**Supplementary Table 1.** Genes included in the complete tPRS (n=332)

**Supplementary Table 2.** Genes in restricted tPRS (*n*=61)

**Supplementary Table 3.** Effects of tPRS on cortical thickness and cortical surface area in the full sample (*n*=4977)

**Supplementary Table 4.** Effects of tPRS on subcortical volume

**Supplementary Figure 1.** Distributions of standardized CBCL Withdrawn/Depressed and Anxious/Depressed Syndrome Scales at baseline (top) and 2-year follow-up (bottom). Solid vertical lines denote scores above the clinical cutoff (t>70). Dashed lines denote elevated scores in the subclinical range.

**Supplementary Table 1.** Genes included in the complete tPRS (n=332)

**Supplementary Table 2. Genes in restricted tPRS (n=61)**

ACOT8

ADH5

AGA

AGL

ALDH4A1

ALMS1

ANKRD10

ARSA

ATF4

ATIC

ATPIF1

BPHL

BRMS1

CAMK2N2

CCNY

CHERP

CLCN3

COQ5

CPNE7

CSRP2

DDT

DGCR2

DIDO1

DPY19L1

DTNBP1

FAM149A

FIGNL1

GALNT13

GAS2L1

GCC2

GGCX

GOSR1

GPR98

HN1L

KCNIP3

KIAA1467

KLHL24

LXN

NEK1

NPHP3

PIK3R1

PILRB

PPM1D

PPP2R3A

PPP3CC

PRSS3

RPA1

RPS26

RRM1

RWDD2B

SFI1

SIN3B

SLC1A1

SNX24

SPATA7

STARD10

SYT7

TAF1C

TBCD

TTC3

WWP2

**Supplementary Table 3. Effects of tPRS on cortical thickness and cortical surface area in the full sample (n=4977)**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Desikan-Killiany cortical region** | **Cortical thickness** | | | | | | **Cortical surface area** | | | | | |
|  | **Main effect** | | | **TPRS x sex interaction** | | | **Main effect** | | | **TPRS x sex interaction** | | |
|  | **t** | **p** | **pFDR** | **t** | **p** | **pFDR** | **t** | **p** | **pFDR** | **t** | **p** | **pFDR** |
| Banks superior temporal sulcus, lh | 0.474 | 0.635 | 0.985 | 0.049 | 0.961 | 0.975 | -0.371 | 0.710 | 0.928 | -0.762 | 0.446 | 0.983 |
| Caudal anterior cingulate, lh | 1.873 | 0.061 | 0.985 | -0.341 | 0.733 | 0.921 | -0.506 | 0.613 | 0.928 | -0.630 | 0.528 | 0.983 |
| Caudal middle frontal, lh | 0.586 | 0.558 | 0.985 | -0.452 | 0.651 | 0.921 | 0.061 | 0.951 | 0.980 | -0.666 | 0.505 | 0.983 |
| Cuneus, lh | 0.066 | 0.947 | 0.996 | 0.341 | 0.733 | 0.921 | 1.609 | 0.108 | 0.822 | -0.715 | 0.475 | 0.983 |
| Entorhinal, lh | 1.527 | 0.127 | 0.985 | 0.124 | 0.901 | 0.943 | -0.771 | 0.441 | 0.926 | -1.386 | 0.166 | 0.983 |
| Fusiform, lh | 0.663 | 0.507 | 0.985 | 0.423 | 0.673 | 0.921 | 0.451 | 0.652 | 0.928 | -0.389 | 0.697 | 0.983 |
| Inferior parietal, lh | -0.726 | 0.468 | 0.985 | -0.189 | 0.850 | 0.921 | 1.202 | 0.230 | 0.869 | 0.477 | 0.633 | 0.983 |
| Inferior temporal, lh | 0.627 | 0.530 | 0.985 | -0.747 | 0.455 | 0.921 | -0.692 | 0.489 | 0.926 | 0.816 | 0.415 | 0.983 |
| Isthmus cingulate, lh | 1.722 | 0.085 | 0.985 | 0.397 | 0.691 | 0.921 | -1.925 | 0.054 | 0.734 | -1.829 | 0.067 | 0.983 |
| Lateral occipital, lh | -0.238 | 0.812 | 0.985 | 0.288 | 0.773 | 0.921 | 0.185 | 0.853 | 0.956 | -0.028 | 0.977 | 0.983 |
| Lateral orbitofrontal, lh | 0.690 | 0.490 | 0.985 | 0.313 | 0.754 | 0.921 | -0.490 | 0.624 | 0.928 | -1.239 | 0.215 | 0.983 |
| Lingual, lh | 0.339 | 0.735 | 0.985 | -0.595 | 0.552 | 0.921 | 1.536 | 0.125 | 0.822 | -1.509 | 0.131 | 0.983 |
| Medial orbitofrontal, lh | -0.744 | 0.457 | 0.985 | 0.502 | 0.616 | 0.921 | -0.106 | 0.915 | 0.980 | -0.821 | 0.411 | 0.983 |
| Middle temporal, lh | -0.201 | 0.840 | 0.985 | -0.185 | 0.853 | 0.921 | -1.102 | 0.271 | 0.926 | -0.726 | 0.468 | 0.983 |
| Parahippocampal, lh | 1.357 | 0.175 | 0.985 | -1.291 | 0.197 | 0.837 | 0.263 | 0.793 | 0.956 | 0.920 | 0.358 | 0.983 |
| Paracentral, lh | -0.783 | 0.434 | 0.985 | -0.221 | 0.825 | 0.921 | 0.812 | 0.417 | 0.926 | -0.057 | 0.955 | 0.983 |
| Pars opercularis, lh | -0.720 | 0.472 | 0.985 | -0.629 | 0.529 | 0.921 | -0.187 | 0.851 | 0.956 | 0.262 | 0.793 | 0.983 |
| Pars orbitalis, lh | -0.008 | 0.994 | 0.996 | 0.269 | 0.788 | 0.921 | 0.179 | 0.858 | 0.956 | -1.141 | 0.254 | 0.983 |
| Pars triangularis, lh | 0.153 | 0.878 | 0.996 | -1.380 | 0.168 | 0.837 | 0.215 | 0.830 | 0.956 | 0.149 | 0.882 | 0.983 |
| Pericalcarine, lh | -0.713 | 0.476 | 0.985 | -0.549 | 0.583 | 0.921 | 1.298 | 0.194 | 0.869 | -1.001 | 0.317 | 0.983 |
| Postcentral, lh | 0.565 | 0.572 | 0.985 | -0.199 | 0.842 | 0.921 | 1.692 | 0.091 | 0.822 | 0.471 | 0.637 | 0.983 |
| **Posterior cingulate, lh** | **3.739** | **<0.001** | **<0.001** | -0.411 | 0.681 | 0.921 | -1.370 | 0.171 | 0.869 | -0.191 | 0.849 | 0.983 |
| Precentral, lh | 0.261 | 0.794 | 0.985 | -1.276 | 0.202 | 0.837 | 0.303 | 0.762 | 0.956 | 0.021 | 0.983 | 0.983 |
| Precuneus, lh | -0.607 | 0.544 | 0.985 | 0.327 | 0.743 | 0.921 | 0.251 | 0.802 | 0.956 | 0.659 | 0.510 | 0.983 |
| Rostral anterior cingulate, lh | -0.409 | 0.683 | 0.985 | -1.385 | 0.166 | 0.837 | -0.720 | 0.472 | 0.926 | 0.252 | 0.801 | 0.983 |
| Rostral middle frontal, lh | -0.042 | 0.966 | 0.996 | -1.066 | 0.286 | 0.846 | -0.598 | 0.550 | 0.928 | -0.225 | 0.822 | 0.983 |
| Superior frontal, lh | 0.675 | 0.500 | 0.985 | -1.446 | 0.148 | 0.837 | 0.720 | 0.472 | 0.926 | 0.313 | 0.754 | 0.983 |
| Superior parietal, lh | -0.091 | 0.928 | 0.996 | -0.225 | 0.822 | 0.921 | 0.693 | 0.488 | 0.926 | 0.739 | 0.460 | 0.983 |
| Superior temporal, lh | -0.820 | 0.412 | 0.985 | -1.008 | 0.314 | 0.890 | -0.904 | 0.366 | 0.926 | 0.387 | 0.699 | 0.983 |
| Supramarginal, lh | -0.570 | 0.569 | 0.985 | 0.898 | 0.369 | 0.921 | -0.388 | 0.698 | 0.928 | 0.570 | 0.569 | 0.983 |
| Frontal pole, lh | -0.357 | 0.721 | 0.985 | -0.437 | 0.662 | 0.921 | -0.545 | 0.586 | 0.928 | 0.528 | 0.598 | 0.983 |
| Temporal pole, lh | -0.212 | 0.832 | 0.985 | -1.567 | 0.117 | 0.837 | -0.614 | 0.539 | 0.928 | 0.624 | 0.533 | 0.983 |
| Transverse temporal, lh | 0.221 | 0.825 | 0.985 | 0.410 | 0.681 | 0.921 | 0.041 | 0.967 | 0.981 | 0.072 | 0.943 | 0.983 |
| Insula, lh | -2.059 | 0.040 | 0.907 | 0.809 | 0.418 | 0.921 | 0.841 | 0.400 | 0.926 | -0.200 | 0.842 | 0.983 |
| Banks superior temporal sulcus, rh | -0.711 | 0.477 | 0.985 | -0.763 | 0.445 | 0.921 | 0.764 | 0.445 | 0.926 | -1.586 | 0.113 | 0.983 |
| Caudal anterior cingulate, rh | -0.686 | 0.493 | 0.985 | -0.802 | 0.423 | 0.921 | -2.047 | 0.041 | 0.734 | -0.639 | 0.523 | 0.983 |
| Caudal middle frontal, rh | 0.548 | 0.584 | 0.985 | -1.234 | 0.217 | 0.837 | -0.465 | 0.642 | 0.928 | -0.134 | 0.893 | 0.983 |
| Cuneus, rh | 0.439 | 0.661 | 0.985 | 0.147 | 0.883 | 0.938 | 0.390 | 0.696 | 0.928 | -0.057 | 0.954 | 0.983 |
| Entorhinal, rh | 1.381 | 0.167 | 0.985 | -0.663 | 0.508 | 0.921 | -0.225 | 0.822 | 0.956 | 0.686 | 0.493 | 0.983 |
| Fusiform, rh | 0.448 | 0.655 | 0.985 | -0.441 | 0.659 | 0.921 | 0.641 | 0.522 | 0.928 | 0.521 | 0.602 | 0.983 |
| Inferior parietal, rh | -0.313 | 0.754 | 0.985 | -0.470 | 0.638 | 0.921 | 0.699 | 0.484 | 0.926 | 0.593 | 0.553 | 0.983 |
| Inferior temporal, rh | -0.109 | 0.913 | 0.996 | -1.933 | 0.053 | 0.837 | -0.859 | 0.390 | 0.926 | 0.194 | 0.846 | 0.983 |
| Isthmus cingulate, rh | 1.324 | 0.185 | 0.985 | -0.009 | 0.993 | 0.993 | -0.419 | 0.675 | 0.928 | 0.170 | 0.865 | 0.983 |
| Lateral occipital, rh | -0.645 | 0.519 | 0.985 | -0.302 | 0.762 | 0.921 | -1.085 | 0.278 | 0.926 | 0.887 | 0.375 | 0.983 |
| Lateral orbitofrontal, rh | 0.908 | 0.364 | 0.985 | 0.745 | 0.457 | 0.921 | -2.012 | 0.044 | 0.734 | -0.559 | 0.576 | 0.983 |
| Lingual, rh | -0.447 | 0.655 | 0.985 | 0.381 | 0.703 | 0.921 | 0.845 | 0.398 | 0.926 | -0.225 | 0.822 | 0.983 |
| Medial orbitofrontal, rh | -0.309 | 0.757 | 0.985 | 1.253 | 0.210 | 0.837 | -1.503 | 0.133 | 0.822 | -0.421 | 0.674 | 0.983 |
| Middle temporal, rh | -0.942 | 0.346 | 0.985 | -1.286 | 0.198 | 0.837 | -1.352 | 0.176 | 0.869 | -0.786 | 0.432 | 0.983 |
| Parahippocampal, rh | 0.780 | 0.436 | 0.985 | -1.605 | 0.108 | 0.837 | 0.109 | 0.913 | 0.980 | 0.544 | 0.586 | 0.983 |
| Paracentral, rh | 0.804 | 0.422 | 0.985 | -1.413 | 0.158 | 0.837 | -0.088 | 0.930 | 0.980 | 0.335 | 0.738 | 0.983 |
| Pars opercularis, rh | -0.110 | 0.912 | 0.996 | -0.799 | 0.425 | 0.921 | 0.883 | 0.377 | 0.926 | 0.517 | 0.605 | 0.983 |
| Pars orbitalis, rh | 0.748 | 0.455 | 0.985 | 0.333 | 0.739 | 0.921 | -2.111 | 0.035 | 0.734 | -1.133 | 0.257 | 0.983 |
| Pars triangularis, rh | 0.005 | 0.996 | 0.996 | -1.084 | 0.279 | 0.846 | 0.524 | 0.600 | 0.928 | -0.739 | 0.460 | 0.983 |
| Pericalcarine, rh | 0.469 | 0.639 | 0.985 | -1.528 | 0.127 | 0.837 | 0.408 | 0.684 | 0.928 | -0.243 | 0.808 | 0.983 |
| Postcentral, rh | 0.326 | 0.744 | 0.985 | -0.731 | 0.465 | 0.921 | 1.601 | 0.109 | 0.822 | -0.349 | 0.727 | 0.983 |
| Posterior cingulate, rh | 2.100 | 0.036 | 0.907 | 0.098 | 0.922 | 0.950 | -1.209 | 0.227 | 0.869 | -0.070 | 0.944 | 0.983 |
| Precentral, rh | -0.327 | 0.744 | 0.985 | -1.530 | 0.126 | 0.837 | -0.077 | 0.939 | 0.980 | 0.456 | 0.648 | 0.983 |
| Precuneus, rh | -0.616 | 0.538 | 0.985 | -0.903 | 0.367 | 0.921 | 1.697 | 0.090 | 0.822 | 0.298 | 0.766 | 0.983 |
| Rostral anterior cingulate, rh | -0.392 | 0.695 | 0.985 | -1.199 | 0.231 | 0.837 | -0.690 | 0.490 | 0.926 | -1.141 | 0.254 | 0.983 |
| Rostral middle frontal, rh | 0.806 | 0.420 | 0.985 | -1.191 | 0.234 | 0.837 | -1.339 | 0.180 | 0.869 | -0.505 | 0.614 | 0.983 |
| Superior frontal, rh | 0.986 | 0.324 | 0.985 | -1.874 | 0.061 | 0.837 | 0.693 | 0.488 | 0.926 | 0.545 | 0.586 | 0.983 |
| Superior parietal, rh | -0.619 | 0.536 | 0.985 | -1.087 | 0.277 | 0.846 | 1.038 | 0.299 | 0.926 | 0.952 | 0.341 | 0.983 |
| Superior temporal, rh | -0.865 | 0.387 | 0.985 | -1.189 | 0.234 | 0.837 | -0.552 | 0.581 | 0.928 | 0.828 | 0.408 | 0.983 |
| Supramarginal, rh | -0.899 | 0.369 | 0.985 | -0.309 | 0.757 | 0.921 | 2.229 | 0.026 | 0.734 | 1.167 | 0.243 | 0.983 |
| Frontal pole, rh | -0.984 | 0.325 | 0.985 | -0.436 | 0.663 | 0.921 | 1.215 | 0.224 | 0.869 | -0.068 | 0.946 | 0.983 |
| Temporal pole, rh | 0.135 | 0.893 | 0.996 | -1.099 | 0.272 | 0.846 | -0.248 | 0.804 | 0.956 | 1.250 | 0.211 | 0.983 |
| Transverse temporal, rh | -0.229 | 0.819 | 0.985 | 1.203 | 0.229 | 0.837 | -0.006 | 0.995 | 0.995 | 1.293 | 0.196 | 0.983 |
| Insula, rh | -0.040 | 0.968 | 0.996 | -0.676 | 0.499 | 0.921 | 0.547 | 0.584 | 0.928 | 1.315 | 0.189 | 0.983 |

*FDR = false discovery rate; lh = left hemisphere; rh = right hemisphere; bold indicates pFDR < 0.05.*

**Supplementary Table 4. Effects of tPRS on subcortical volume**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Region** | **Main effect, full sample**  **(n = 4977)** | | | **TPRS x sex interaction, full sample**  **(n = 4977)** | | | **Main effect, female subsample**  **(n = 2320)** | | | **Main effect, male subsample**  **(n = 2657)** | | |
|  | **t** | **p** | **pFDR** | **t** | **p** | **pFDR** | **t** | **p** | **pFDR** | **t** | **p** | **pFDR** |
| Thalamus, lh | -0.308 | 0.758 | 0.816 | -0.930 | 0.352 | 0.448 |  |  |  |  |  |  |
| Caudate, lh | -1.271 | 0.204 | 0.504 | -1.943 | 0.052 | 0.104 |  |  |  |  |  |  |
| Putamen, lh | 2.065 | 0.039 | 0.322 | -2.134 | 0.033 | 0.092 |  |  |  |  |  |  |
| Pallidum, lh | -0.987 | 0.324 | 0.504 | -1.991 | 0.046 | 0.104 |  |  |  |  |  |  |
| Hippocampus, lh | -0.866 | 0.386 | 0.504 | -2.551 | 0.011 | 0.051 |  |  |  |  |  |  |
| Amygdala, lh | 0.637 | 0.524 | 0.611 | -2.196 | 0.028 | 0.092 |  |  |  |  |  |  |
| Accumbens area, lh | -0.858 | 0.391 | 0.504 | -0.288 | 0.773 | 0.832 |  |  |  |  |  |  |
| Thalamus, rh | -0.849 | 0.396 | 0.504 | -1.117 | 0.264 | 0.370 |  |  |  |  |  |  |
| Caudate, rh | -1.824 | 0.068 | 0.322 | -1.637 | 0.102 | 0.178 |  |  |  |  |  |  |
| Putamen, rh | 1.817 | 0.069 | 0.322 | -1.430 | 0.153 | 0.238 |  |  |  |  |  |  |
| **Pallidum, rh** | -1.132 | 0.258 | 0.504 | **-2.808** | **0.005** | **0.035** | **-3.112** | **0.002** | **0.002** | 1.208 | 0.227 | 0.227 |
| **Hippocampus, rh** | -0.930 | 0.353 | 0.504 | **-3.087** | **0.002** | **0.028** | **-3.058** | **0.002** | **0.002** | 1.379 | 0.168 | 0.227 |
| Amygdala, rh | 0.946 | 0.344 | 0.504 | -0.728 | 0.467 | 0.545 |  |  |  |  |  |  |
| Accumbens area, rh | 0.191 | 0.848 | 0.848 | 0.196 | 0.844 | 0.844 |  |  |  |  |  |  |

*FDR = false discovery rate; lh = left hemisphere; rh = right hemisphere; bold indicates pFDR < 0.05*

**Supplementary Figure 1.** Distributions of standardized CBCL Withdrawn/Depressed and Anxious/Depressed Syndrome Scales at baseline (top) and 2-year follow-up (bottom). Solid vertical lines denote scores above the clinical cutoff (t≥70). Dashed lines denote elevated scores in the subsyndromal range (t≥55).

A screenshot of a graph

Description automatically generated