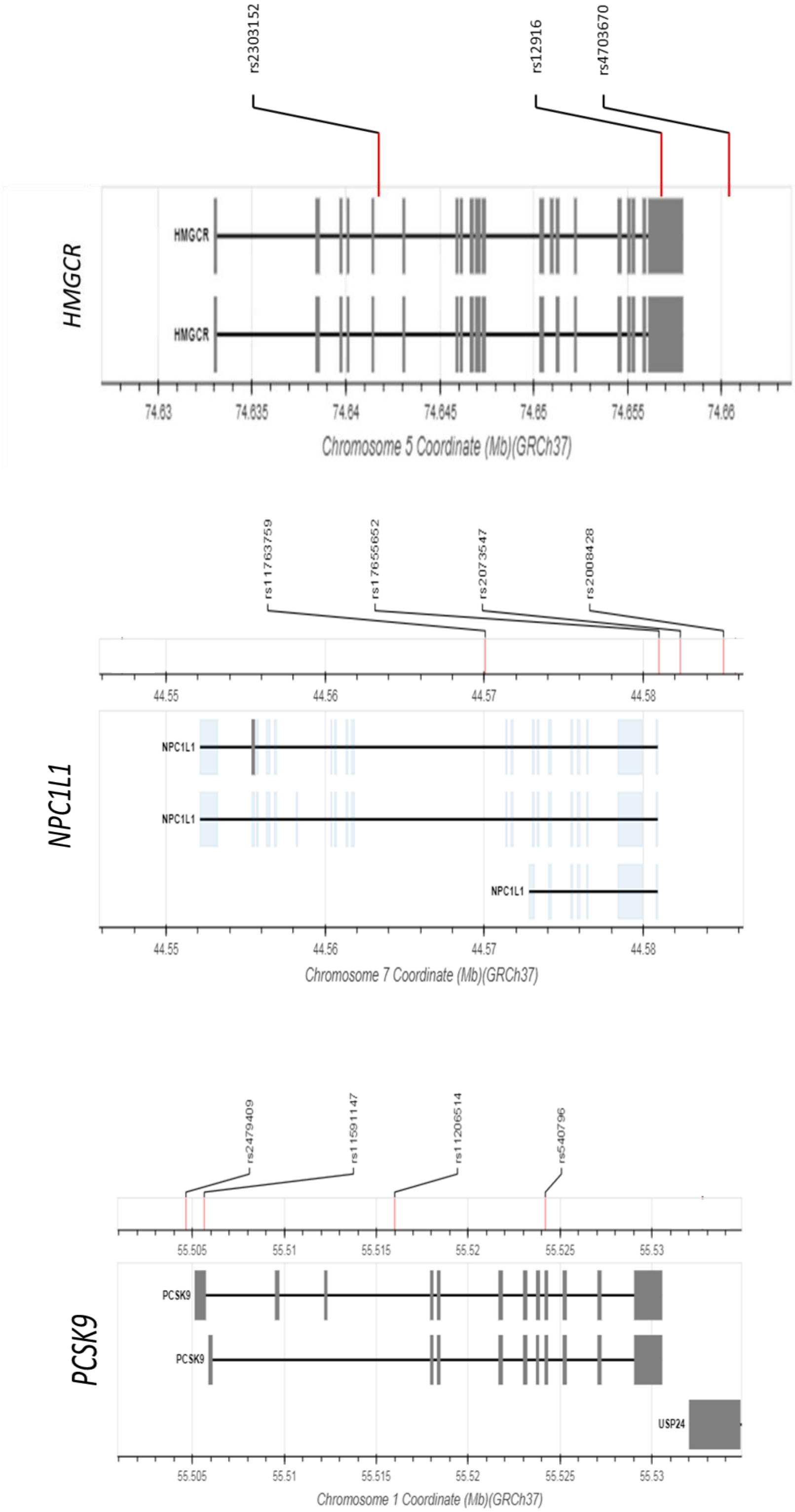
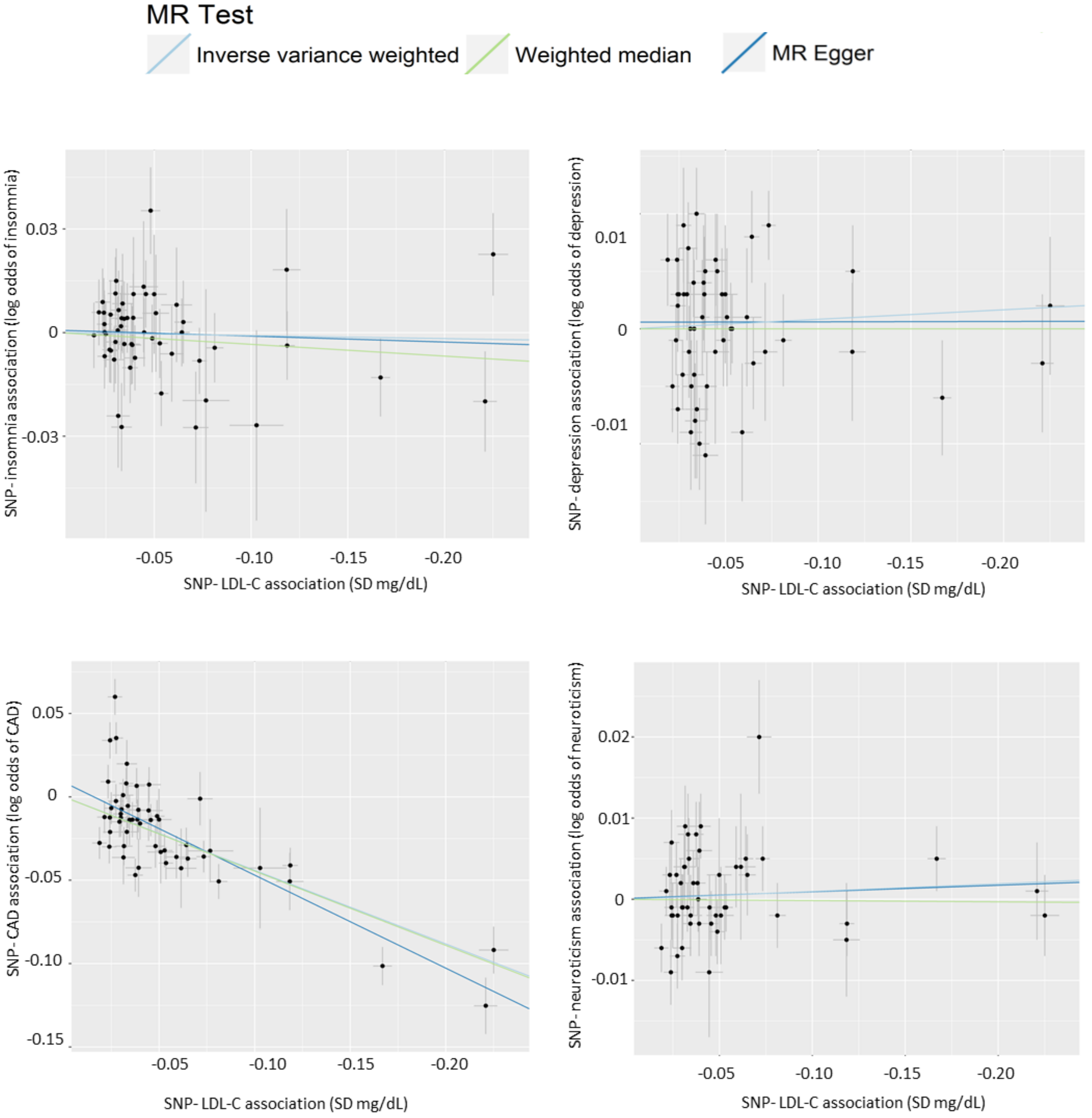
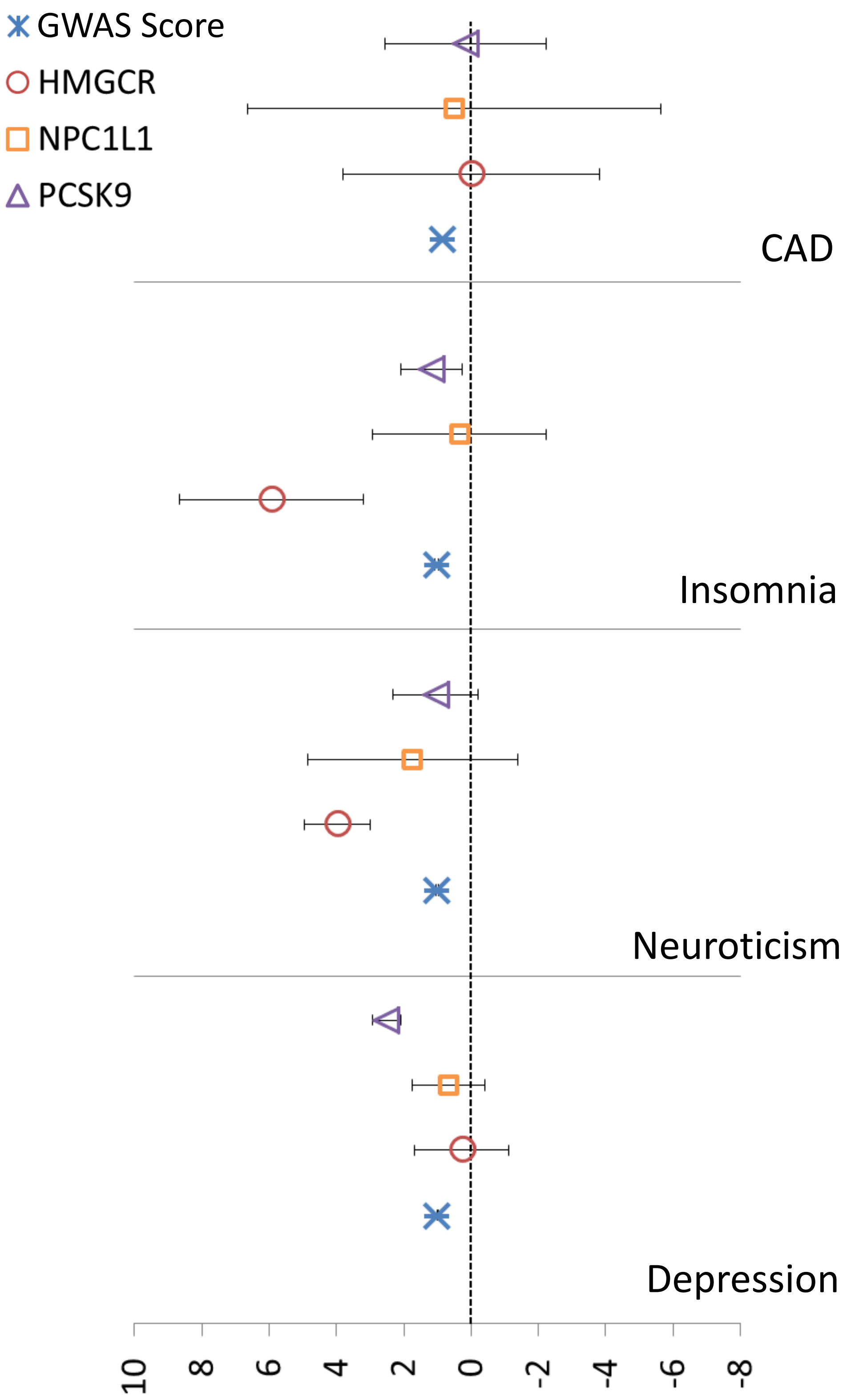


Supplementary Figure S1: Genomic locations of the SNPs included in the Genetic risk scores of *HMGCR*, *NPC1L1*, and *PCSK9*



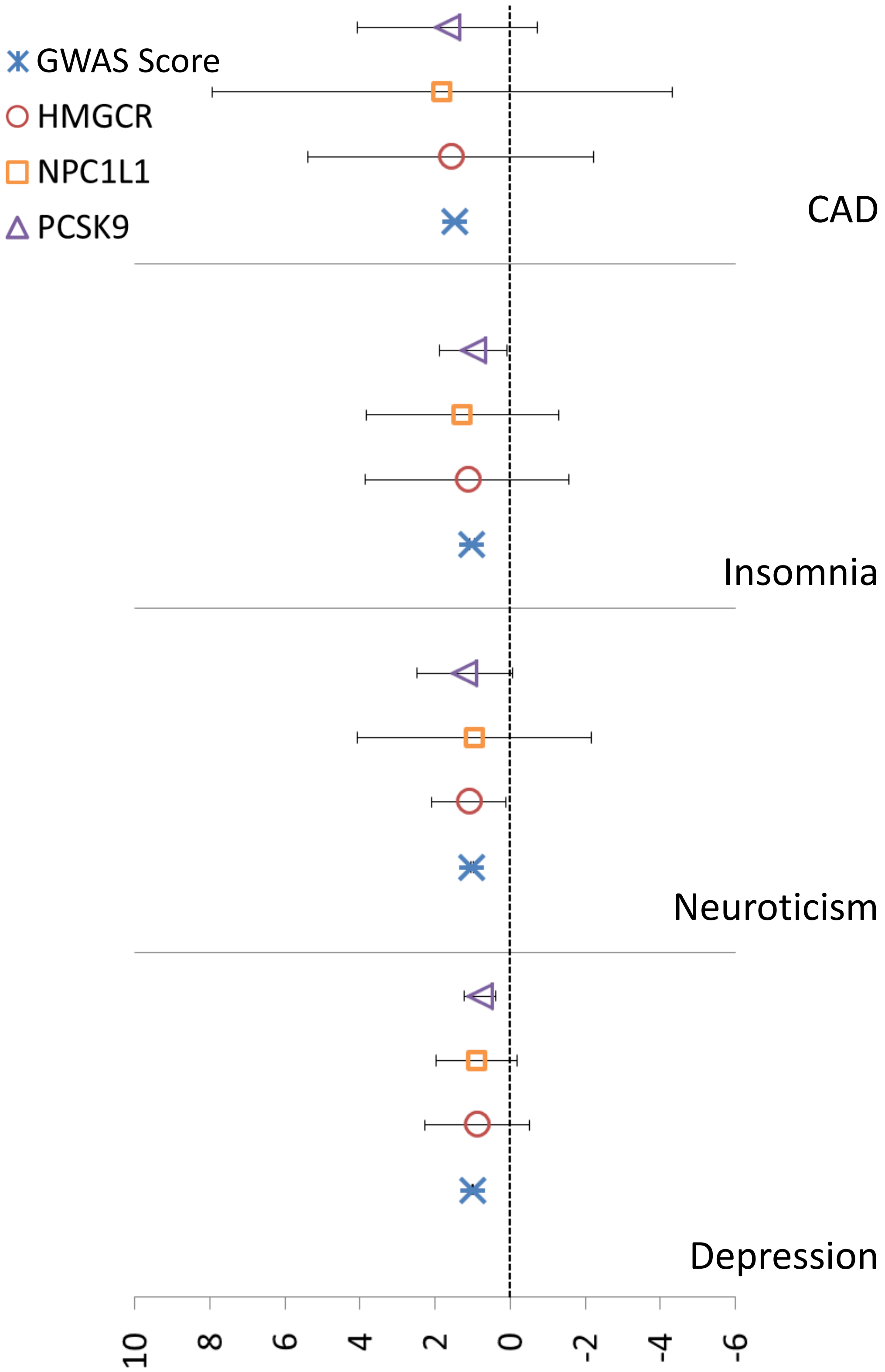
Supplementary Figure S2: MR-analyses using different statistical methods for regression scatterplot for LDL-C on risk of depression, insomnia, neuroticism, and CAD.

The results of inverse-variance weighting (IVW), weighted median, and MR-Egger regression lines. Each point represents the per allele association of one SNP, lines from each point are 95% confidence interval for the association. The association with LDL-C is in in standard deviation units (38 mg/dL) and association with the different outcomes in log(odds ratios).



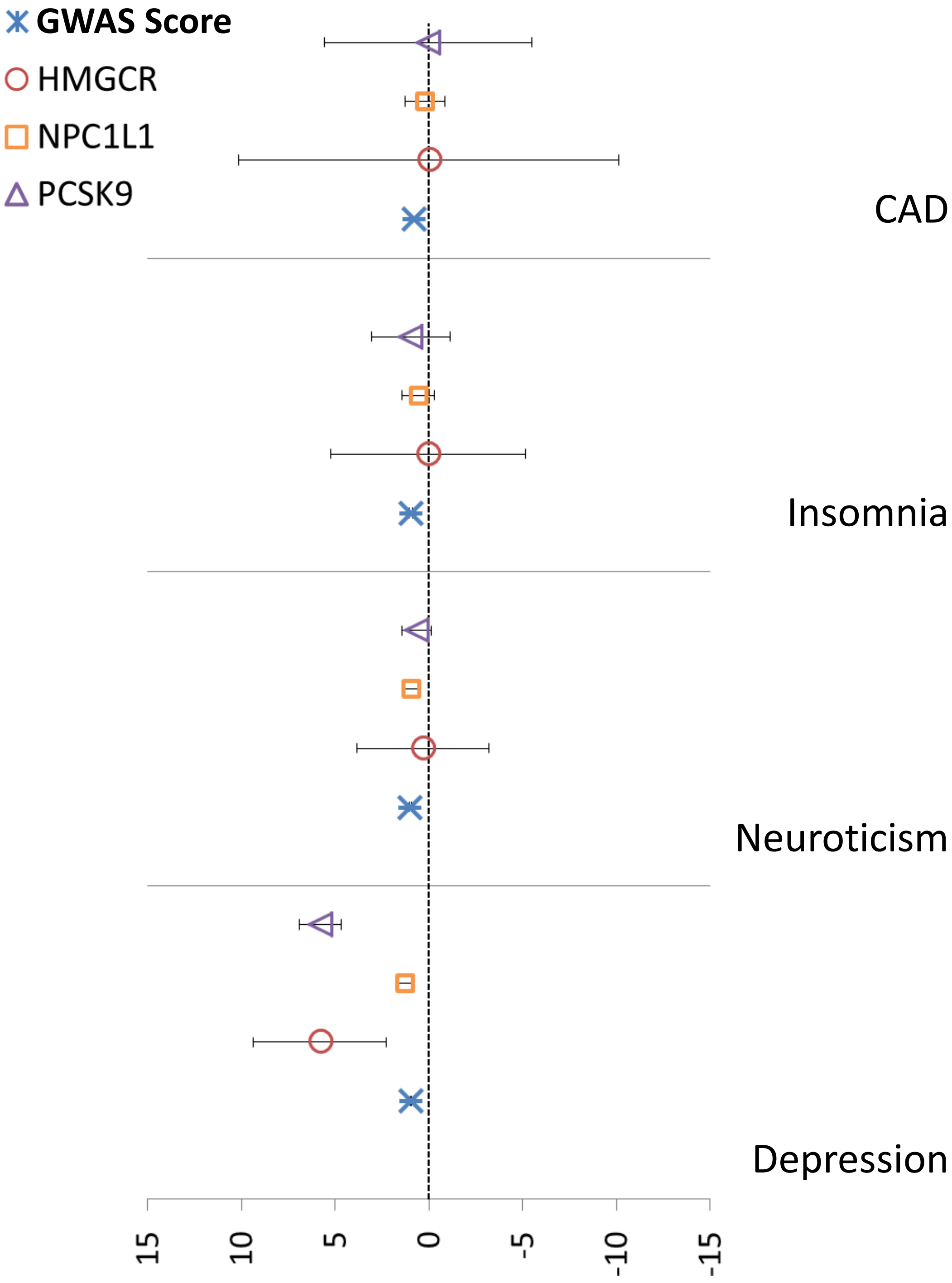
Supplementary Figure S3: Effect of lowering HDL-C mediated by the four genetic risk scores.

Points represent the summary point estimates of effect for the association between each exposure GRS and outcome outcome per 1 SD reduction of HDL-c (mg/dL), Bars represent the 95% confidence interval.



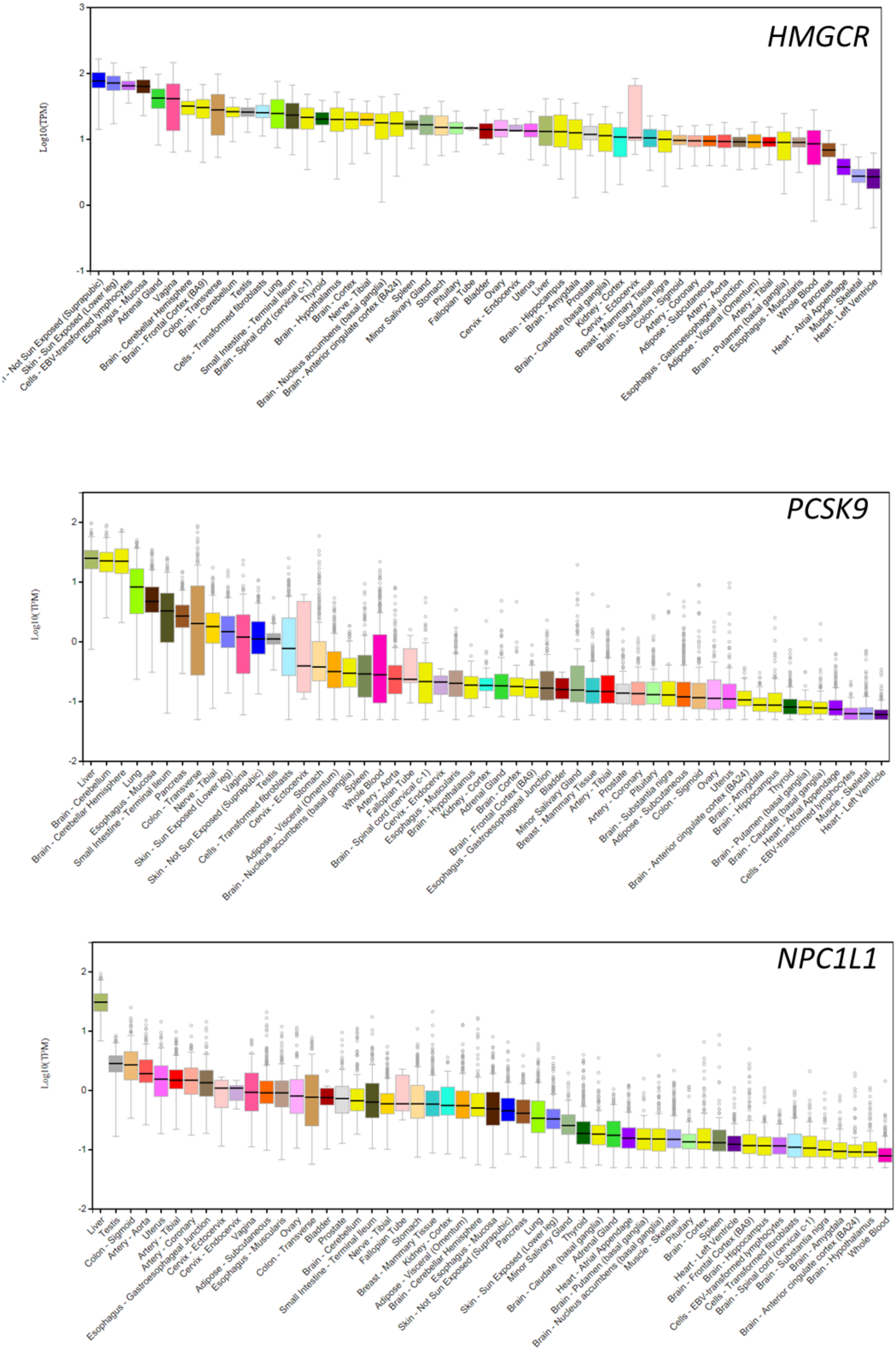
Supplementary Figure S4: Effect of lowering TC mediated by the four genetic risk scores.

Points represent the summary point estimates of effect for the association between each exposure GRS and outcome outcome per 1 SD reduction of TC (mg/dL), Bars represent the 95% confidence interval.

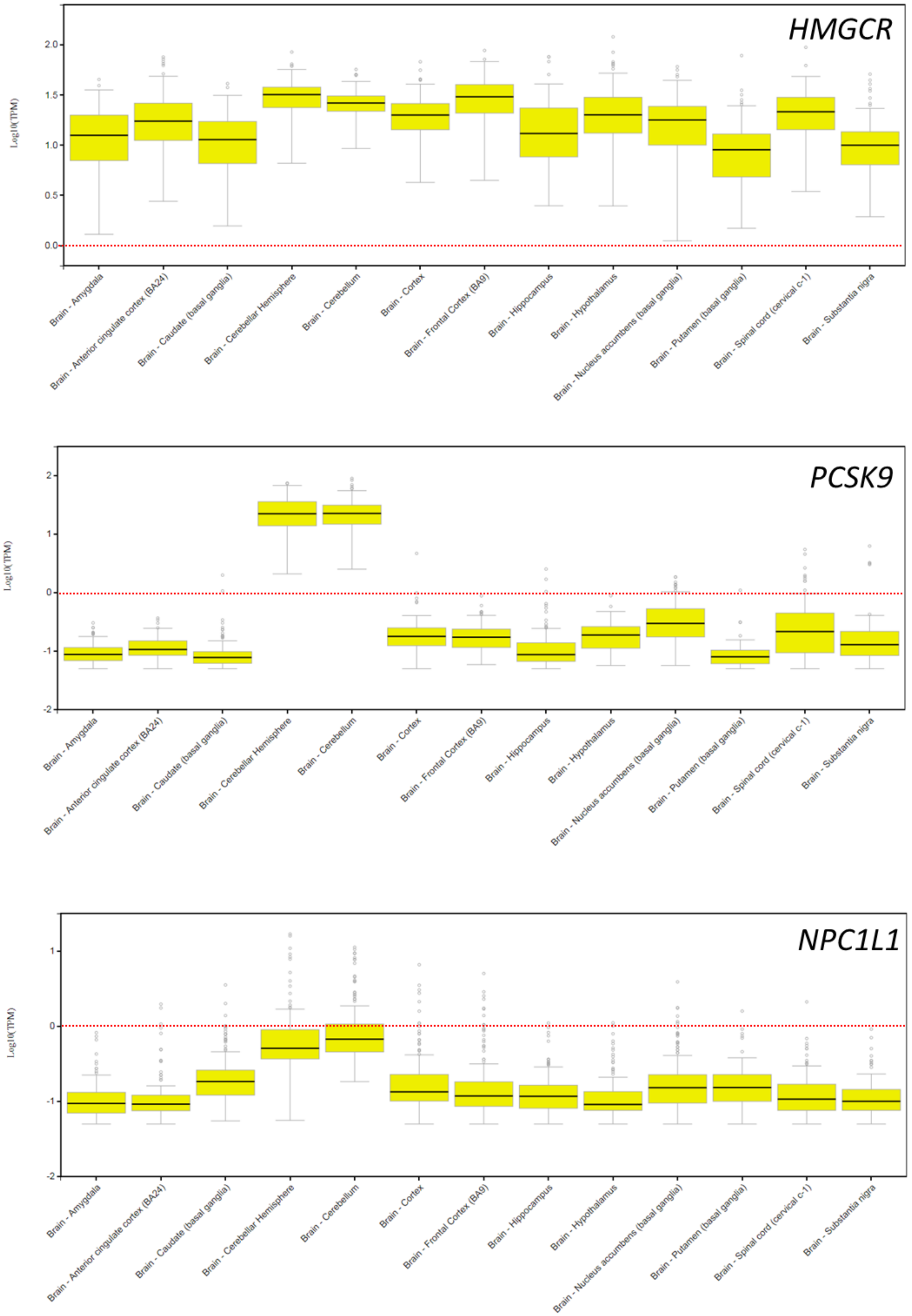


Supplementary Figure S5: Effect of lowering TG mediated by the four genetic risk scores.

Points represent the summary point estimates of effect for the association between each exposure GRS and outcome outcome per 1 SD reduction of TG(mg/dL), Bars represent the 95% confidence interval.



Supplementary Figure S6: Gene expression for *HMGCR*, *PCSK9*, and *NPC1L1* ranked by their log10(transcript per million) values in the different body parts.



Supplementary Figure S7: Gene expression for *HMGCR*, *PCSK9*, and *NPC1L1* ranked by their log10(transcript per million) values in the central nervous system.