Association between genotype variants and 44 MRI measurement was evaluated with linear regression adjusted with covariate of average age.

In our analysis, 1,031,667 variants removed due to MAF<0.01 and eventually 1,618,874 variants and 249 samples passed filters and quality control (low call rate, gender discrepancy, twin data remove, duplicated samples remove, family data random selection) .

Phen ~ case/control

**Linear regression with Non-Permutation Analysis Mode**

We have 44 MRI measurements, however, we only identified significant association (P<3.1×10-8) between genotype variation with BCC.MD.Z (N=2038), GCC.RD.Z(N=1), lPLIC.MD.Z(N=1), rSLF.RD.Z(N=1), GCC.MD.Z(N=30) and BCC.RD.Z(N=789) in non-permutation analysis.

rs8011867 was significantly identified in 4 different MRI measurements (BCC.MD, BCC.RD, GCC.MD and GCC.RD). rs35802157 was significantly identified in lPLIC.MD measurement. rs6500552 was significantly identified in 2 different MRI measurements (BCC.MD.Z and rSLF.RD.Z)

rs8011867 might associated with RNA gene RP11-168L7.1 or TCONS\_00022880 and the functions for this SNPs have never been touched before since the difficulty of the function validation for noncoding-RNA. rs35802157 located in intron regions of FOXN3 which significantly differential expression in different brain region (high in cerebellar hemisphere and cerebellum and quite low in other brain regions). rs6500552 located in TRAP1 exon regions and the previous research found Autism is significantly present in many of the boys with TRAP1-related disease (R.G. Boles et al. / Mitochondrion 23 (2015) 64–70).

**Linear regression with Permutation Analysis Mode**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | CHR | SNP | EMP1 | EMP2 | Gene |
| BCC.MD.Z.assoc.linear.mperm | chr5 | kgp334896 | 0.00175 | 0.02686 |  |
| lALIC.AD.Z.assoc.linear.mperm | chr19 | kgp12379442 | 0.00293 | 0.01876 |  |
| lRLIC.AD.Z.assoc.linear.mperm | chr1 | rs11161438 | 0.00196 | 0.0033 | SSX2IP,LPAR3,C1orf180,CTBS |
| lSLF.AD.Z.assoc.linear.mperm | chr14 | kgp8810402 | 0.00268 | 0.01324 |  |
| lSLF.MD.Z.assoc.linear.mperm | chr2 | kgp5133951 | 0.00327 | 0.04488 |  |
| rALIC.FA.Z.assoc.linear.mperm | chr18 | rs3018274 | 0.00311 | 0.02312 | DOK6 |

**Gene based analysis:**

**SKAT analysis:**

**Compound heterozygote analysis**