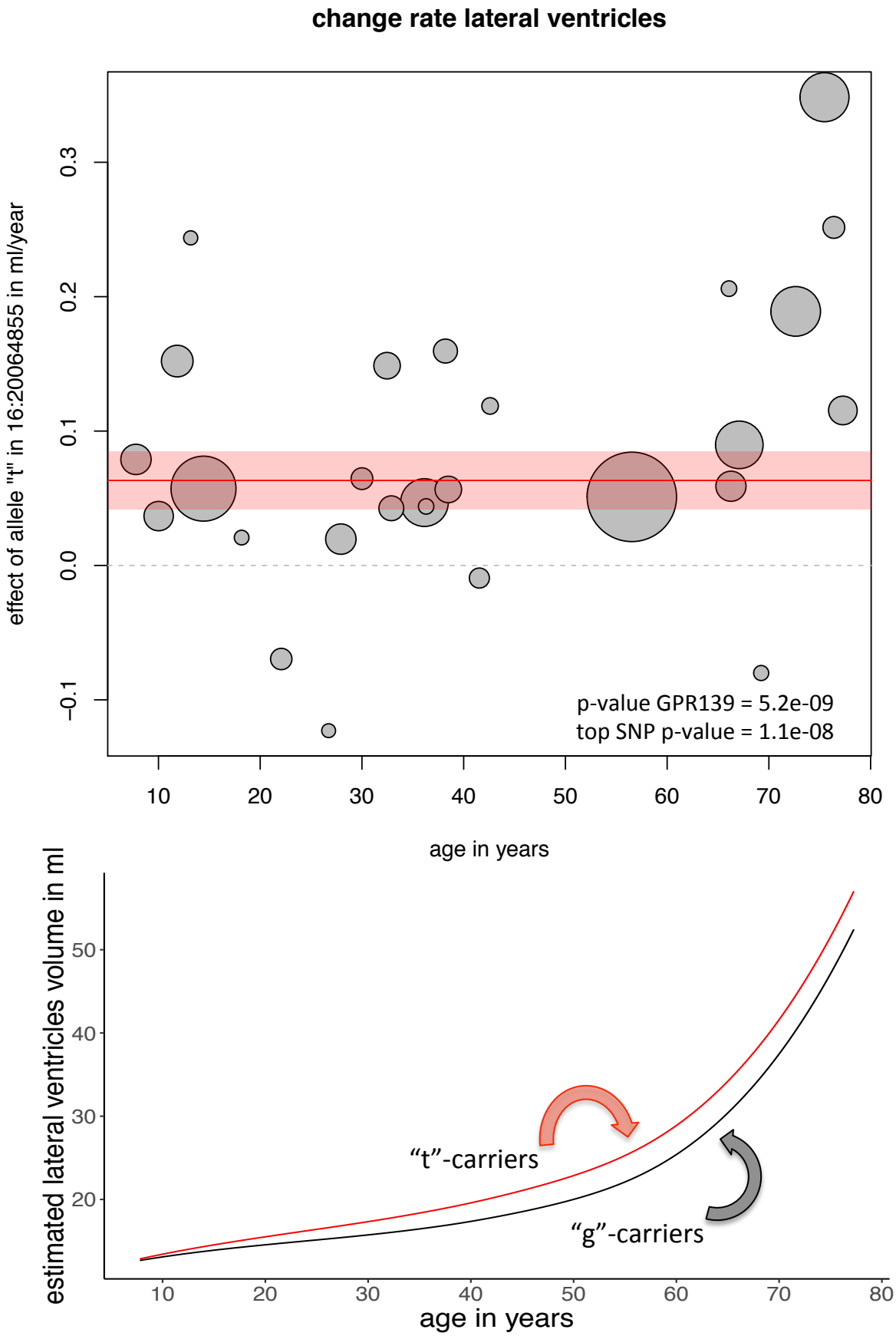

change rate cerebellum white matter
effect of allele "g" in 12:72717608 in ml/year
0.2
0.1
0.0
−0.1
−0.2
p-value rs10674957 = 1.3e-08
10
20
30
40
50
60
70
80
age in years
estimated cerebellum white matter volume in ml
28
26
24
"gagat"-carriers
"g"-carriers
10
20
30
40
50
60
70
80
age in years

S5J

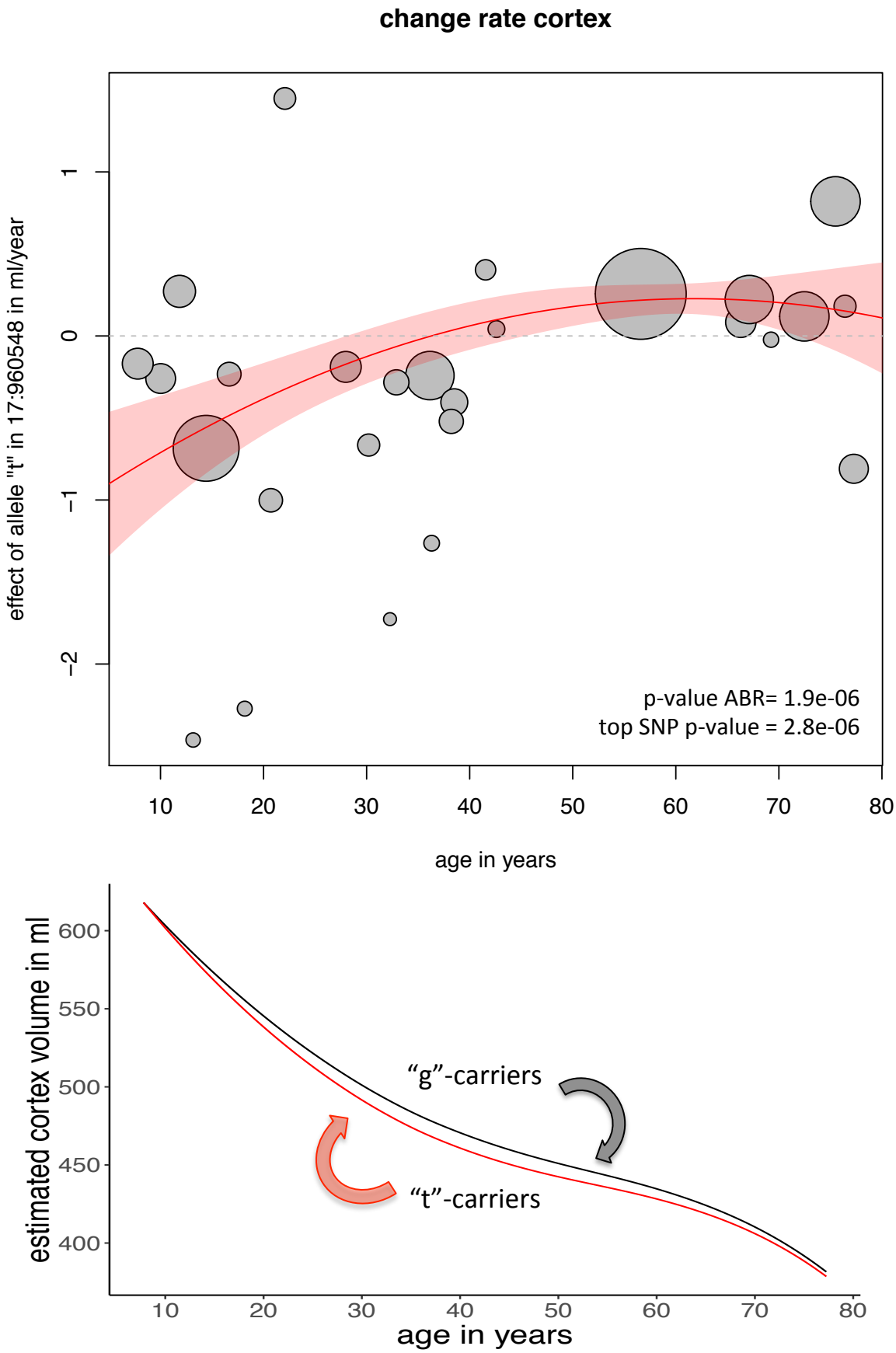

change rate cerebral white matter
effect of allele "a" in 13:72353395 in ml/year
1.0
0.5
0.0
−0.5
−1.0
−1.5
−2.0
10
20
30
40
50
60
70
80
p-value DACH1= 3.1e-07
top SNP p-value = 1.4e-09


estimated cerebral white matter volume in ml
480
460
440
420
400
"a"-carriers
"g"-carriers
10
20
30
40
50
60
70
80
age in years

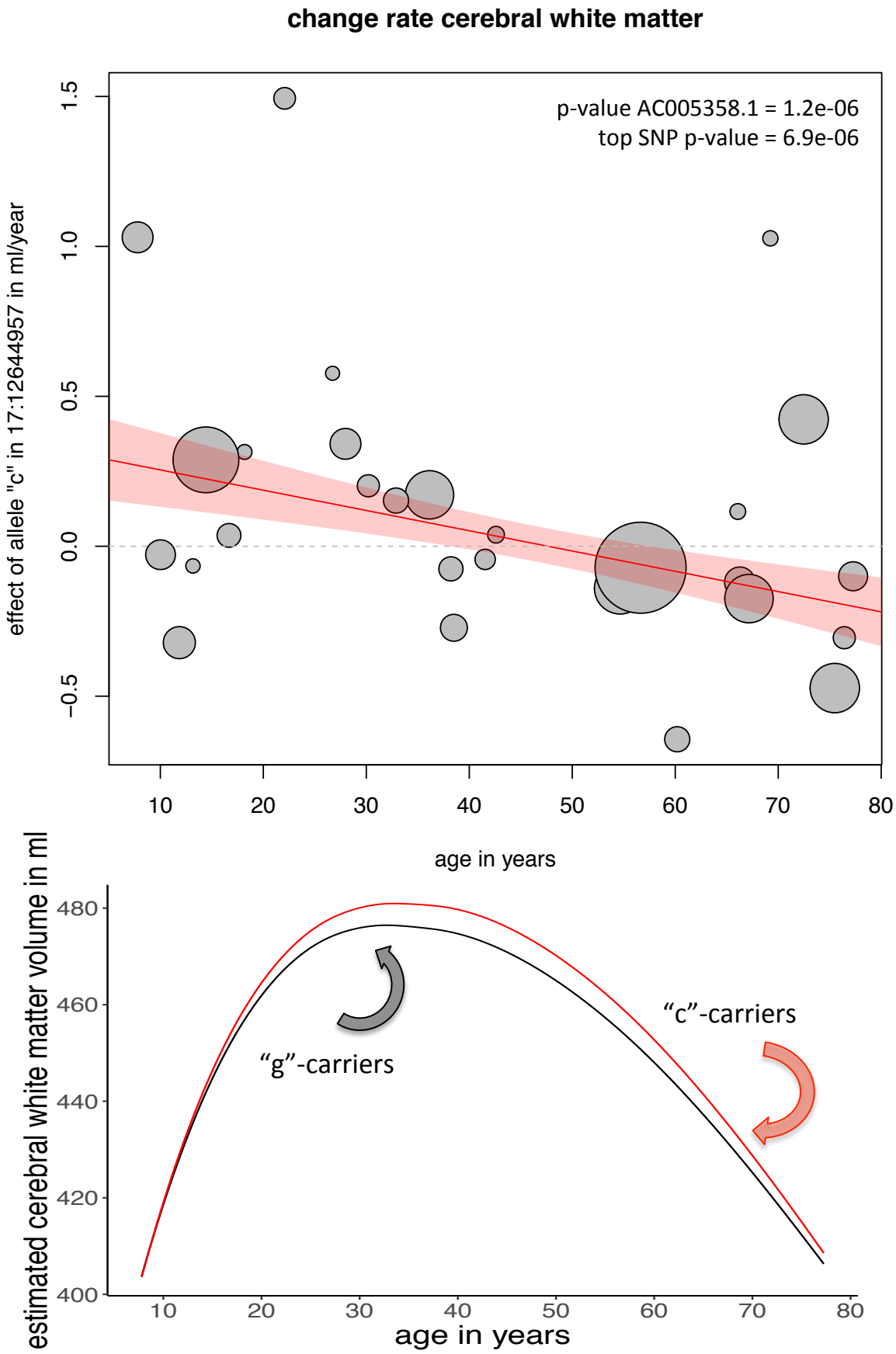
S5K


change rate lateral ventricles
effect of allele "t" in 16:20064855 in ml/year
0.3
0.2
0.1
0.0
−0.1
p-value GPR139 = 5.2e-09
top SNP p-value = 1.1e-08
10
20
30
40
50
60
70
80
age in years
estimated lateral ventricles volume in ml
50
40
30
20
“t”-carriers
“g”-carriers
10
20
30
40
50
60
70
80
age in years

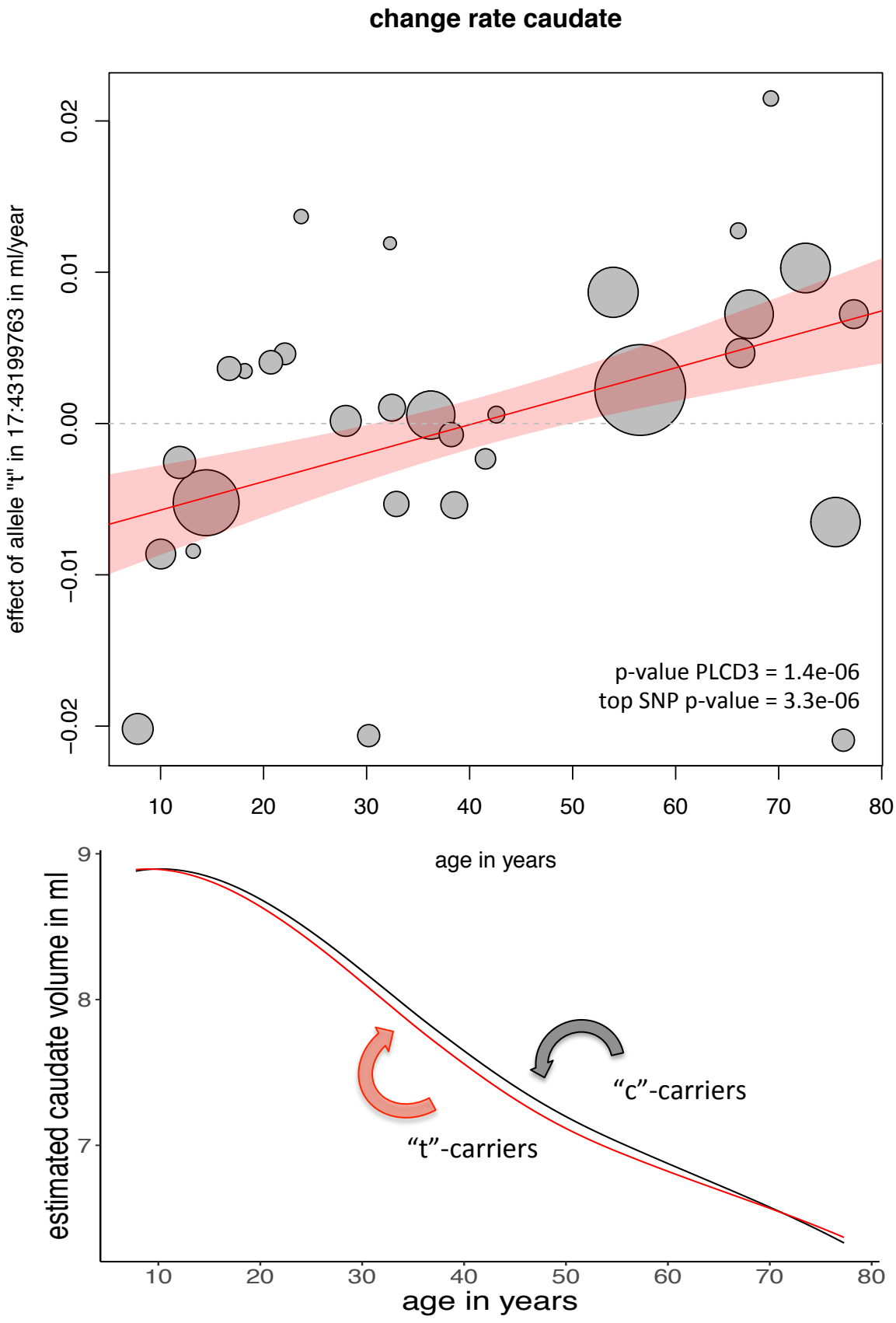
S5L

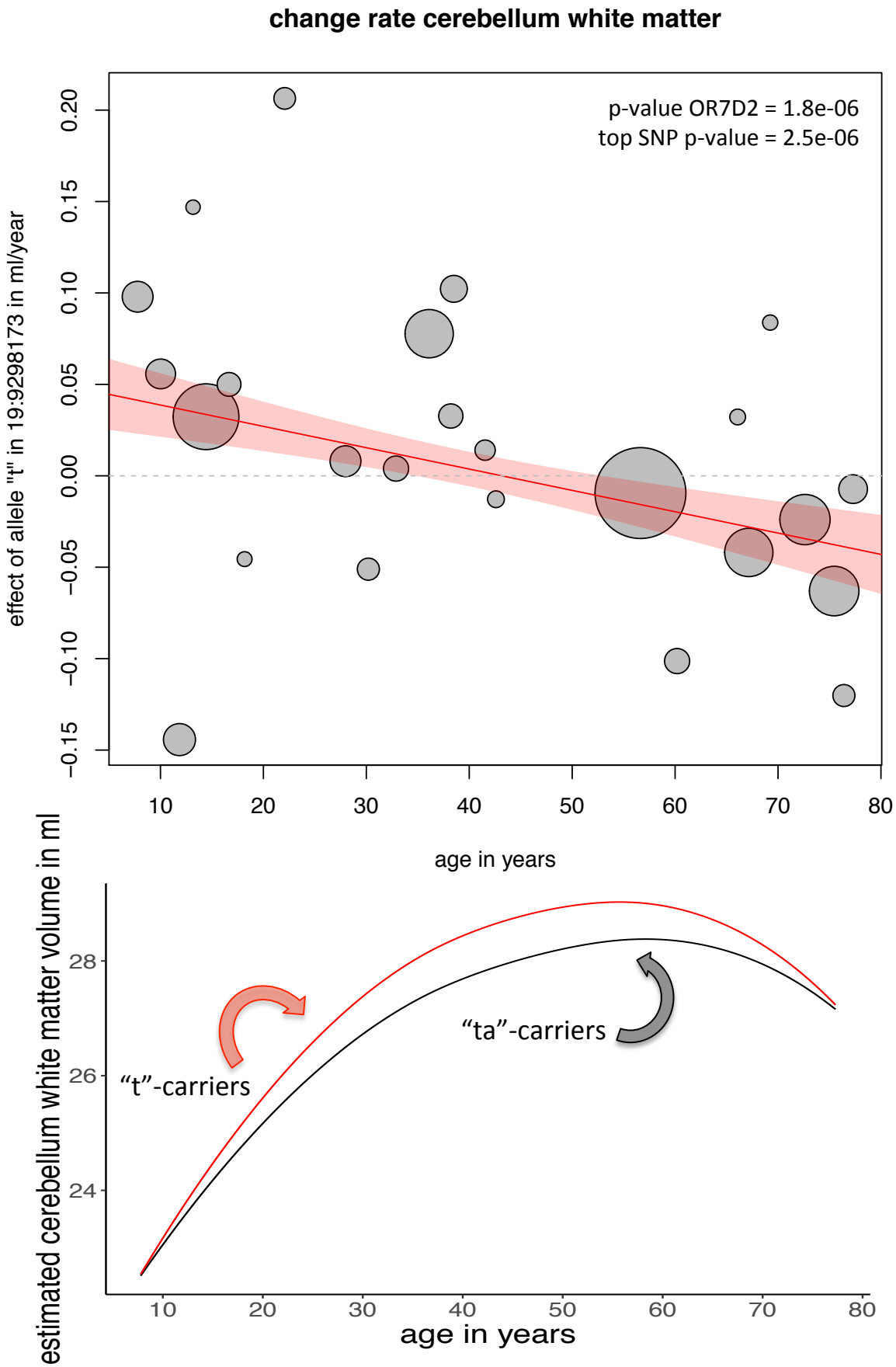

change rate cortex
effect of allele "t" in 17:960548 in ml/year
1
0
−1
−2
p-value ABR= 1.9e-06
top SNP p-value = 2.8e-06
10
20
30
40
50
60
70
80
age in years
estimated cortex volume in ml
600
550
500
450
400
“g”-carriers
“t”-carriers
10
20
30
40
50
60
70
80
age in years

S5M

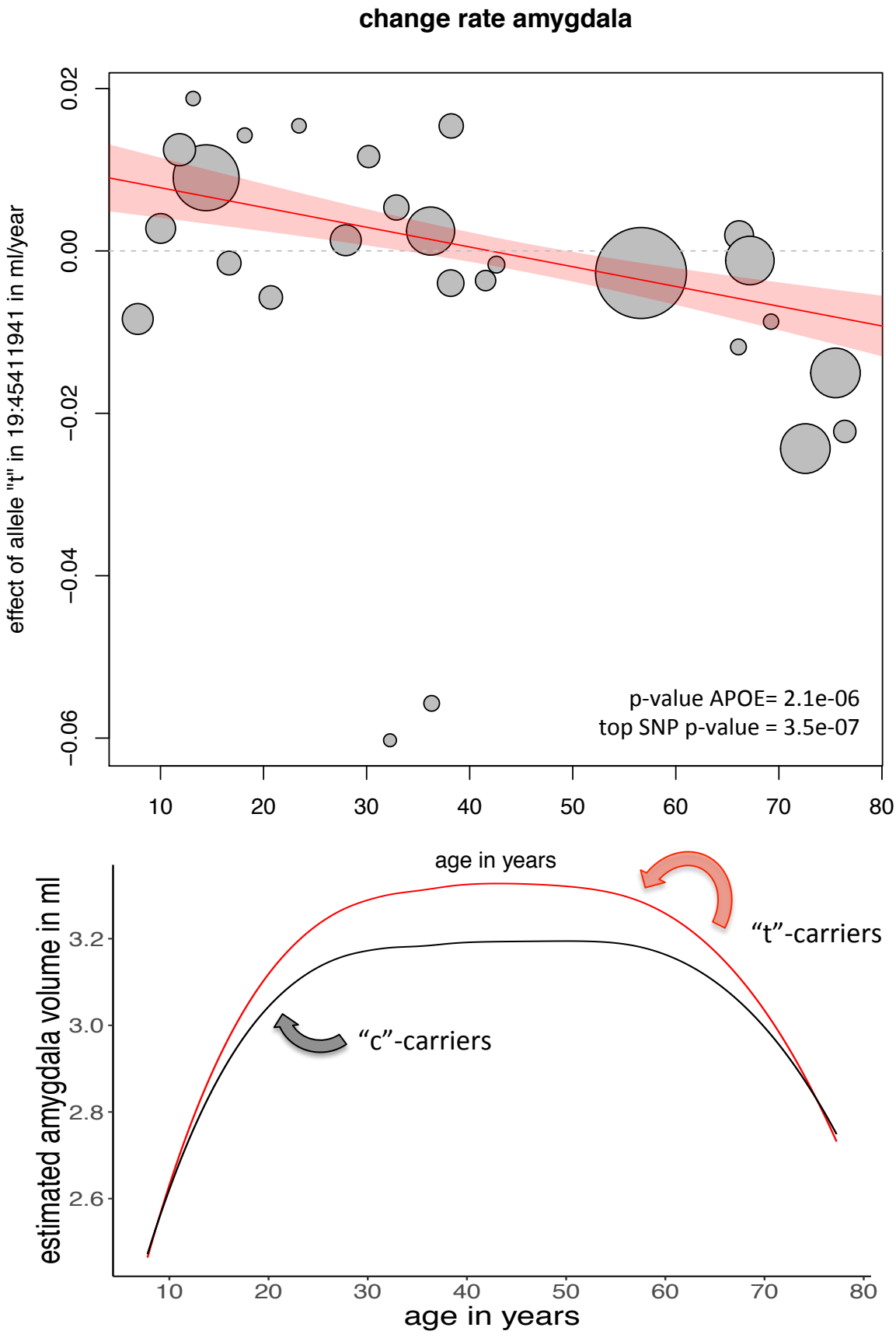

change rate cerebral white matter
p-value AC005358.1 = 1.2e-06
top SNP p-value = 6.9e-06
effect of allele "c" in 17:12644957 in ml/year
1.5
1.0
0.5
0.0
−0.5
10
20
30
40
50
60
70
80
age in years
estimated cerebral white matter volume in ml
480
460
440
420
400
"g"-carriers
"c"-carriers
10
20
30
40
50
60
70
80
age in years

S5N

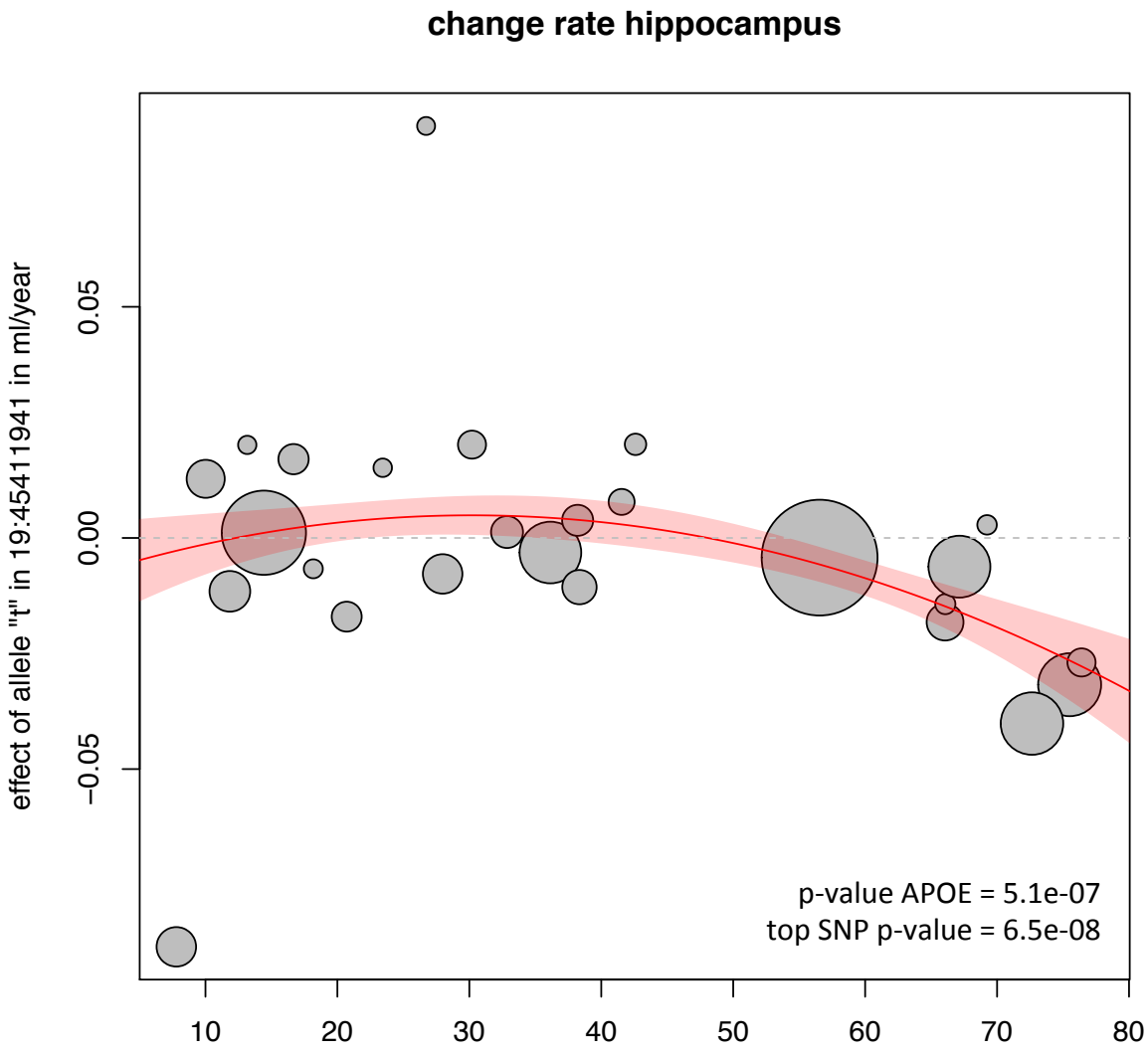

change rate caudate
effect of allele "t" in 17:43199763 in ml/year
0.02
0.01
0.00
−0.01
−0.02
p-value PLCD3 = 1.4e-06
top SNP p-value = 3.3e-06
10
20
30
40
50
60
70
80
age in years
estimated caudate volume in ml
9
8
7
“c”-carriers
“t”-carriers
age in years

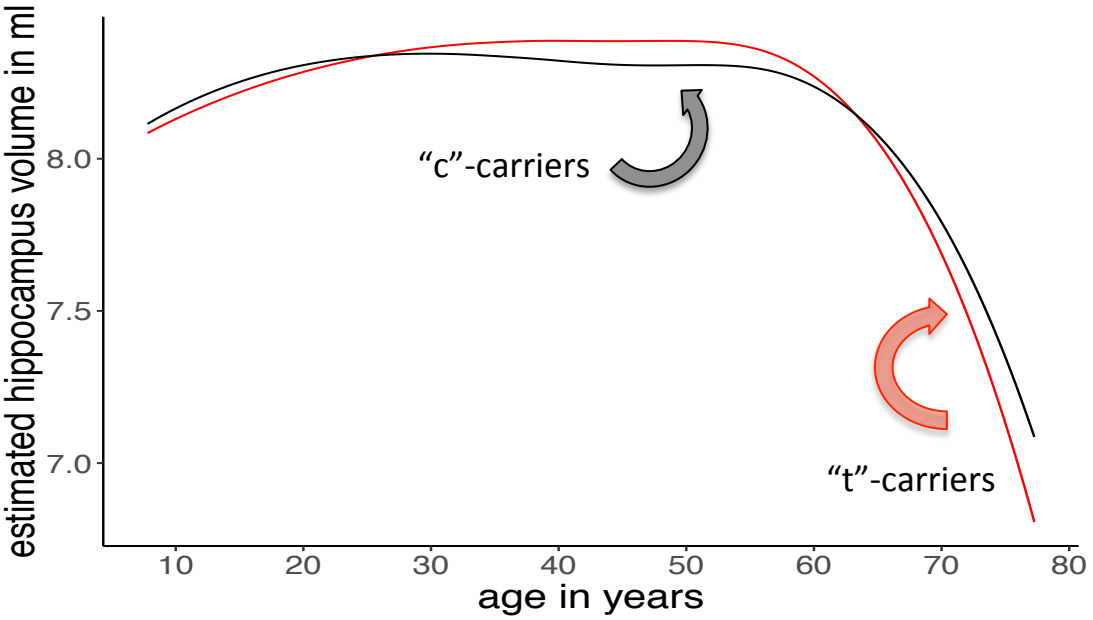

change rate cerebellum white matter
p-value OR7D2 = 1.8e-06
top SNP p-value = 2.5e-06
effect of allele "t" in 19:9298173 in ml/year
0.20
0.15
0.10
0.05
0.00
−0.05
−0.10
−0.15
10
20
30
40
50
60
70
80
age in years
estimated cerebellum white matter volume in ml
28
26
24
“t”-carriers
“ta”-carriers
10
20
30
40
50
60
70
80
age in years

S5P

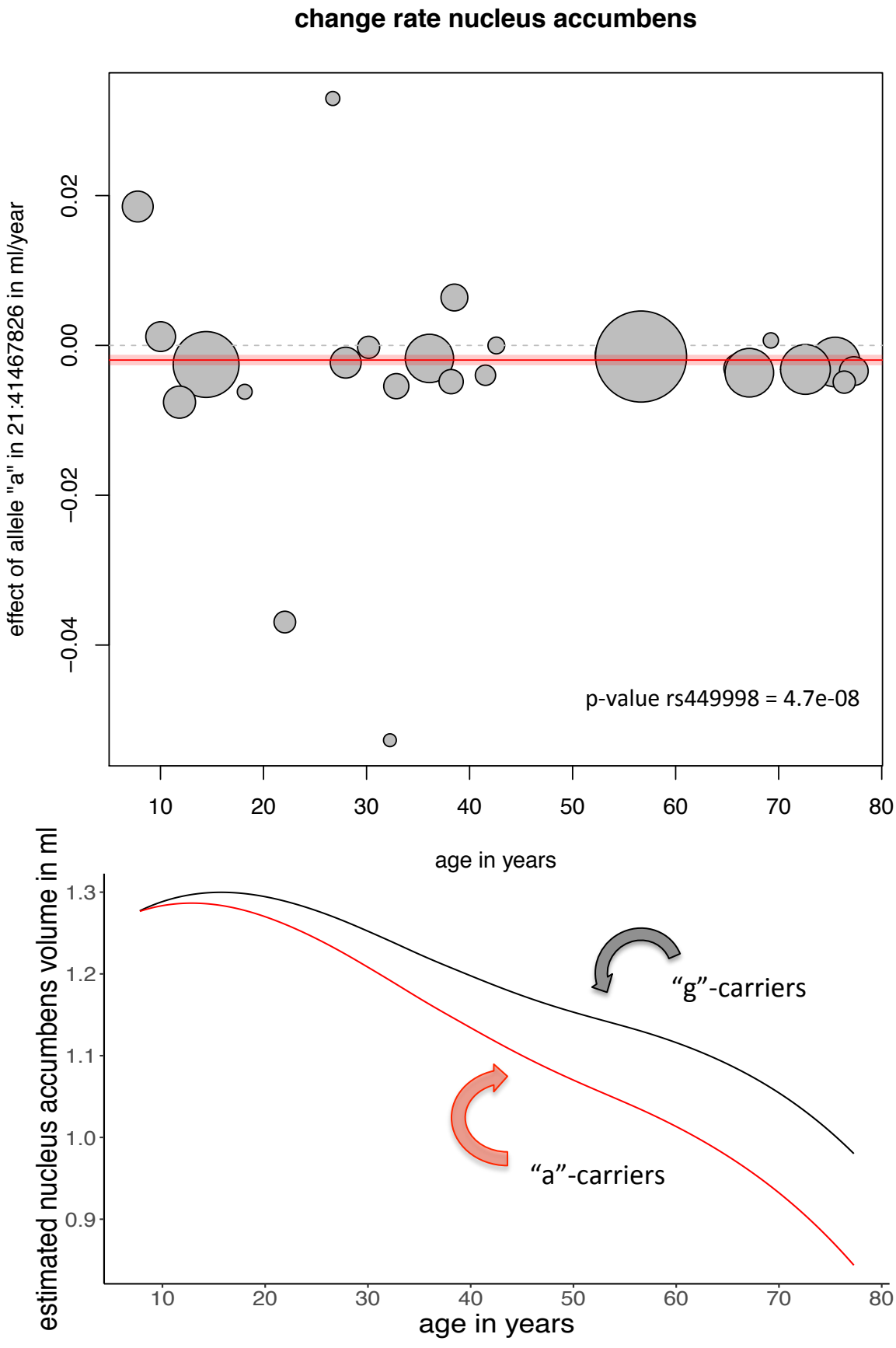

change rate amygdala
effect of allele "t" in 19:45411941 in ml/year
0.02
0.00
−0.02
−0.04
−0.06
p-value APOE= 2.1e-06
top SNP p-value = 3.5e-07
10
20
30
40
50
60
70
80
age in years
estimated amygdala volume in ml
3.2
3.0
2.8
2.6
“t”-carriers
“c”-carriers
age in years

S5Q

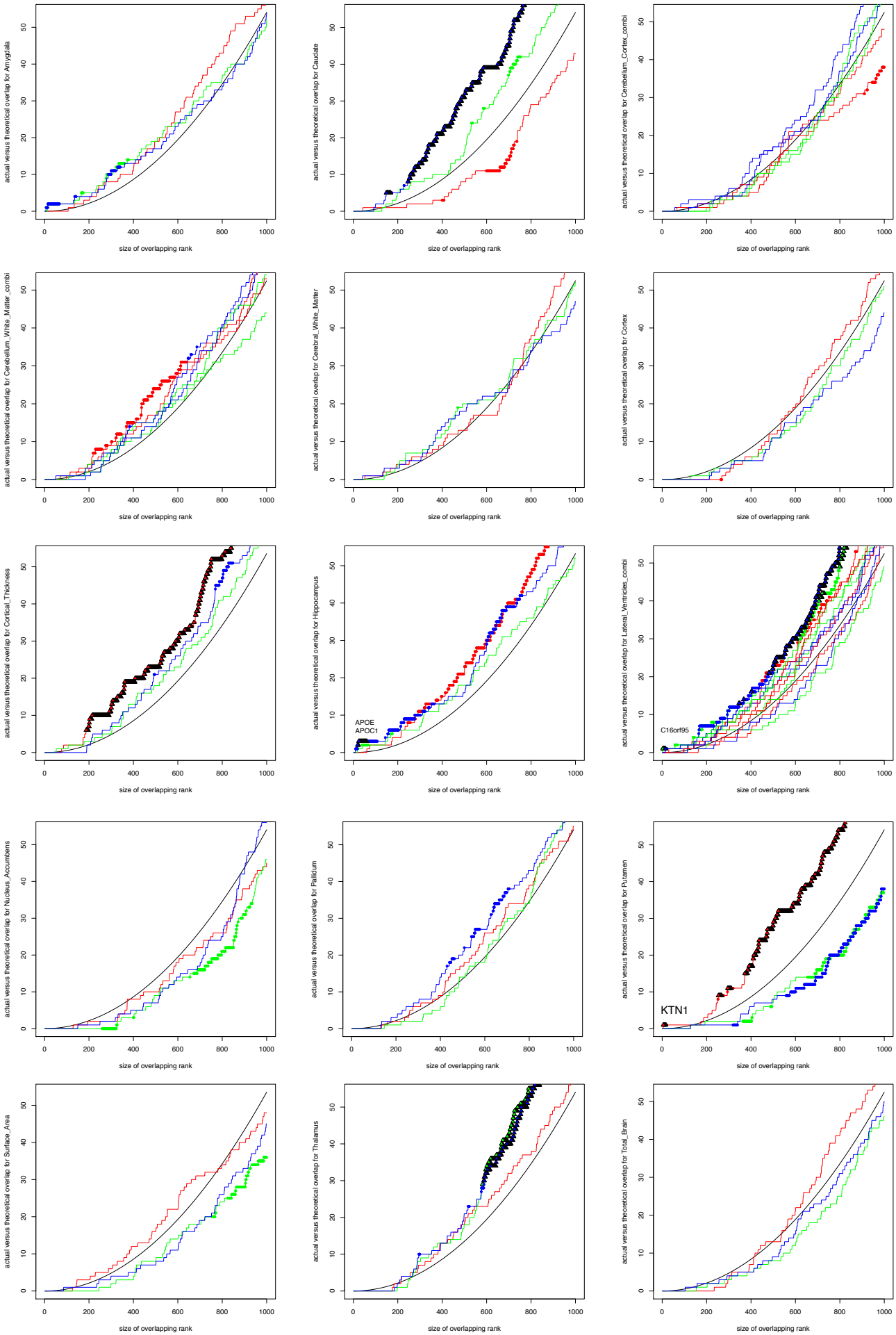

change rate hippocampus
effect of allele "t" in 19:45411941 in ml/year
0.05
0.00
−0.05
p-value APOE = 5.1e-07
top SNP p-value = 6.5e-08
10
20
30
40
50
60
70
80


estimated hippocampus volume in ml
8.0
7.5
7.0
“c”-carriers
“t”-carriers
10
20
30
40
50
60
70
80
age in years

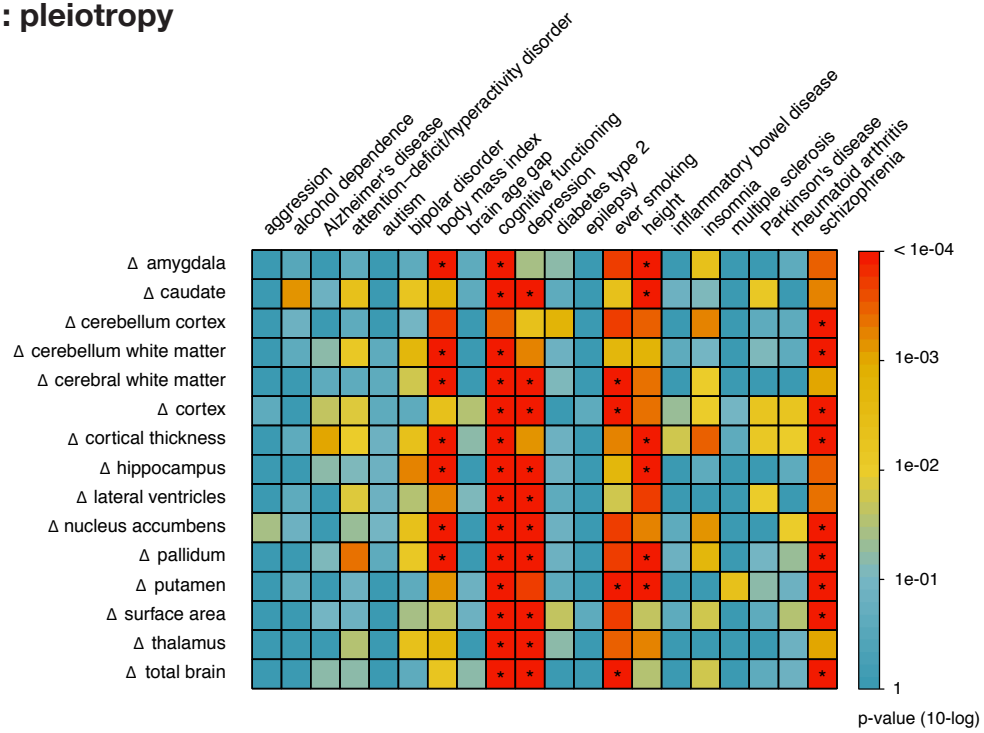
S5R


change rate nucleus accumbens
effect of allele "a" in 21:41467826 in ml/year
0.02
0.00
−0.02
−0.04
p-value rs449998 = 4.7e-08
10
20
30
40
50
60
70
80
age in years
estimated nucleus accumbens volume in ml
1.3
1.2
1.1
1.0
0.9
“g”-carriers
“a”-carriers
10
20
30
40
50
60
70
80
age in years

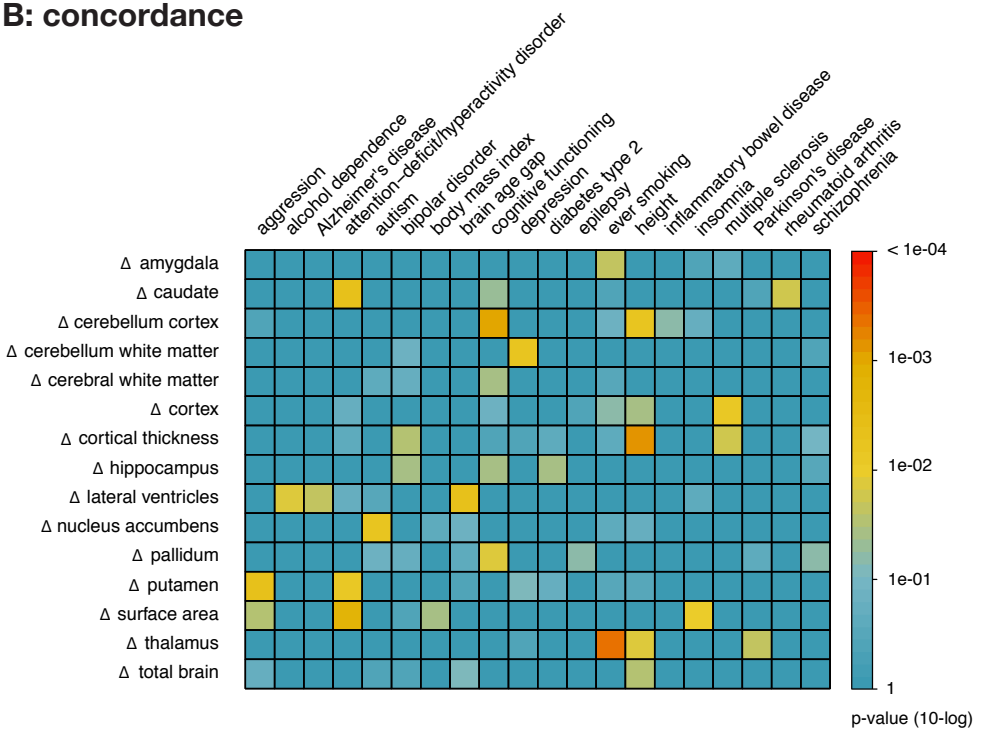
S6


actual versus theoretical overlap for Amygdala
actual versus theoretical overlap for Caudate
actual versus theoretical overlap for Cerebellum_Cortex_combi
actual versus theoretical overlap for Cerebellum_White_Matter_combi
actual versus theoretical overlap for Cerebral_White_Matter
actual versus theoretical overlap for Cortex
actual versus theoretical overlap for Cortical_Thickness
actual versus theoretical overlap for Hippocampus
APOE
APOC1
actual versus theoretical overlap for Lateral_Ventricles_combi
C16orf95
actual versus theoretical overlap for Nucleus_Accumbens
actual versus theoretical overlap for Pallidum
actual versus theoretical overlap for Putamen
KTN1
actual versus theoretical overlap for Surface_Area
actual versus theoretical overlap for Thalamus
actual versus theoretical overlap for Total_Brain
size of overlapping rank
0
200
400
600
800
1000
10
20
30
40
50

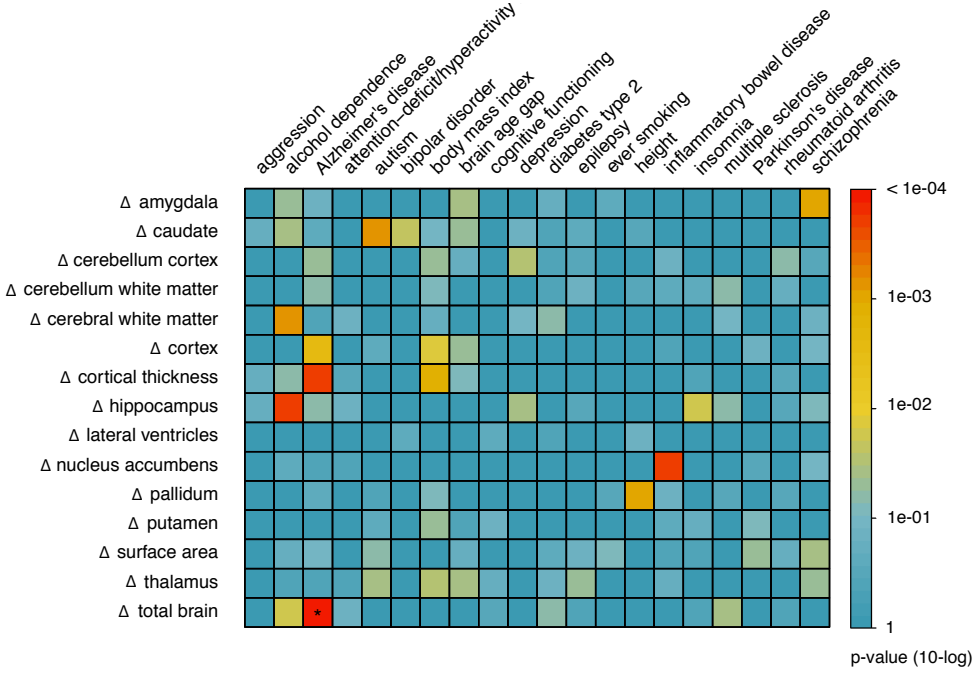
S7A : pleiotropy



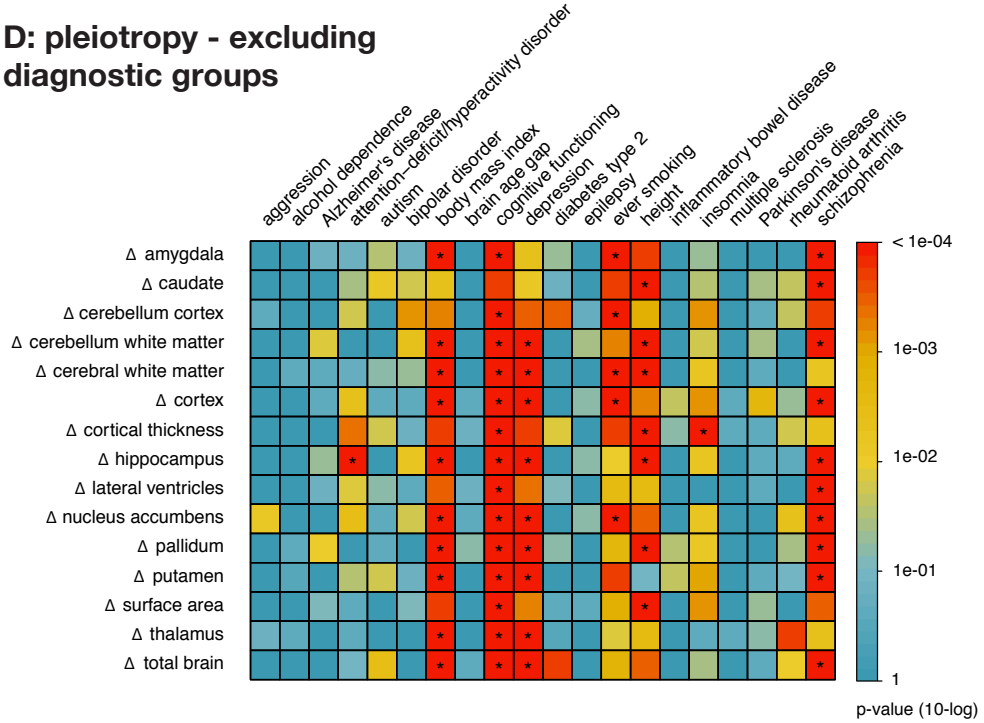
B: concordance



C: discordance



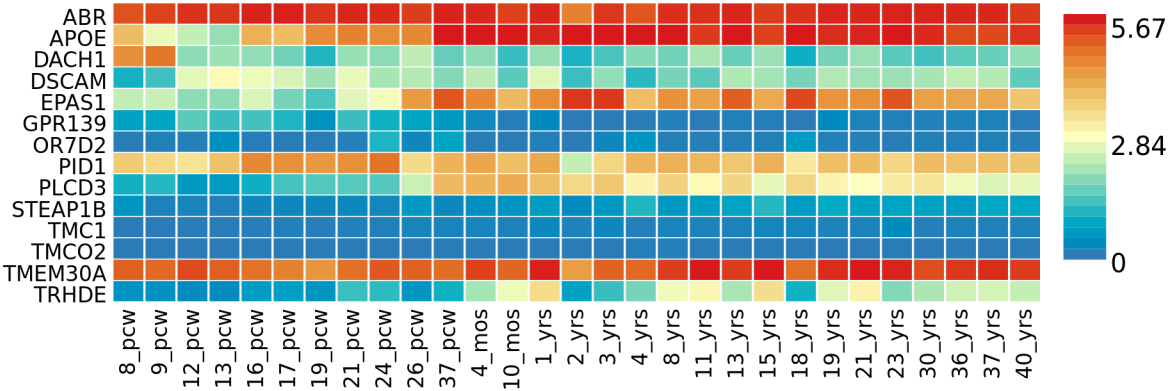
D: pleiotropy - excluding diagnostic groups



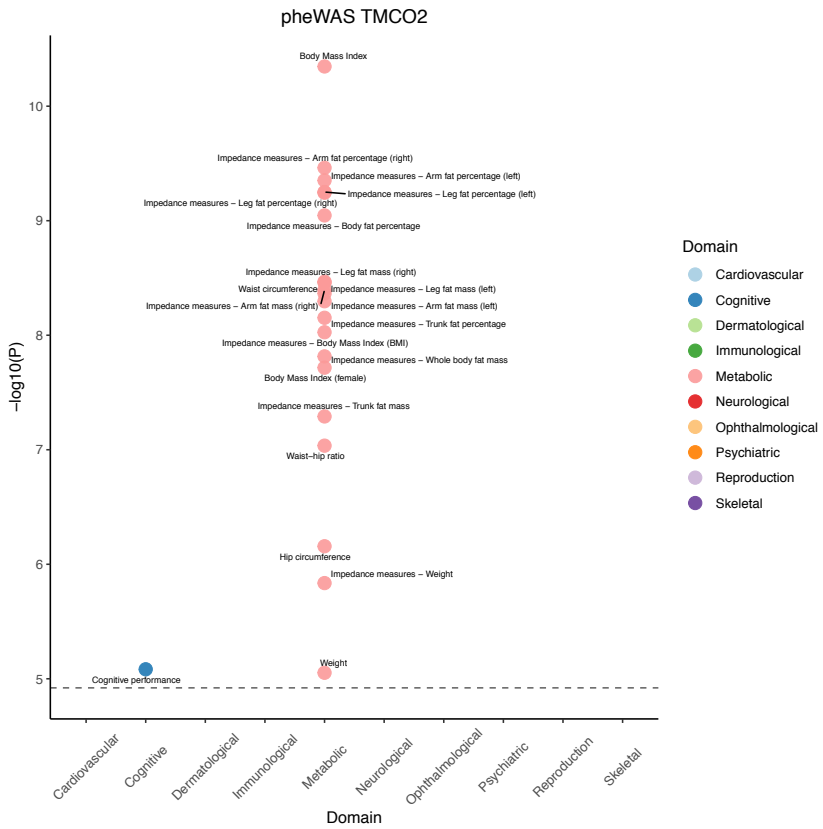
S8A


ABR
APOE
DSCAM
EPAS1
GPR139
OR7D2
PID1
PLCD3
STEAP1B
TMC1
TMCO2
TMEM30A
TRHDE
5.67
2.84
0
Adipose_Subcutaneous
Adipose_Visceral_Omentum
Adrenal_Gland
Artery_Aorta
Artery_Coronary
Artery_Tibial
Bladder
Brain_Amygdala
Brain_Anterior_cingulate_cortex_BA24
Brain_Caudate_basal_ganglia
Brain_Cerebellar_Hemisphere
Brain_Cerebellum
Brain_Cortex
Brain_Frontal_Cortex_BA9
Brain_Hippocampus
Brain_Hypothalamus
Brain_Nucleus_accumbens_basal_ganglia
Brain_Putamen_basal_ganglia
Brain_Spinal_cord_cervical_c-1
Brain_Substantia_nigra
Breast_Mammary_Tissue
Cells_Cultured_fibroblasts
Cells_EBV-transformed_lymphocytes
Cervix_Ectocervix
Cervix_Endocervix
Colon_Sigmoid
Colon_Transverse
Esophagus_Gastroesophageal_Junction
Esophagus_Mucosa
Esophagus_Muscularis
Fallopian_Tube
Heart_Atrial_Appendage
Heart_Left_Ventricle
Kidney_Cortex
Kidney_Medulla
Liver
Lung
Minor_Salivary_Gland
Muscle_Skeletal
Nerve_Tibial
Ovary
Pancreas
Pituitary
Prostate
Skin_Not_Sun_Exposed_Suprapubic
Skin_Sun_Exposed_Lower_leg
Small_Intestine_Terminal_Ileum
Spleen
Stomach
Testis
Thyroid
Uterus
Vagina
Whole_Blood

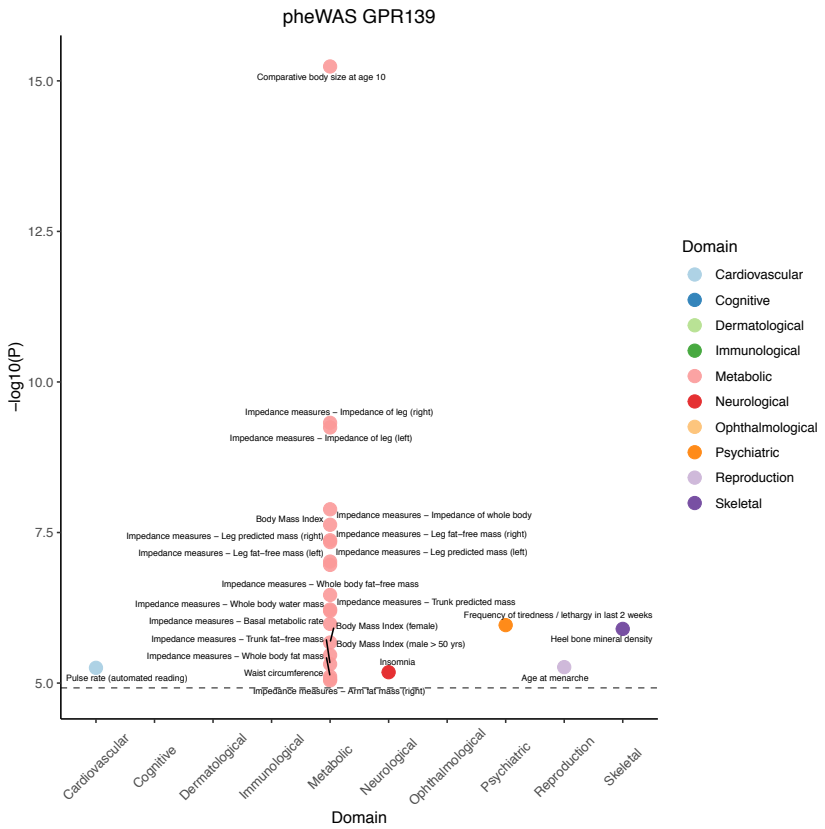
S8B


ABR
APOE
DACH1
DSCAM
EPAS1
GPR139
OR7D2
PID1
PLCD3
STEAP1B
TMC1
TMCO2
TMEM30A
TRHDE
8_pcw
9_pcw
12_pcw
13_pcw
16_pcw
17_pcw
19_pcw
21_pcw
24_pcw
26_pcw
37_pcw
4_mos
10_mos
1_yrs
2_yrs
3_yrs
4_yrs
8_yrs
11_yrs
13_yrs
15_yrs
18_yrs
19_yrs
21_yrs
23_yrs
30_yrs
36_yrs
37_yrs
40_yrs
5.67
2.84
0

S9A


pheWAS TMCO2
Body Mass Index
Impedance measures – Arm fat percentage (right)
Impedance measures – Arm fat percentage (left)
Impedance measures – Leg fat percentage (left)
Impedance measures – Leg fat percentage (right)
Impedance measures – Body fat percentage
Impedance measures – Leg fat mass (right)
Waist circumference
Impedance measures – Leg fat mass (left)
Impedance measures – Arm fat mass (right)
Impedance measures – Arm fat mass (left)
Impedance measures – Trunk fat percentage
Impedance measures – Body Mass Index (BMI)
Impedance measures – Whole body fat mass
Body Mass Index (female)
Impedance measures – Trunk fat mass
Waist–hip ratio
Hip circumference
Impedance measures – Weight
Weight
Cognitive performance
−log10(P)
10
9
8
7
6
5
Cardiovascular
Cognitive
Dermatological
Immunological
Metabolic
Neurological
Ophthalmological
Psychiatric
Reproduction
Skeletal
Domain
Domain
Cardiovascular
Cognitive
Dermatological
Immunological
Metabolic
Neurological
Ophthalmological
Psychiatric
Reproduction
Skeletal

B


pheWAS GPR139
Comparative body size at age 10
Impedance measures – Impedance of leg (right)
Impedance measures – Impedance of leg (left)
Body Mass Index
Impedance measures – Impedance of whole body
Impedance measures – Leg predicted mass (right)
Impedance measures – Leg fat–free mass (right)
Impedance measures – Leg fat–free mass (left)
Impedance measures – Leg predicted mass (left)
Impedance measures – Whole body fat–free mass
Impedance measures – Whole body water mass
Impedance measures – Trunk predicted mass
Impedance measures – Basal metabolic rate
Frequency of tiredness / lethargy in last 2 weeks
Body Mass Index (female)
Impedance measures – Trunk fat–free mass
Body Mass Index (male > 50 yrs)
Heel bone mineral density
Impedance measures – Whole body fat mass
Insomnia
Waist circumference
Pulse rate (automated reading)
Age at menarche
Impedance measures – Arm fat mass (right)
−log10(P)
15.0
12.5
10.0
7.5
5.0
Cardiovascular
Cognitive
Dermatological
Immunological
Metabolic
Neurological
Ophthalmological
Psychiatric
Reproduction
Skeletal
Domain
Domain
Cardiovascular
Cognitive
Dermatological
Immunological
Metabolic
Neurological
Ophthalmological
Psychiatric
Reproduction
Skeletal