**Supplementary Material**

**Supplementary Table S1.** Associations with sample retention (genotype data)

|  |  |  |  |
| --- | --- | --- | --- |
|  | OR | (95% CI) | p |
| *Characteristics collected during pregnancy* |
|  Female sex | 0.98 | (0.90-1.06) | 0.541 |
|  Region | 1.00 | (0.89-1.13) | 0.950 |
|  Birth weight | 1.00 | (1.00-1.00) | 0.565 |
|  Maternal age | 1.00 | (0.99-1.00) | 0.997 |
|  Maternal marital status | 1.15 | (0.90-1.47) | 0.259 |
|  Maternal education | 0.91 | (0.83-1.00) | 0.056 |
|  Smoking in pregnancy | 1.09 | (1.00-1.19) | 0.061 |
|  Social class | 0.97 | (0.87-1.08) | 0.590 |
| *Emotional problems* |  |  |  |
|  Age 7 | 1.02 | (0.97-1.06) | 0.510 |
|  Age 11 | 1.01 | (0.97-1.06) | 0.652 |
|  Age 16 | 0.98 | (0.93-1.04) | 0.457 |
|  Age 23 | 0.97 | (0.94-0.99) | 0.014 |
|  Age 33 | 0.96 | (0.94-0.99) | 0.007 |
|  Age 42 | 0.98 | (0.96-1.00) | 0.024 |

Total N=9377. Region = Wales/Scotland vs. England; maternal marital status = married/stable union vs. unmarried/separated/widowed; maternal education = schooling after minimum leaving age; social class = husband’s social class I/II vs III/IV/V (Registrar General’s classification).

**Supplementary Table S2.** Malaise emotional items

|  |
| --- |
| *All depression/anxiety items* |
| * Do you feel tired most of the time?
 |
| * Do you often feel miserable or depressed?
 |
| * Do you often get worried about things?
 |
| * Do you usually have great difficulty in falling or staying asleep?
 |
| * Do you usually wake unnecessarily early in the morning?
 |
| * Do you wear yourself out worrying about your health?
 |
| * Do you often suddenly become scared for no good reason?
 |
| * Are you scared to be alone when there are no friends near you?
 |
| * Are you frightened of going out alone or of meeting people?
 |
| * Are you constantly keyed up or jittery?
 |
| * Is your appetite poor?
 |

**Supplementary Table S3.** Overlapping items

|  |  |  |  |
| --- | --- | --- | --- |
|  | Ages 7 and 11 years | Age 16 years | Ages 23, 33 and 42 years |
| Measure | (Modified Rutter A scale) | (Rutter A scale) | (Malaise ) |
| Depression item | Is miserable or tearful. | Often appears miserable, unhappy, tearful or distressed. | Do you often feel miserable or depressed? |
| Anxiety item | Worries about many things. | Often worried, worries about many things. | Do you often get worried about things? |
| Coding | Frequently = 2Sometimes = 1Never = 0 | Certainly applies = 2Applies somewhat = 1Doesn’t apply = 0 | Yes = 1No = 0 |

**Supplementary Table S4.** Correlations between emotional problems at different ages

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | 1. | 2. | 3. | 4. | 5. | 6. | 7. | 8. | 9. |
| *Primary outcome measures* |
|  1. Age 7 | 1 |  |  |  |  |  |  |  |  |
|  2. Age 11 | 0.389 | 1 |  |  |  |  |  |  |  |
|  3. Age 16 | 0.243 | 0.325 | 1 |  |  |  |  |  |  |
|  4. Age 23 | 0.085 | 0.105 | 0.184 | 1 |  |  |  |  |  |
|  5. Age 33 | 0.056 | 0.089 | 0.177 | 0.454 | 1 |  |  |  |  |
|  6. Age 42 | 0.083 | 0.094 | 0.163 | 0.414 | 0.517 | 1 |  |  |  |
| *Restricted items* |  |  |  |  |  |  |  |  |  |
|  7. Age 23 | 0.099 | 0.116 | 0.192 | 0.798 | 0.399 | 0.360 | 1 |  |  |
|  8. Age 33 | 0.048 | 0.093 | 0.186 | 0.397 | 0.778 | 0.423 | 0.416 | 1 |  |
|  9. Age 42 | 0.079 | 0.100 | 0.161 | 0.364 | 0.427 | 0.796 | 0.365 | 0.429 | 1 |

Spearman’s rho correlations. N=3558-5059

**Supplementary Table S5.** Associations between polygenic risk scores and the restricted set of total emotional problems for each age

|  |  |  |  |
| --- | --- | --- | --- |
|  | Schizophrenia risk alleles |  | MDD risk alleles |
|  | OR | (95% CI) | p |  | OR | (95% CI) | p |
| Age 7 | 1.09 | (1.03-1.15) | 0.003 |  | 1.03 | (0.98-1.09) | 0.228 |
| Age 11 | 1.00 | (0.95-1.06) | 0.925 |  | 0.98 | (0.93-1.04) | 0.551 |
| Age 16 | 1.09  | (1.02-1.16) | 0.012 |  | 0.98  | (0.92-1.04) | 0.450 |
| Age 23 | 1.08 | (1.02-1.15) | 0.013 |  | 1.06 | (1.00-1.13) | 0.066 |
| Age 33 | 1.08 | (1.01-1.15) | 0.030 |  | 1.07 | (1.01-1.14) | 0.032 |
| Age 42 | 1.11 | (1.05-1.18) | <0.001 |  | 1.03 | (0.98-1.09) | 0.215 |

MDD = Major Depressive Disorder.

**Supplementary Table S6.** Associations between polygenic risk scores and emotional problems for each age, using weight adjusting for biases associated with nonresponse

|  |  |  |  |
| --- | --- | --- | --- |
|  | Schizophrenia risk alleles |  | MDD risk alleles |
|  | OR | (95% CI) | p |  | OR | (95% CI) | p |
| Age 7 | 1.09 | (1.02-1.15) | 0.006 |  | 1.04 | (0.99-1.11) | 0.131 |
| Age 11 | 1.00 | (0.95-1.07) | 0.874 |  | 0.98 | (0.92-1.04) | 0.486 |
| Age 16 | 1.07 | (1.00-1.14) | 0.067 |  | 0.97 | (0.91-1.04) | 0.417 |
| Age 23 | 1.08 | (1.01-1.14) | 0.021 |  | 1.03 | (0.97-1.09) | 0.343 |
| Age 33 | 1.08 | (1.00-1.15) | 0.020 |  | 1.06 | (1.00-1.13) | 0.052 |
| Age 42 | 1.10 | (1.04-1.16) | 0.002 |  | 1.05 | (0.99-1.11) | 0.090 |

MDD = Major Depressive Disorder. Weights were estimated using logistic regression including variables assessed in pregnancy (sex, region, birth weight, maternal age, maternal marital status, maternal education, smoking in pregnancy and social class: all with less than 10% missing values) and polygenic risk scores (population stratification components and batch), i.e. comparing those with data to those without. Separate weights generated for each time point. The top 1% of weights were trimmed to the next highest value to reduce the impact of extreme outliers.

|  |
| --- |
| **Supplementary Figure S1.** Associations between polygenic risk scores and emotional problems, using a range of p-value thresholds from the discovery sample  |
| a) Schizophrenia risk alleles |
|  |
| b) Major depressive disorder risk alleles |
|  |

**Supplementary Figure S2.** Frequencies for the restricted set of total emotional problems by age

NB. Ages 7 and 11 (modified Rutter scale) and 16 years (Rutter scale) are scored 0-4, ages 23, 33 and 42 years (Malaise) are scored 0-2.

**Supplementary Figure S3.** Polygenic risk scores (PRS) for emotional problems persistence/age-at-onset across childhood and adulthood

NB. Estimated means at mean covariate values. MDD = Major Depressive Disorder. RRR=relative risk ratio (with 95% confidence intervals) from multinomial regression for elevated emotional symptoms (top decile) in childhood only (age 7 or 11 years, but not later), in adulthood only (ages 33 or 42, but not earlier) and persistently elevated scores (age 7 or 11 and age 33, 42 or 44), compared to those that never had elevated symptoms (age 7, 11, 16, 23, 33, or 42).