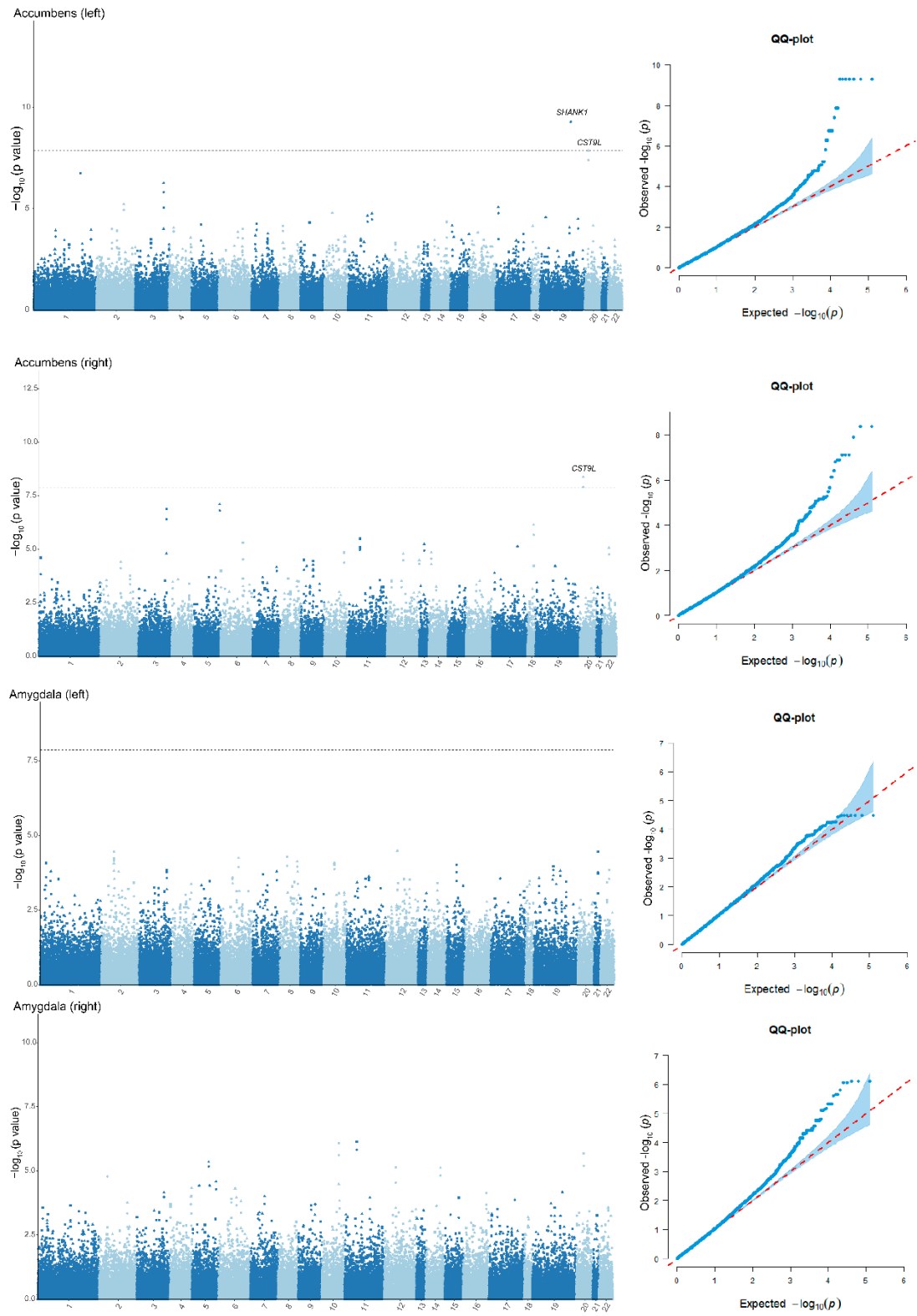
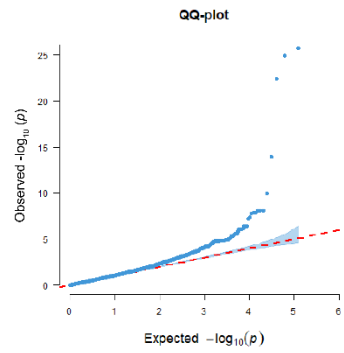
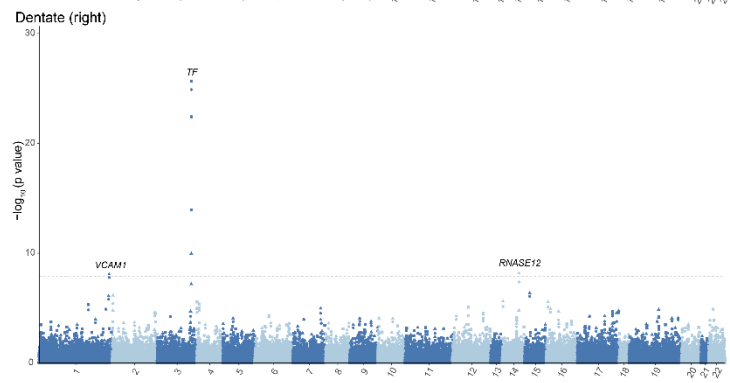
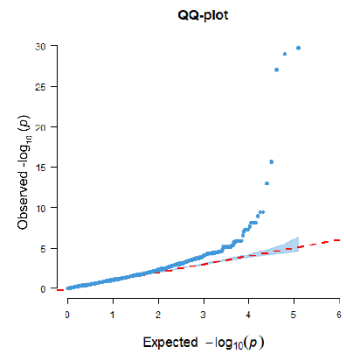
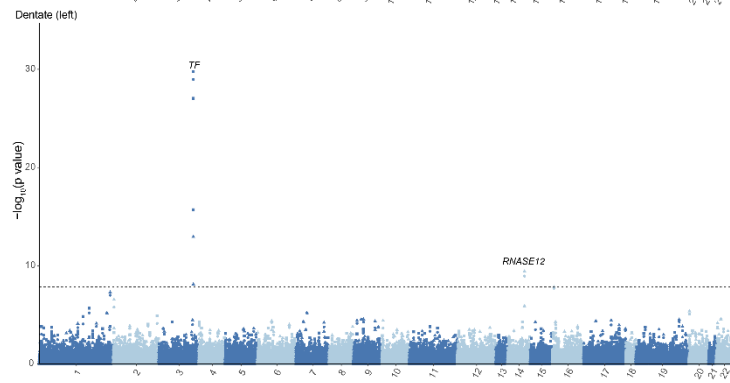
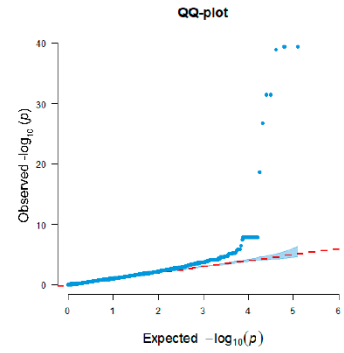
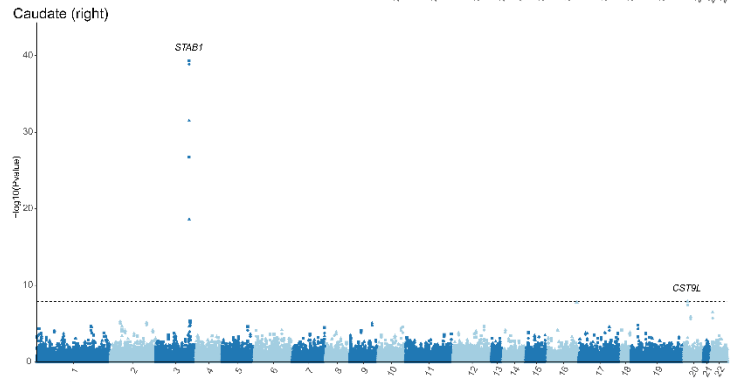
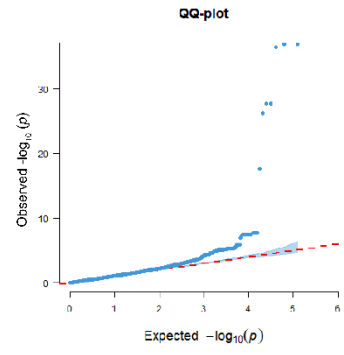
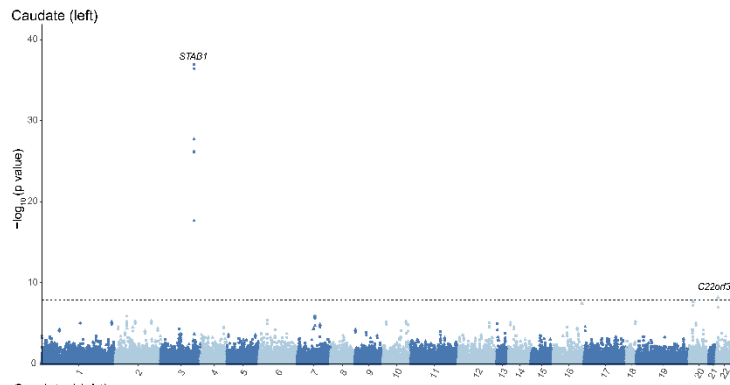
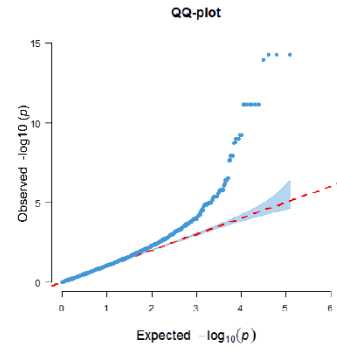
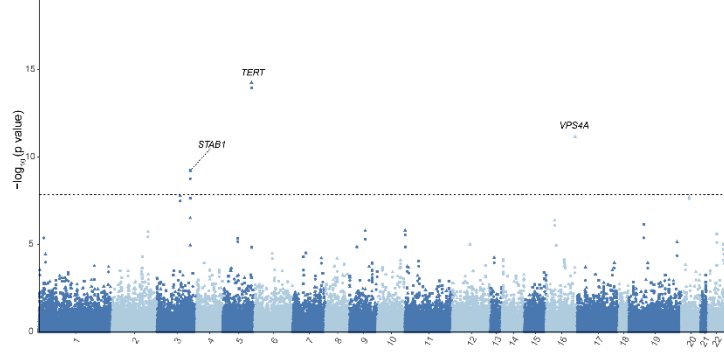


# Supplementary Material for “Whole-Exome Sequencing Identifies Protein-Coding Variants Associated with Brain Iron in 29,828 Individuals”

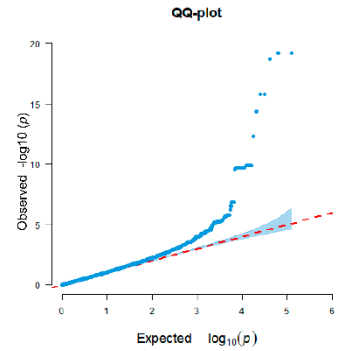
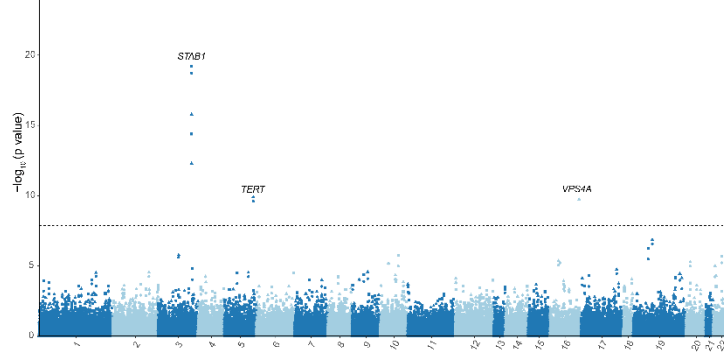




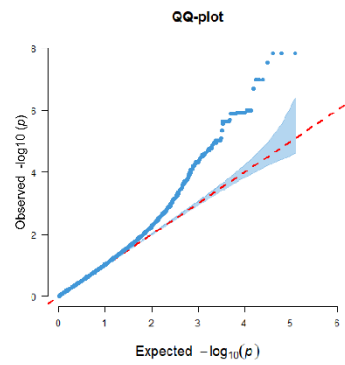
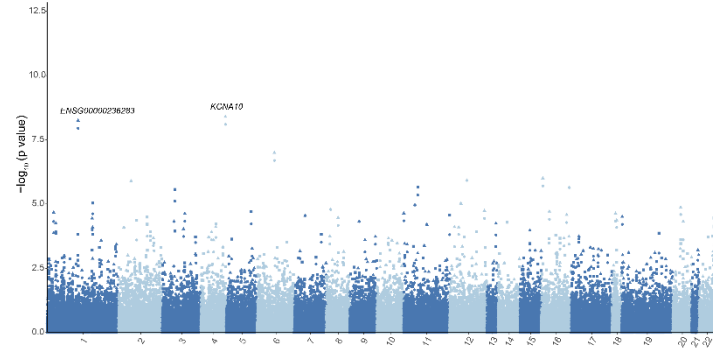
Globus pallidus externa (left)



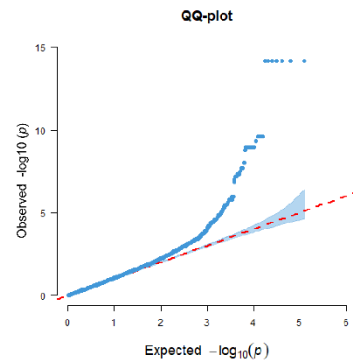
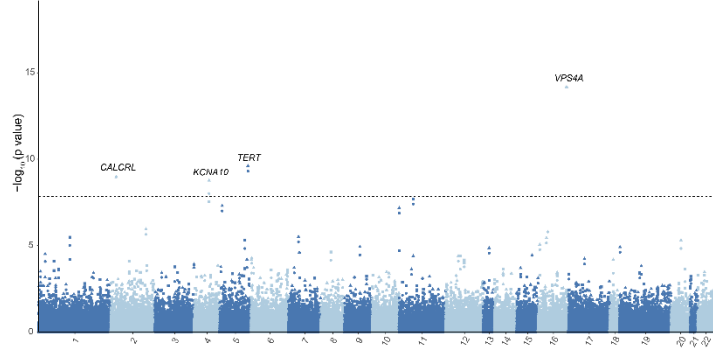
Globus pallidus externa (right)



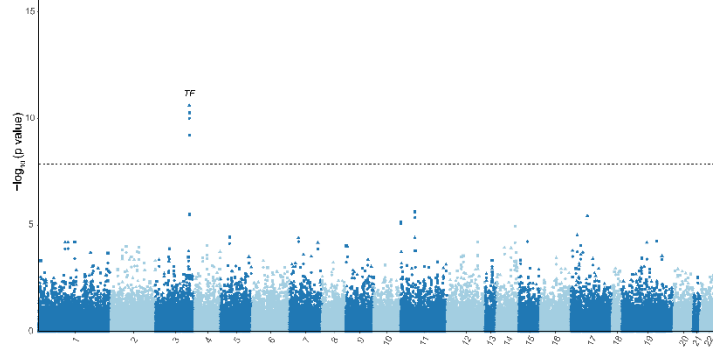
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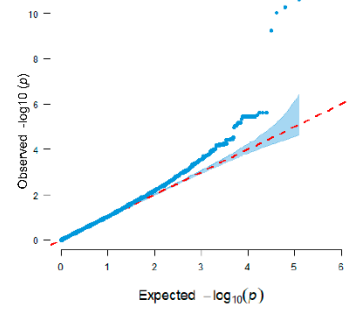
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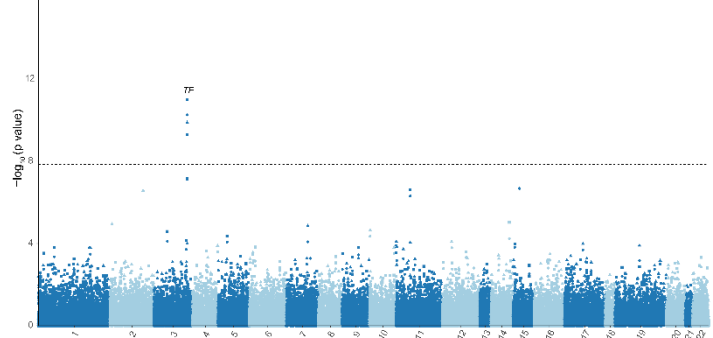
Hippocampus (left)



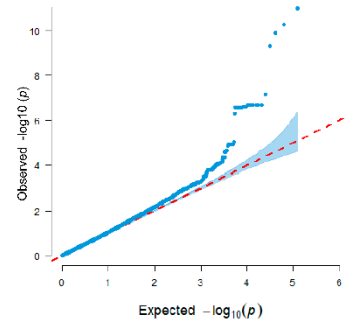
QQ-plot



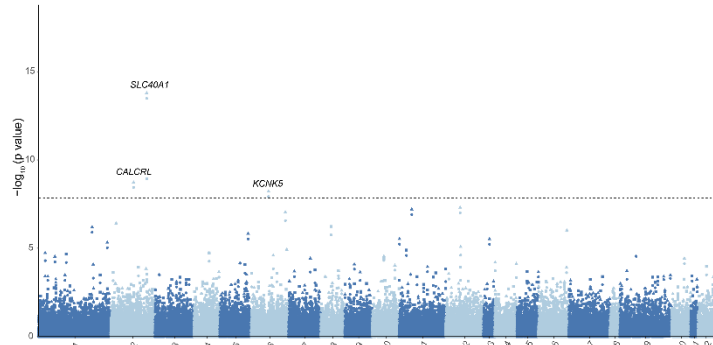
Hippocampus (right)



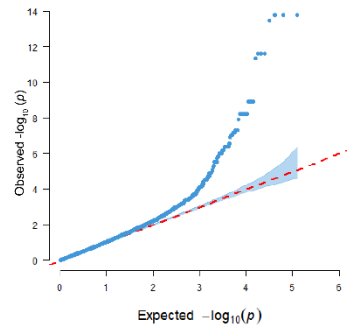
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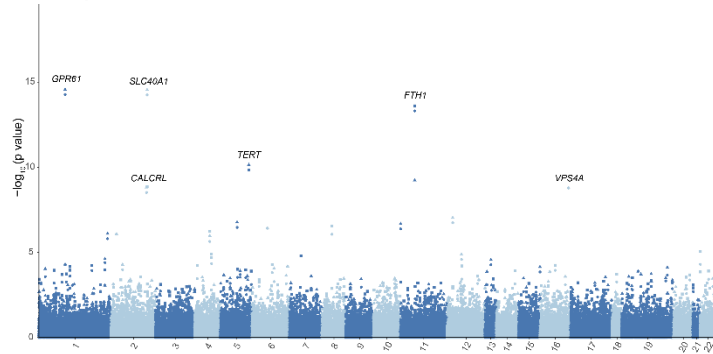
Pallidum (left)



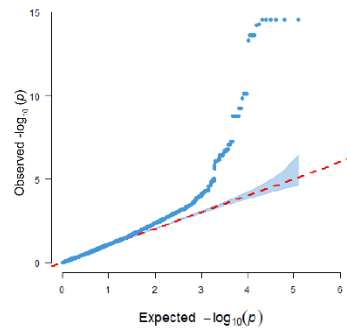
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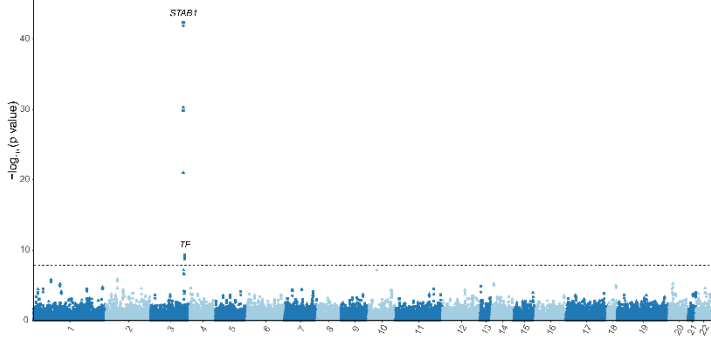
Pallidum (right)



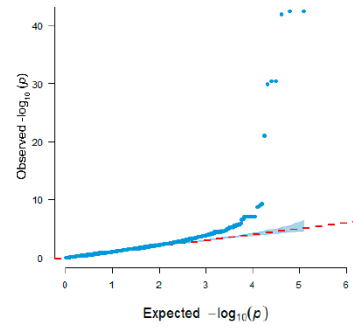
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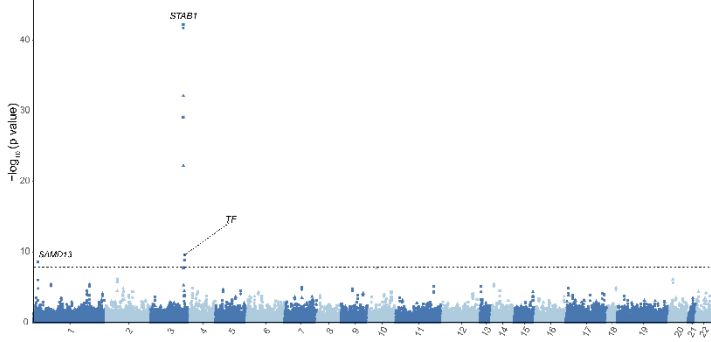
Putamen (left)



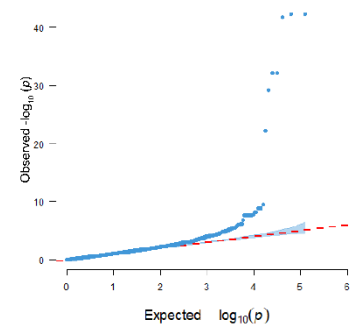
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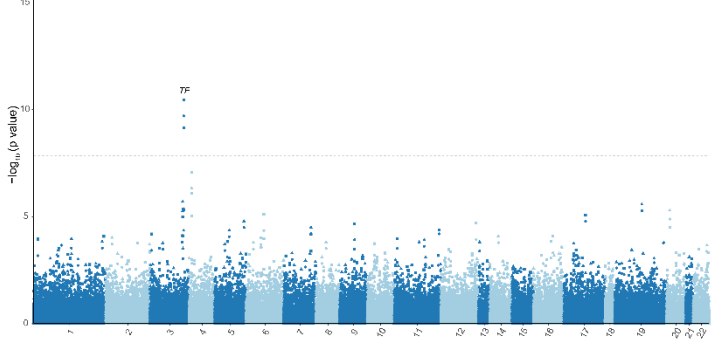
Putamen (right)



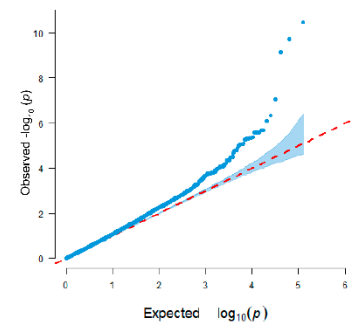
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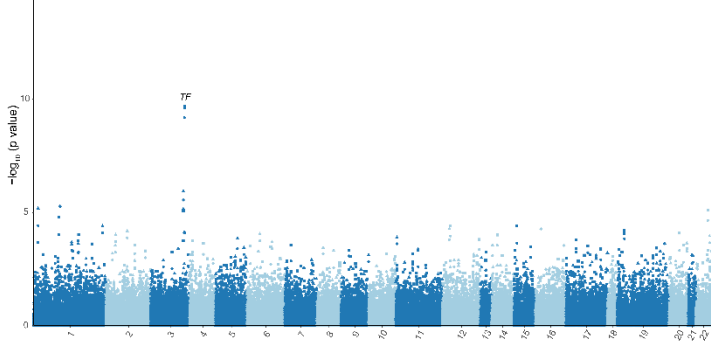
Red nucleus (left)



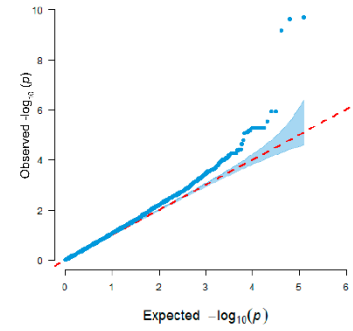
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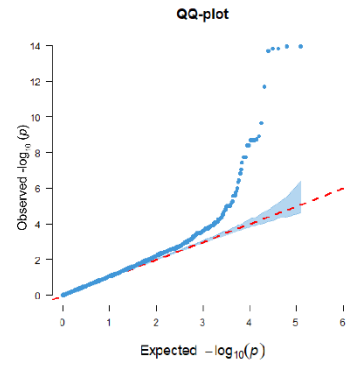
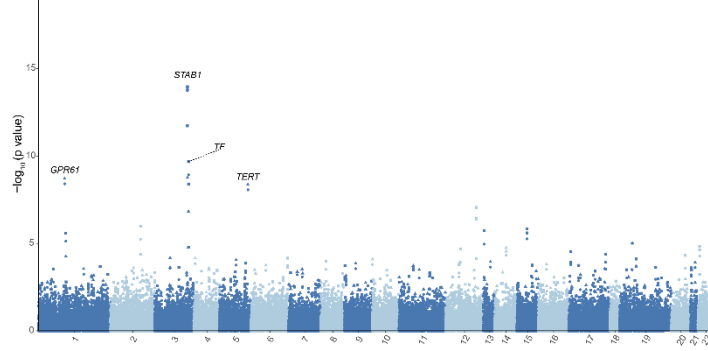
Red nucleus (right)



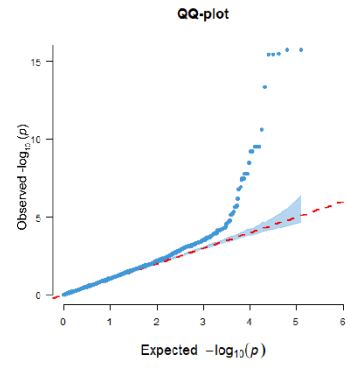
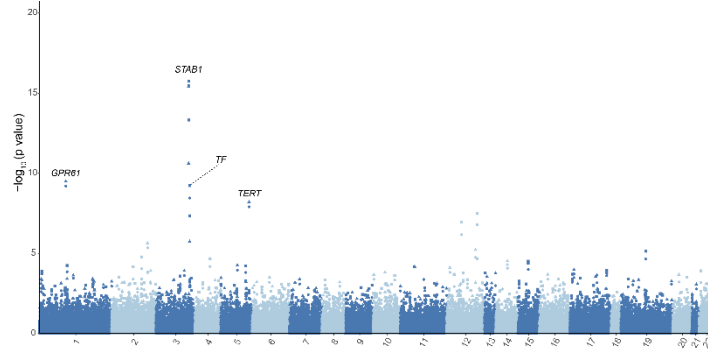
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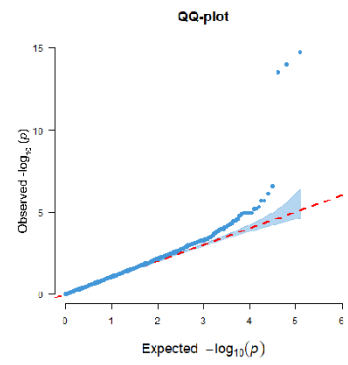
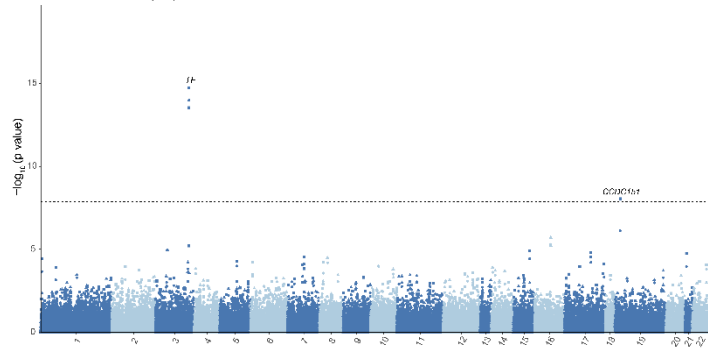
Substantia nigra (left)



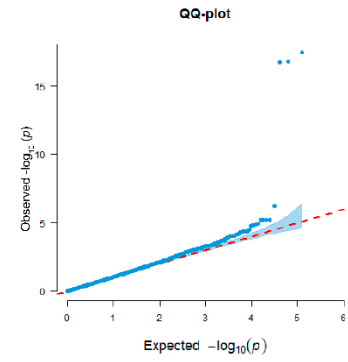
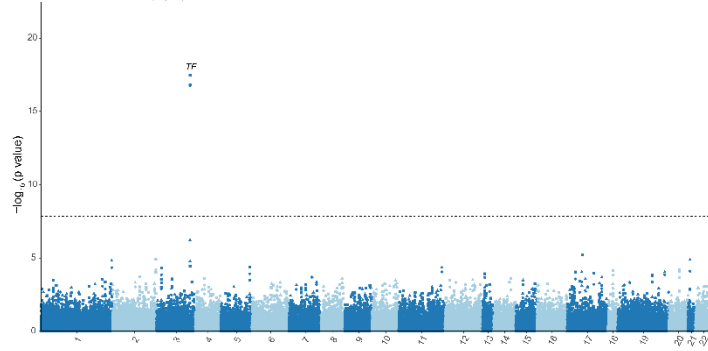
Substantia nigra (right)

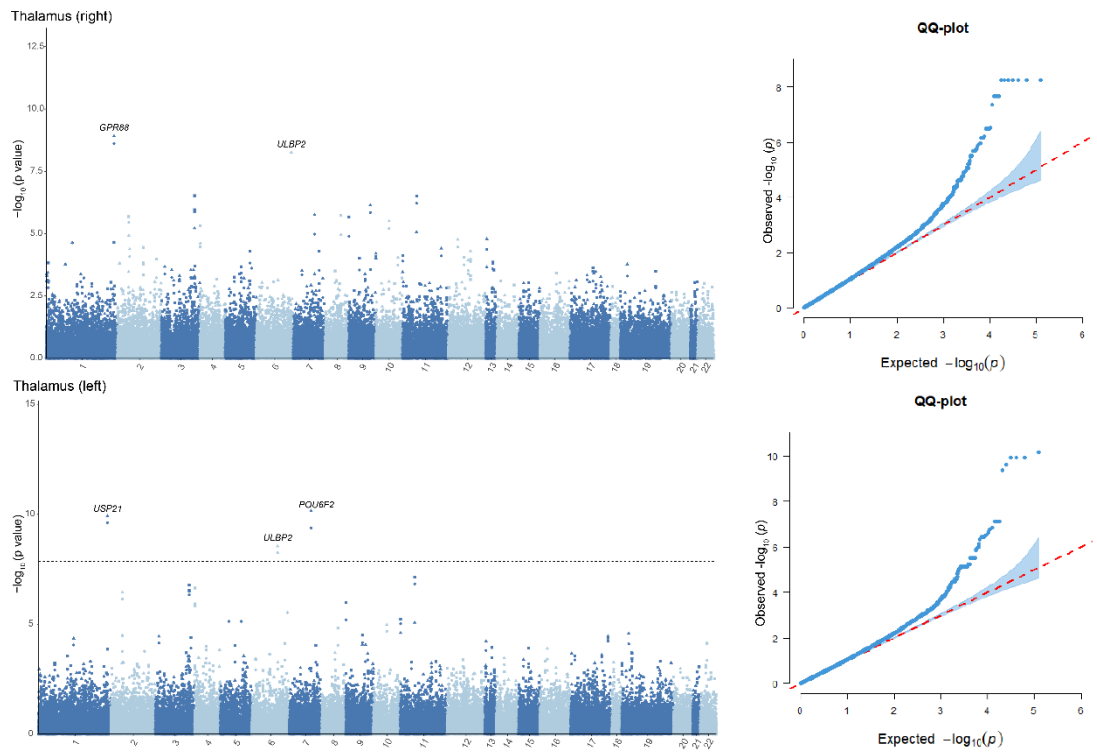


Subthalamic nucleus (left)

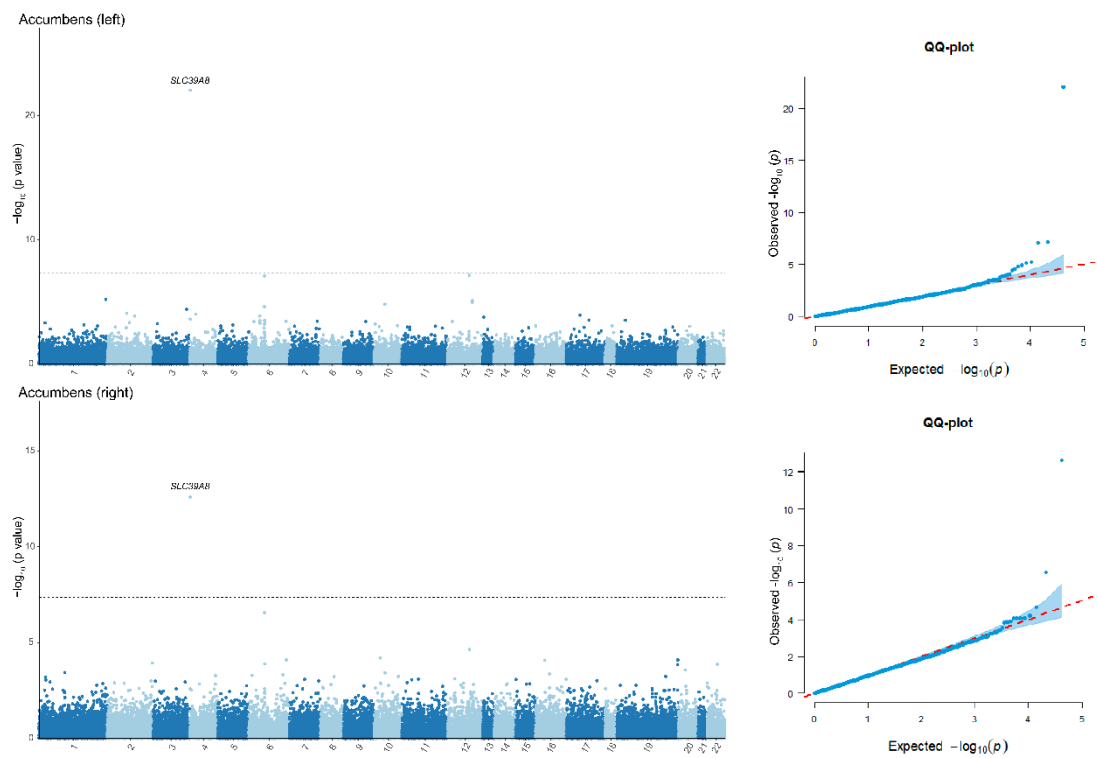


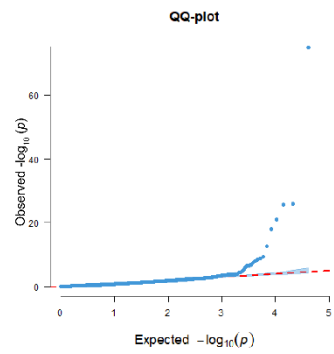
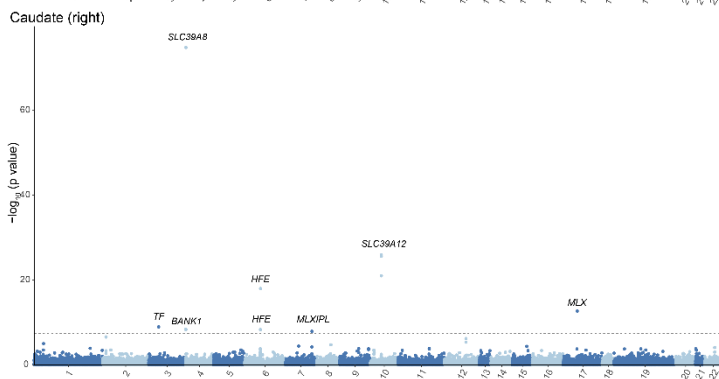
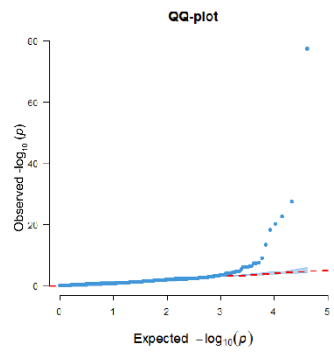
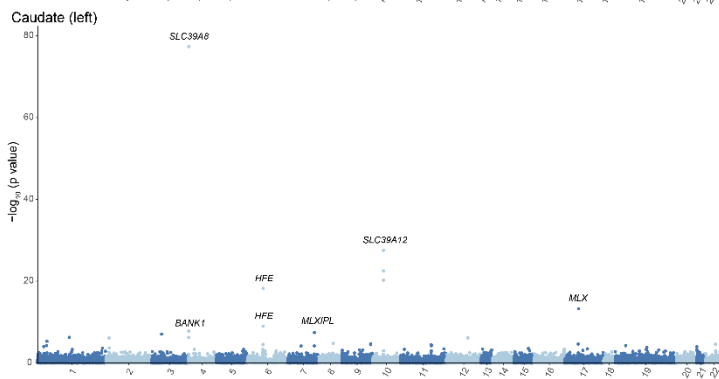
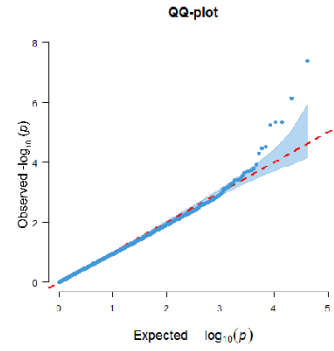
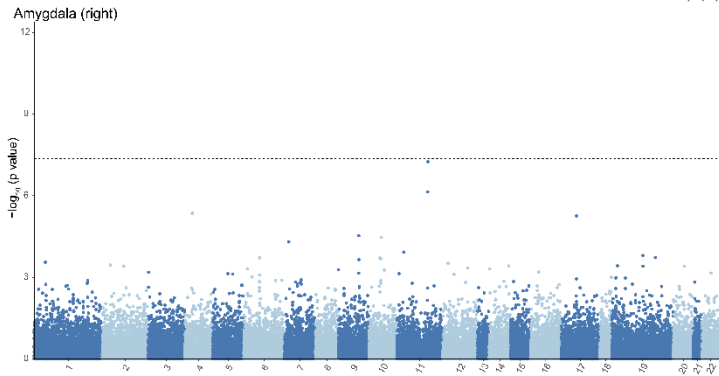
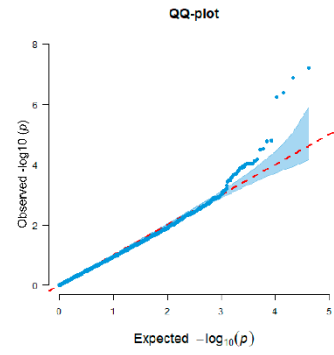
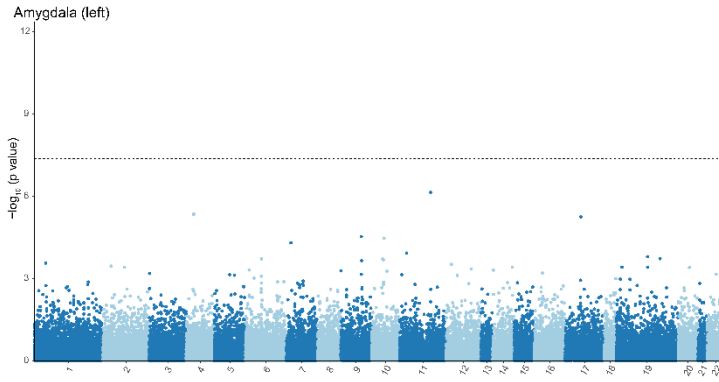
Subthalamic nucleus (right)



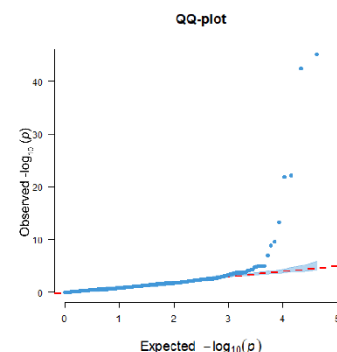
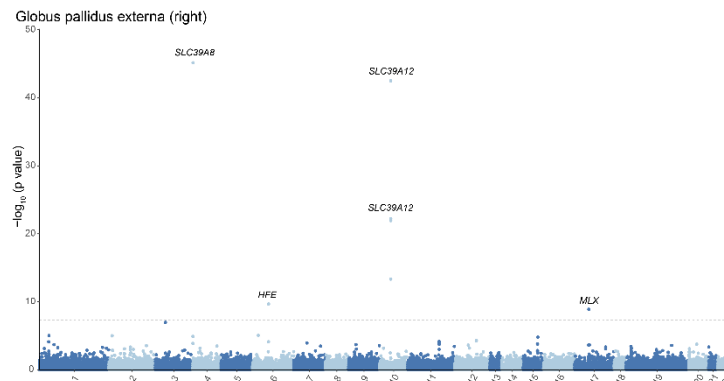
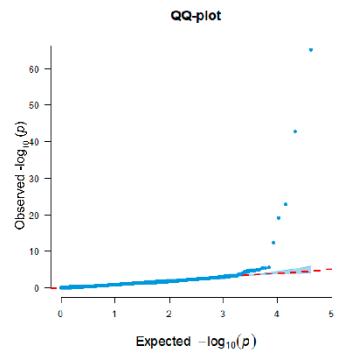
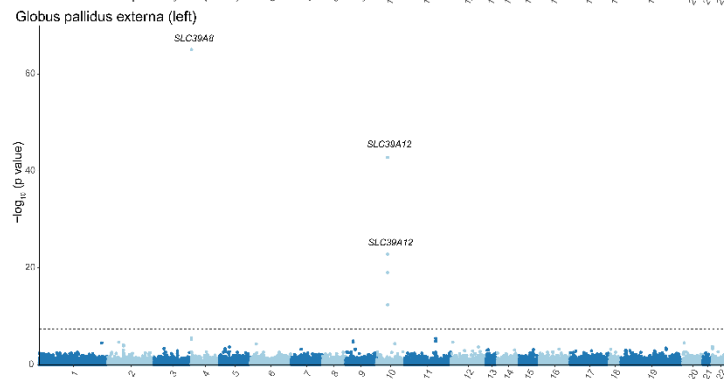
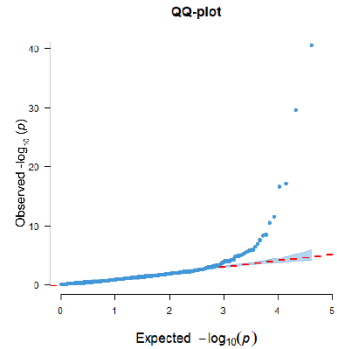
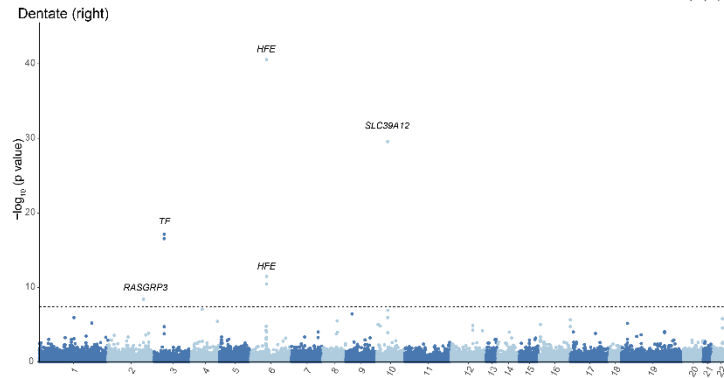
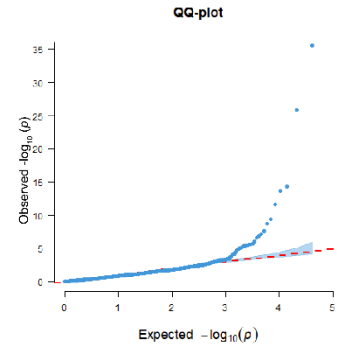
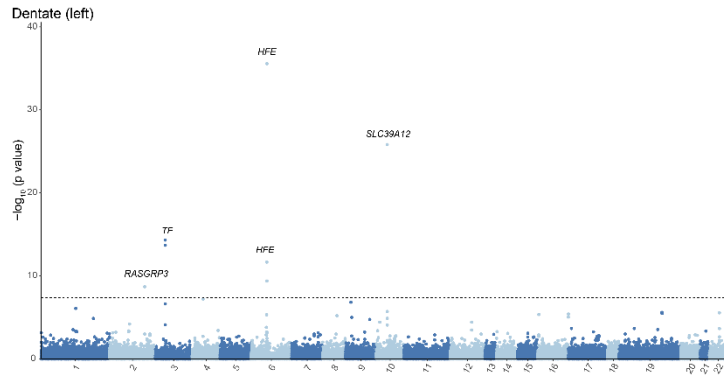


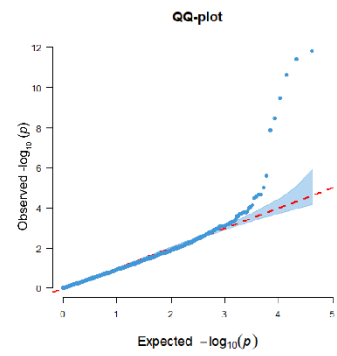
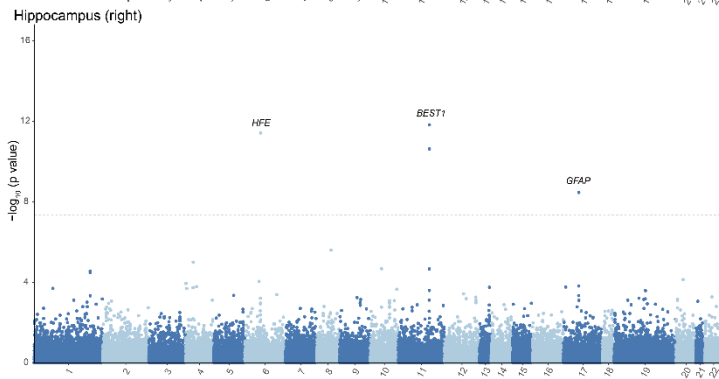
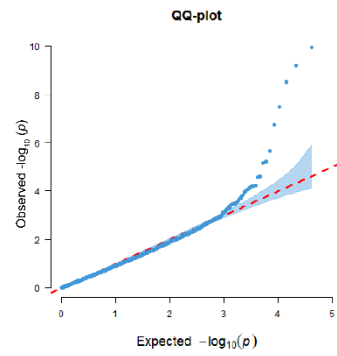
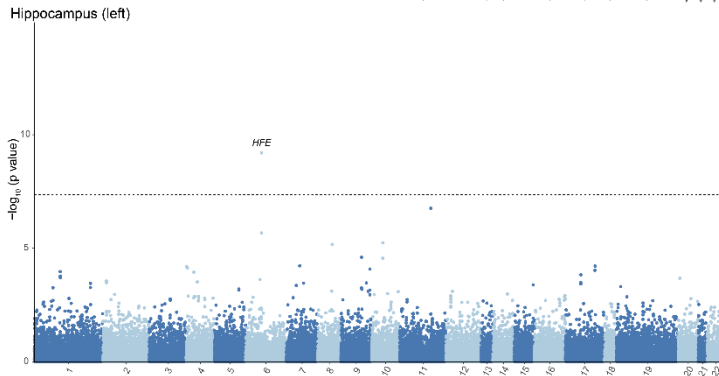
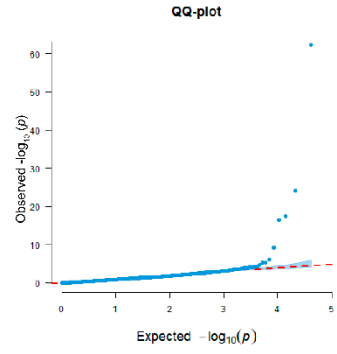
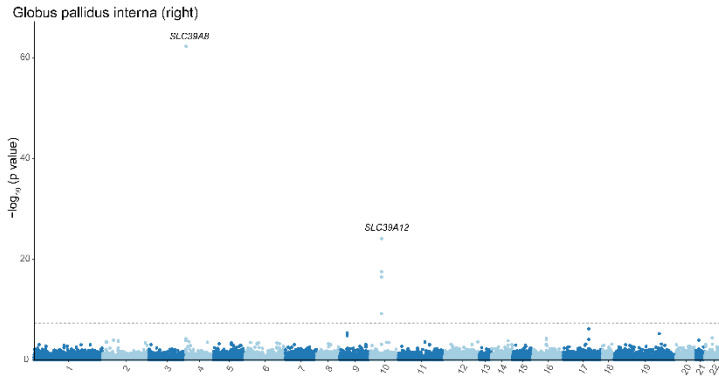
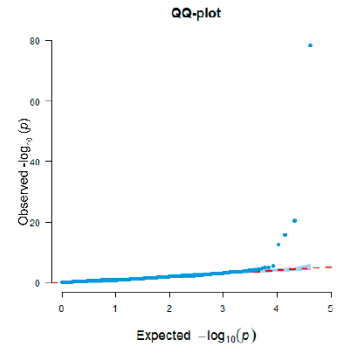
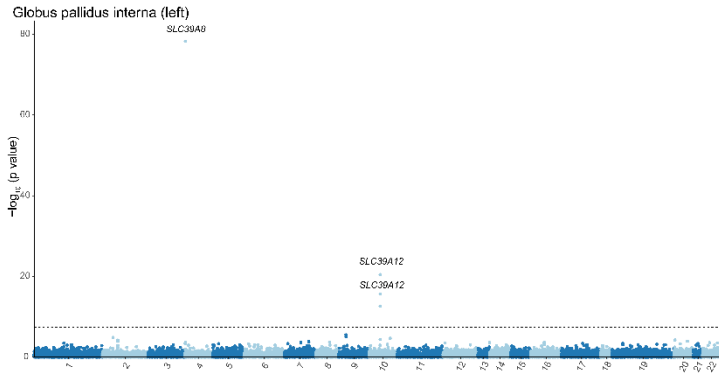
**Supplementary Figure 1.** Manhattan plots of every exome-wide association analysis of rare protein-coding variants performed for QSM in 26 brain regions, in 26789 participants. P values shown are two-sided and Bonferroni correction were used. The dotted horizontal line represents the significance threshold ( $1.7 \times 10^{-8}$ ).

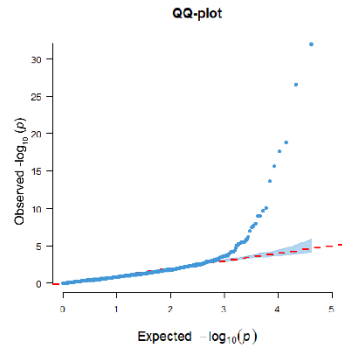
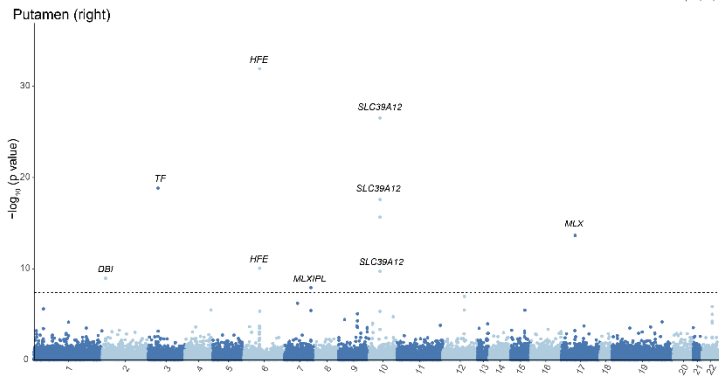
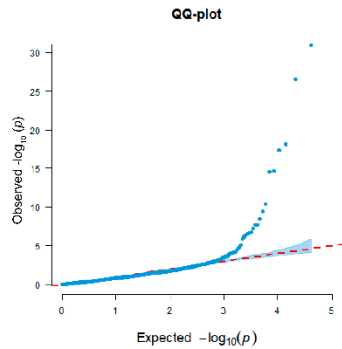
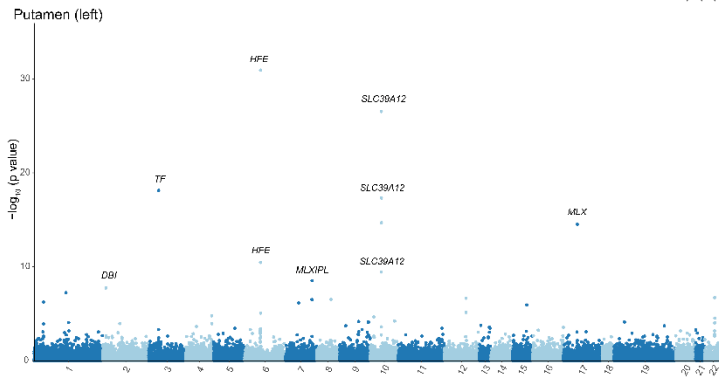
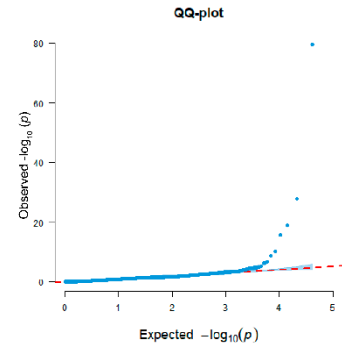
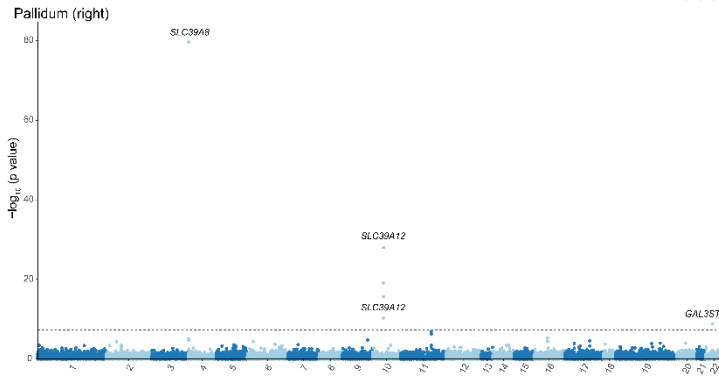
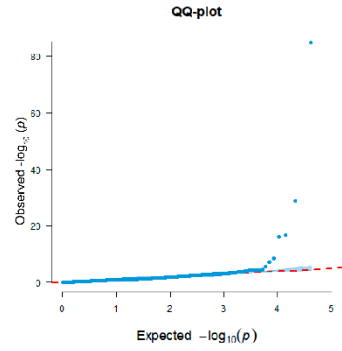
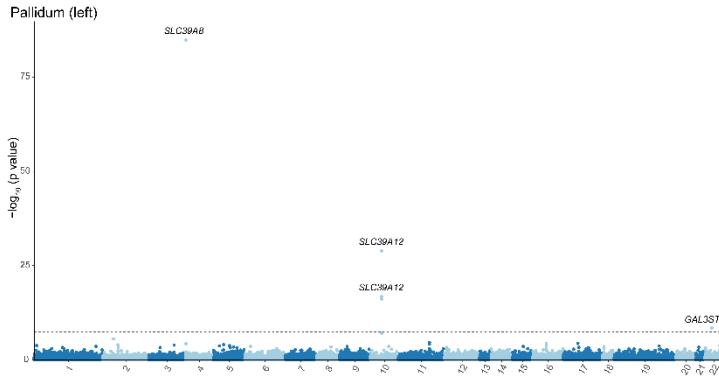


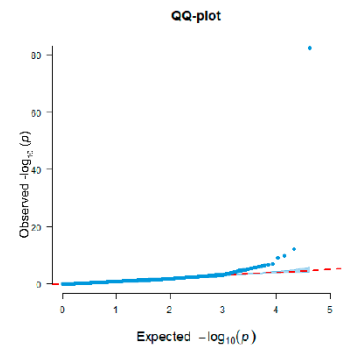
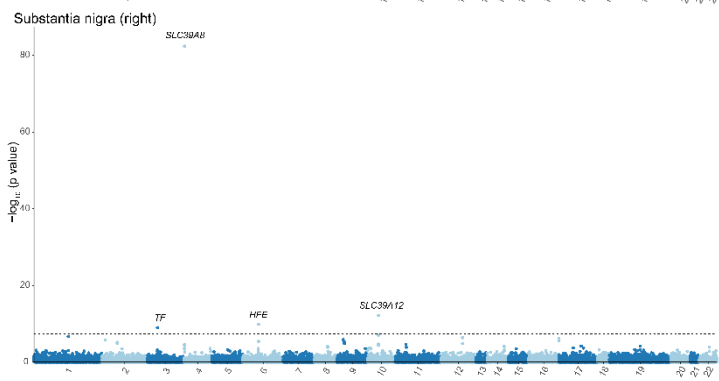
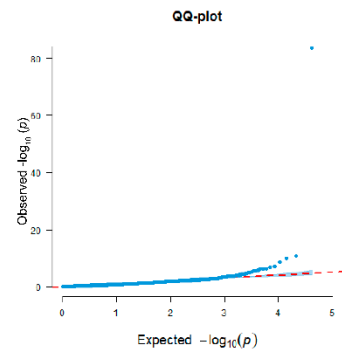
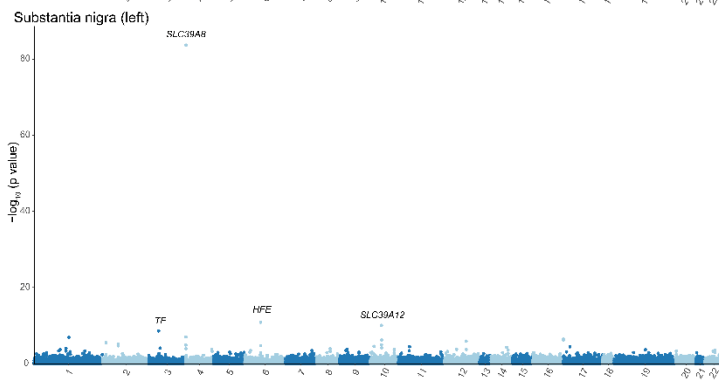
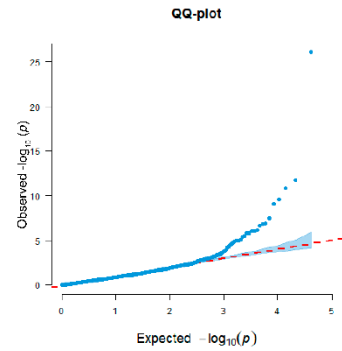
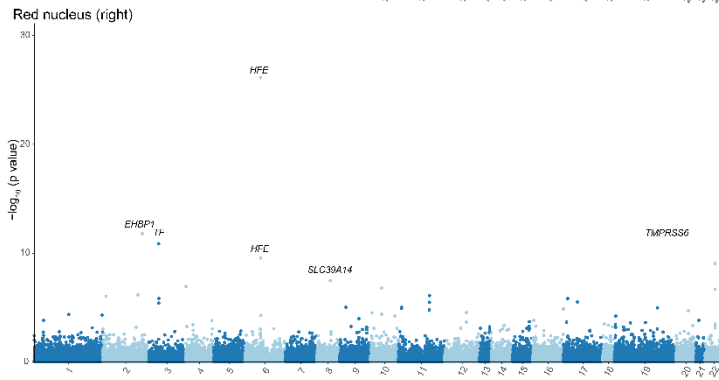
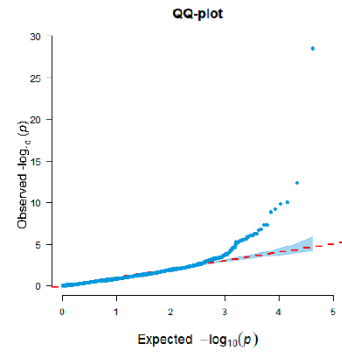
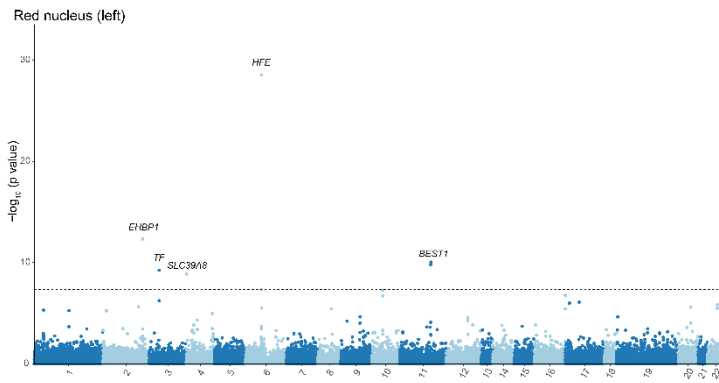


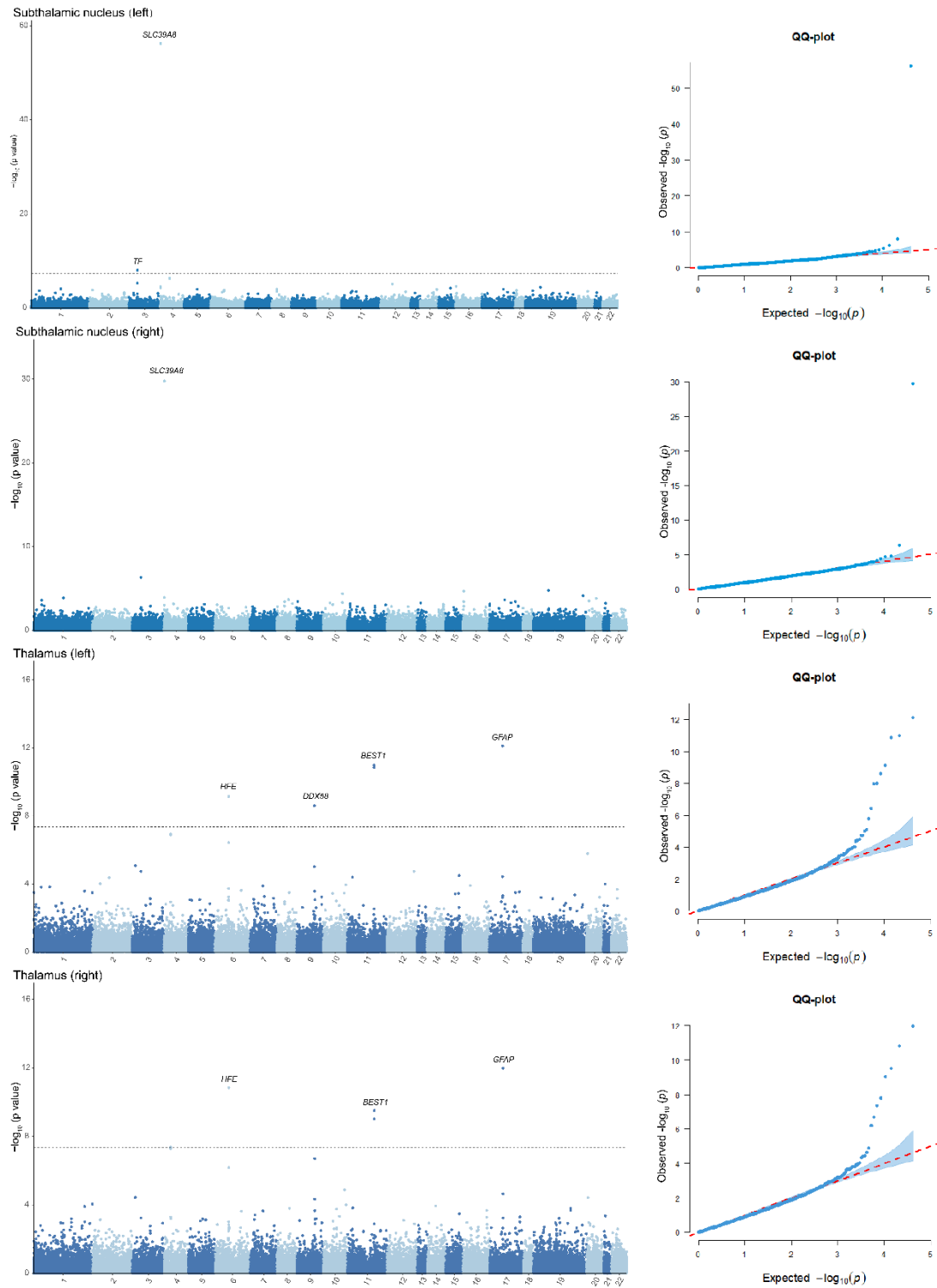




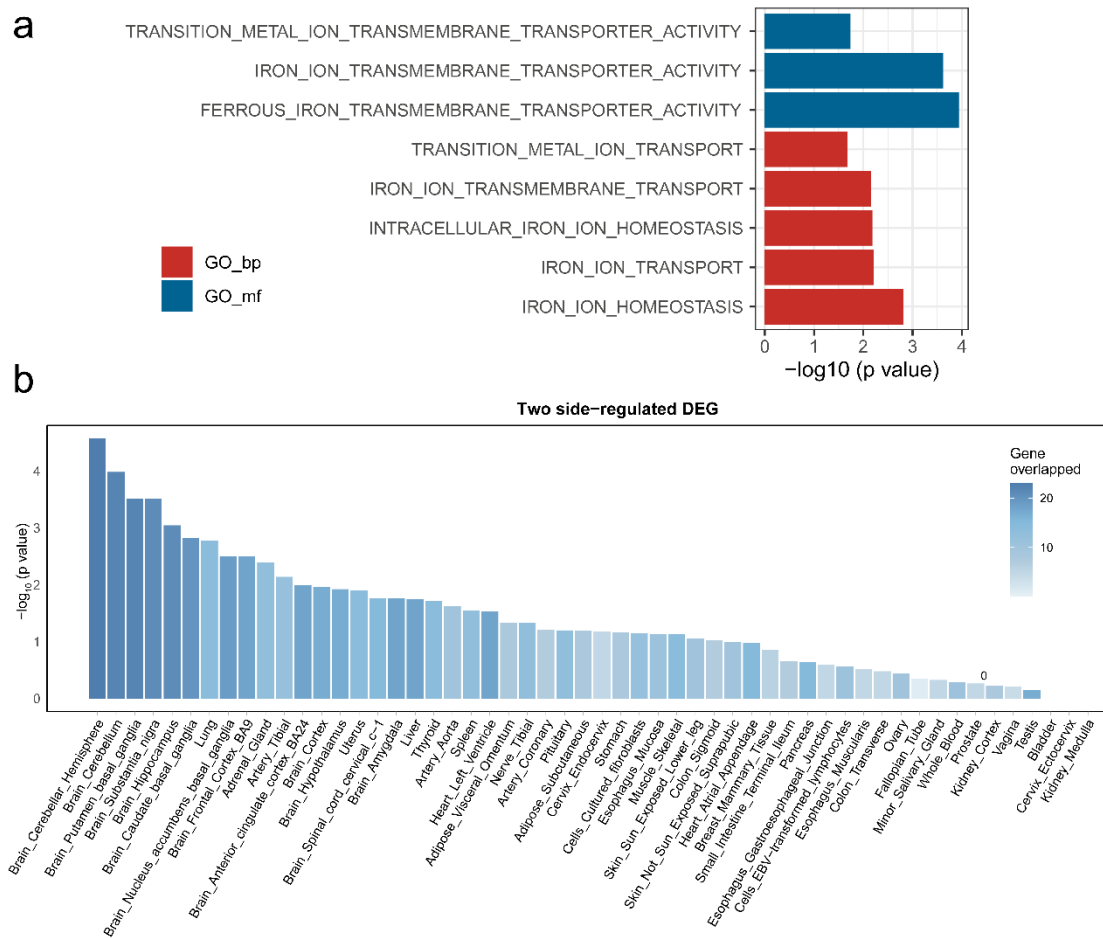








**Supplementary Figure S2.** Manhattan plots of every exome-wide association analysis of common protein-coding variants performed for QSM of 26 brain regions in 26789 participants. P values shown are two-sided and Bonferroni correction were used. The dotted horizontal line represents the significance threshold ( $4.6 \times 10^{-8}$ ).



**Supplementary Figure S3. Tissue and pathway enrichment analysis of genes (exclude top 5 genes) with brain iron.** a) Gene set enrichment analysis of significant genes identified in the exome-wide association analysis, using Gene Ontology and KEGG Ontology database. b) Tissue-wide differential expression analysis of significant brain iron-related genes (exclude top 5 significant genes) using GTEx dataset. The p-values reported are two-sided and unadjusted. GOBP, Gene ontology biological process; GOMF, Gene ontology molecular function.