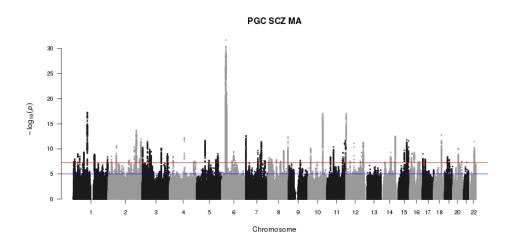
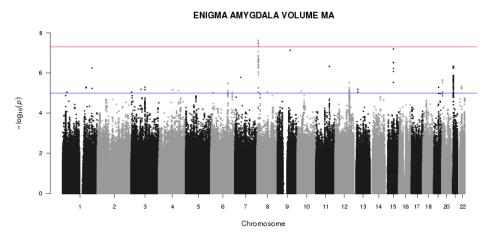


P-value-based meta-analysis between PGC schizophrenia (SCZ) and ENIGMA nucleus accumbens volume

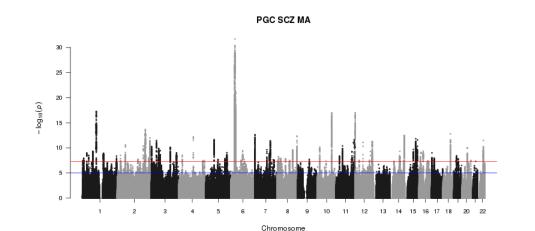


ENIGMA AMYGDALA - PGC SCZ MA - log₁₀(*p*) 13 14 15 16 17 18 Chromosome



Supplementary Figure 2

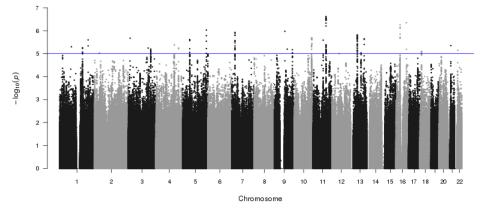
P-value-based meta-analysis between PGC schizophrenia (SCZ) and ENIGMA amygdala volume.



ENIGMA CAUDATE - PGC SCZ MA - log₁₀(*p*) 13 14 15 16 17 18



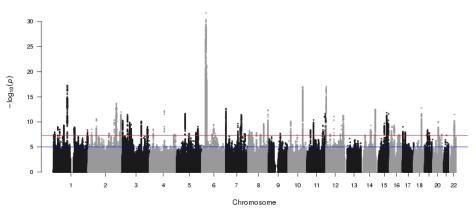
Chromosome



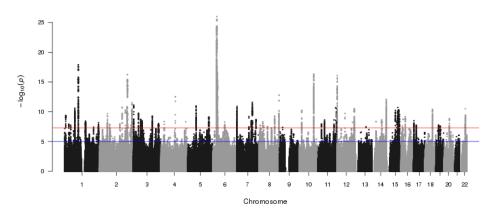
Supplementary Figure 3

P-value-based meta-analysis between PGC schizophrenia (SCZ) and ENIGMA caudate nucleus volume.

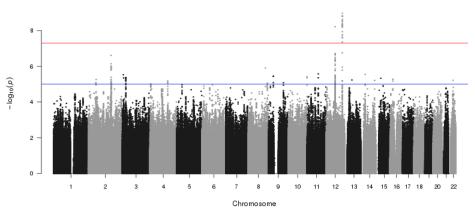






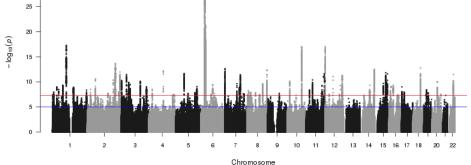






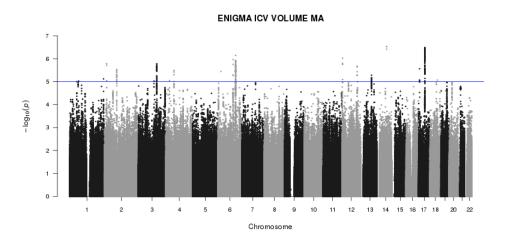
P-value-based meta-analysis between PGC schizophrenia (SCZ) and ENIGMA hippocampus volume.





ENIGMA ICV - PGC SCZ MA - log₁₀(*p*) 13 14 15 16 17 18

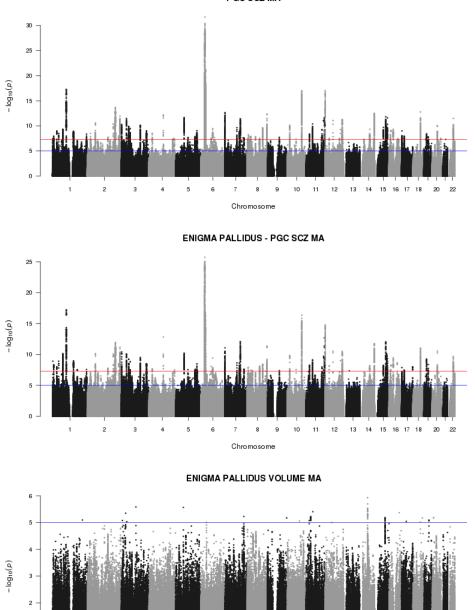
Chromosome



Supplementary Figure 5

P-value-based meta-analysis between PGC schizophrenia (SCZ) and ENIGMA ICV.





1 -

1

2

P-value-based meta-analysis between PGC schizophrenia (SCZ) and ENIGMA pallidum volume.

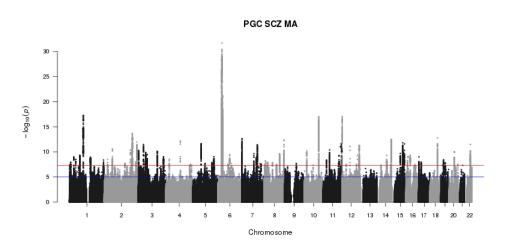
3

4 5 6 7 8 9

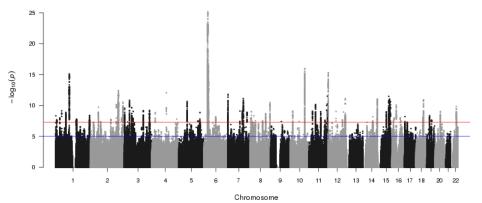
PGC SCZ MA is shown in the top panel, the MA between PGC and ENIGMA is shown in the middle panel, and the ENIGMA MA is shown in the lower panel.

Chromosome

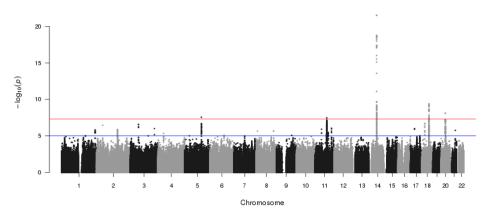
10 11 12 13 14 15 16 17 18 20 22



ENIGMA PUTAMEN - PGC SCZ MA

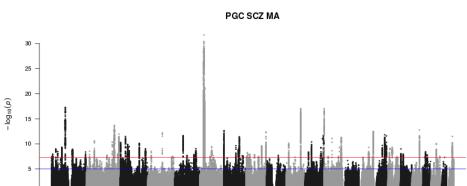


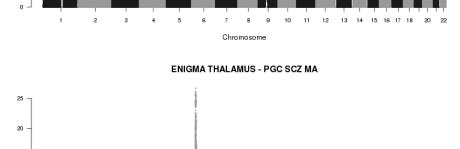
ENIGMA PUTAMEN VOLUME MA

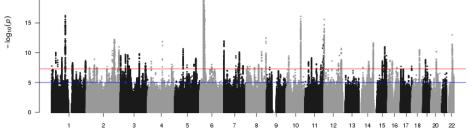


Supplementary Figure 7

P-value-based meta-analysis between PGC schizophrenia (SCZ) and ENIGMA putamen volume.

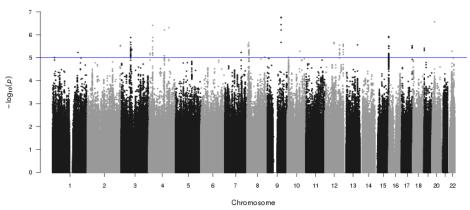






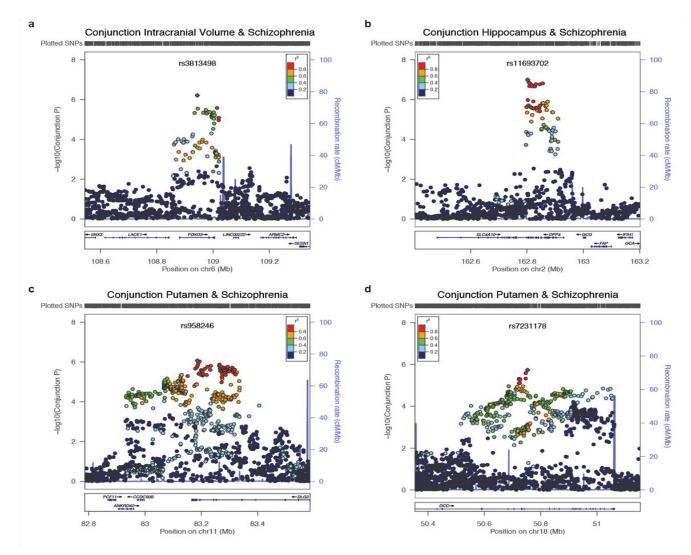
ENIGMA THALAMUS VOLUME MA

Chromosome



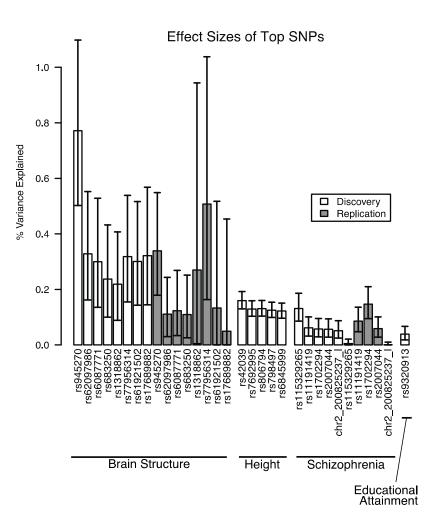
Supplementary Figure 8

P-value-based meta-analysis between PGC schizophrenia (SCZ) and ENIGMA thalamus volume.



Conjunction analysis: regional plots of genetic loci that influence both risk for schizophrenia and brain structure

We used a conjunction test to identify specific genetic variants influencing both risk for schizophrenia and changes in brain structure genome-wide. The conjunction test was run genome-wide using 7,510,842 SNPs found in both the ENIGMA2 and PGC2 studies with MAF \geq 0.01. Conjunction results are then corrected for a downward bias in significance using the relaxed intersection union test. No SNP demonstrated genome-wide significant association to both schizophrenia and brain structure. Several sub-threshold loci did arise from this analysis that bear comment given the possibility that stronger significance may be achieved in future studies. (a) First, the conjunction between intracranial volume and schizophrenia was associated with a locus on chromosome 6 marked by rs381349, where the T allele increases ICV and decreases schizophrenia risk, in the expected direction for a schizophrenia risk factor. This locus is found intronic in the FOXO3 gene known to be involved in neural stem cell proliferation and renewal. (b) The conjunction between hippocampal volume and schizophrenia was associated with a previously mentioned locus on chromosome 2 marked by rs11693702, although in the opposite direction expected for a schizophrenia risk factor (A allele increases schizophrenia risk and increases hippocampal volume). (c,d) The conjunction between putamen volume and schizophrenia was associated with two interesting loci in the expected direction for schizophrenia risk factors marked by rs958246 (chromosome 11; A allele is associated with increased schizophrenia risk and increased putamen volume) and rs7231178 (chromosome 18; A allele is associated with increased schizophrenia risk and increased putamen volume). These SNPs are found in intronic regions of the DLG2 gene, which encodes a key component of the post-synaptic density, and the DCC gene, a netrin receptor involved in axon guidance.



Comparison of SNP effect sizes

Effect sizes of individual SNPs having achieved replicated evidence for association with the phenotypes indicated. For brain structure phenotypes and schizophrenia, effect sizes for both, discovery and replication analyses are shown. For schizophrenia, only the five top SNPs from the 128 recently described genome-wide significant findings were included in the comparison. Height and educational attainment are shown as additional comparators. Effect sizes were measured in percent variance explained (for quantitative traits) or percent variance explained on the liability scale (for disease categories).

Supplementary Table 4.

Correlations of intracranial volume (ICV) and seven subcortical brain volumes (corrected for ICV).

	Nucleus Accumbens	Amygdala	Caudate Nucleus	Hippocampus	Pallidum	Putamen	Thalamus	ICV
Nucleus Accumbens	1	0.222	0.023	0.224	0.201	0.079	0.162	0
Amygdala	-	1	0.058	0.396	0.205	0.282	0.229	0
Caudate Nucleus	-	-	1	0.241	0.098	-0.042	0.124	0
Hippocampus	-	-	-	1	0.153	0.215	0.309	0
Pallidum	-	-	-	-	1	0.134	0.167	0
Putamen	-	-	-	-	-	1	0.147	0
Thalamus	-	-	-	-	-	-	1	0
ICV	-	-	-	-	-	-	-	1