**SUPPLEMENTARY MATERIALS**

Waszczuk, M. A., Docherty, A. R., Shabalin, A. R., Miao, J., Yang, X., Kuan, P.-F., Bromet, E., Kotov, R.\*, & Luft, B. J.\*. *Polygenic prediction of PTSD trajectories in 9/11 responders*.

Supplementary Table S1 – Sensitivity analyses - PRS prediction of PTSD symptoms, diagnoses, and trajectories, at multiple PRS p-value thresholds

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | PTSD-PRS | | REXP-PRS | | GAD-PRS | | SZ-PRS | | DEP-PRS | | N-PRS | |
|  | *β* | *p* | *β* | *p* | *β* | *p* | *β* | *p* | *β* | *p* | *β* | *p* |
|  | **P-value threshold = 0.01** | | | | | | | | | | | |
| PTSD Total | .034 | .802 | **.107** | **.006** | **.095** | **.006** | **.107** | **.003** | .056 | .173 | .054 | .173 |
|  | **P-value threshold = 0.05** | | | | | | | | | | | |
| PTSD Total | .040 | .836 | **.101** | **.028** | **.096** | **.013** | **.085** | **.028** | **.074** | **.034** | .064 | .079 |
|  | **P-value threshold = 0.10** | | | | | | | | | | | |
| PTSD Total | .067 | .206 | **.103** | **.028** | **.090** | **.021** | **.100** | **.009** | **.072** | **.049** | .059 | .112 |
|  | **P-value threshold = 0.50** | | | | | | | | | | | |
| PTSD Total | .066 | .301 | **.098** | **.024** | **.096** | **.004** | **.100** | **.003** | **.099** | **.003** | .062 | .079 |
|  | *OR*  *(95% CI)* | *p* | *OR*  *(95% CI)* | *p* | *OR*  *(95% CI)* | *p* | *OR*  *(95% CI)* | *p* | *OR*  *(95% CI)* | *p* | *OR*  *(95% CI)* | *p* |
|  | **P-value threshold = 0.01** | | | | | | | | | | | |
| PTSD Diagnosis | 1.06  (.89-1.25) | 1.00 | 1.12  (.93-1.35) | .802 | 1.04  (.89-1.22) | 1.00 | 1.20  (1.02-1.41) | .168 | 1.17  (1.00-1.38) | .197 | 1.02  (.87-1.19) | 1.00 |
| PTSD Trajectory | 1.03  (.89-1.20) | 1.00 | **1.29**  **(1.10-1.51)** | **.011** | **1.24**  **(1.08-1.43)** | **.025** | **1.22**  **(1.05-1.41)** | **.049** | 1.07  (.93-1.24) | 1.00 | 1.08  (.94-1.24) | .940 |
|  | **P-value threshold = 0.05** | | | | | | | | | | | |
| PTSD Diagnosis | 1.10  (.91-1.32) | 1.00 | 1.07  (.89-1.30) | 1.00 | 1.06  (.90-1.24) | 1.00 | 1.09  (.93-1.28) | .934 | 1.22  (1.04-1.42) | .079 | 1.07  (.91-1.24) | 1.00 |
| PTSD Trajectory | .99  (.84-1.18) | 1.00 | 1.24  (1.05-1.46) | .070 | **1.23**  **(1.07-1.42)** | **.034** | 1.16  (1.01-1.34) | .191 | 1.12  (.97-1.28) | .496 | 1.08  (.94-1.24) | .934 |
|  | **P-value threshold = 0.10** | | | | | | | | | | | |
| PTSD Diagnosis | 1.14  (.93-1.40) | .752 | 1.09  (.90-1.32) | 1.00 | .99  (.85-1.16) | 1.00 | 1.11  (.94-1.29) | .756 | 1.21  (1.04-1.42) | .084 | 1.05  (.89-1.22) | 1.00 |
| PTSD Trajectory | 1.02  (.85-1.22) | 1.00 | **1.28**  **(1.08-1.51)** | **.042** | **1.22**  **(1.06-1.41)** | **.049** | 1.21  (1.05-1.40) | .054 | 1.08  (.94-1.24) | .859 | 1.07  (.93-1.23) | .963 |
|  | **P-value threshold = 0.50** | | | | | | | | | | | |
| PTSD Diagnosis | 1.13  (.90-1.42) | .792 | 1.02  (.83-1.24) | 1.00 | .99  (.85-1.15) | 1.00 | 1.16  (.98-1.36) | .301 | **1.36**  **(1.16-1.60)** | **.003** | 1.11  (.95-1.30) | .594 |
| PTSD Trajectory | 1.03  (.85-1.26) | 1.00 | **1.29**  **(1.09-1.53)** | **.021** | **1.25**  **(1.08-1.44)** | **.017** | 1.20  (1.04-1.39) | .074 | 1.13  (.98-1.30) | .301 | 1.12  (.98-1.29) | .336 |

*Notes:*

REXP- Re-experiencing symptoms of PTSD, GAD – Generalized Anxiety, SZ – Schizophrenia, DEP- Depression, N – Neuroticism

Linear regressions were conducted for symptoms, logistic regressions for diagnoses and trajectories.

All analyses account for the first ten components of population stratification.

All significant results at 5% FDR multiple testing correction are in bold.

Supplementary Table S2 – Sensitivity analyses - PRS prediction of PTSD symptoms, diagnoses, and trajectories, controlling for the first 100 principle components of the population structure

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | PTSD-PRS | | REXP-PRS | | GAD-PRS | | SZ-PRS | | DEP-PRS | | N-PRS | |
| Symptoms: | *β* | *p* | *β* | *p* | *β* | *p* | *β* | *p* | *β* | *p* | *β* | *p* |
| PTSD Total | .065 | .109 | **.113** | **.002** | **.103** | **.001** | **.101** | **.001** | **.104** | **.001** | **.080** | **.004** |
| PTSD Re-experiencing | .048 | .235 | **.111** | **.004** | **.109** | **.001** | **.104** | **.001** | **.092** | **.002** | **.084** | **.004** |
| PTSD Avoidance | .070 | .089 | **.080** | **.034** | .056 | .053 | **.082** | **.005** | **.102** | **.001** | .055 | .053 |
| PTSD Numbing | .055 | .166 | **.107** | **.004** | **.098** | **.001** | **.091** | **.002** | **.092** | **.002** | **.065** | **.023** |
| PTSD Hyperarousal | .069 | .094 | **.111** | **.002** | **.104** | **.001** | **.094** | **.002** | **.103** | **.001** | **.084** | **.004** |
|  | *OR*  *(95% CI)* | *p* | *OR*  *(95% CI)* | *p* | *OR*  *(95% CI)* | *p* | *OR*  *(95% CI)* | *p* | *OR*  *(95% CI)* | *p* | *OR*  *(95% CI)* | *p* |
| PTSD Lifetime Dx | 1.29  (.99-1.69) | .076 | 1.05  (.82-1.35) | .725 | 1.06  (.88-1.27) | .559 | 1.22  (1.01-1.49) | .057 | **1.48**  **(1.22-1.80)** | **.001** | 1.18  (.98-1.42) | .108 |
| PTSD Trajectory | 1.03  (.82-1.29) | .815 | **1.47**  **(1.20-1.80)** | **.001** | **1.28**  **(1.09-1.47)** | **.004** | **1.27**  **(1.08-1.49)** | **.008** | 1.14  (.97-1.33) | .120 | **1.20**  **(1.02-1.41)** | **.039** |

*Notes:*

REXP- Re-experiencing symptoms of PTSD, GAD – Generalized Anxiety, SZ – Schizophrenia, DEP- Depression, N – Neuroticism

Linear regressions were conducted for symptoms, logistic regressions for diagnoses and trajectories.

P-value threshold =1.

All significant results at 5% FDR multiple testing correction are in bold.

Supplementary Table S3 - Growth mixture model analysis results: fit statistics and N per class.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| N classes | N parameters | Fit statistics | | | | Class size (N) | | | | |
| AIC | SABIC | entropy | LMRLRT *p*-value | 1 | 2 | 3 | 4 | 5 |
| 2 | 31 | 340490.29 | 340615.00 | .90 |  | 1219 | 255 |  |  |  |
| 3 | 35 | 339265.02 | 339405.82 | .88 | .23 | 1191 | 161 | 122 |  |  |
| 4 | 39 | 337880.60 | 338037.49 | .87 | <.001 | 1094 | 155 | 144 | 81 |  |
| 5 | 43 | 337247.92 | 337420.90 | .87 | .04 | 1060 | 183 | 110 | 92 | 29 |

*Notes:*

AIC - Akaike Information Criterion, SABIC – sample-size adjusted Bayesian Information Criterion, LMRLRT - Lo–Mendell–Rubin Likelihood Ratio Test

Lower AIC and SABIC indicate better statistical model fit (Wagenmakers & Farrell, 2004). Entropy with values approaching 1 indicate clear delineation of classes (Celeux & Soromenho, 1996). LMRLRT *p* < .05 indicates that the model provides a significantly better fit to the observed data than the model with one class fewer (Lo, Mendell, & Rubin, 2001).

Supplementary Table S4 – PRS prediction of WTC-related PTSD symptoms at visit 1

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | PTSD-PRS | | REXP-PRS | | GAD-PRS | | SZ-PRS | | DEP-PRS | | N-PRS | |
| Symptoms at 1st visit: | *β* | *p* | *β* | *p* | *β* | *p* | *β* | *p* | *β* | *p* | *β* | *p* |
| PTSD Total | .039 | .496 | .067 | .097 | **.068** | **.036** | **.084** | **.011** | **.131** | **2.22E-5** | **.077** | **.013** |
| PTSD Reexp | .024 | .746 | .071 | .077 | **.081** | **.011** | .062 | .060 | **.105** | **4.62E-4** | **.075** | **.015** |
| PTSD Avoidance | .029 | .647 | .046 | .308 | .024 | .560 | .059 | .070 | **.112** | **1.20E-4** | .035 | .308 |
| PTSD Numbing | .042 | .454 | .063 | .126 | .059 | .067 | **.089** | **.007** | **.122** | **6.30E-5** | .062 | .050 |
| PTSD Hyperarousal | .035 | .560 | .053 | .227 | .064 | .050 | **.080** | **.013** | **.115** | **1.40E-4** | **.072** | **.018** |

*Notes:*

REXP- Re-experiencing symptoms of PTSD, GAD – Generalized Anxiety, SZ – Schizophrenia, DEP- Depression, N – Neuroticism

All analyses are adjusted for the time between the first monitoring visit, and 9/11 exposure severity. Adjusting for 9/11 exposure severity did not affect significant findings.

All significant results at 5% FDR multiple testing correction are in bold.

Supplementary Table S5 - Prediction of PTSD trajectory class membership by Polygenic Risk Scores and Exposure severity.

|  |  |  |  |
| --- | --- | --- | --- |
| Model | Predictors | *OR (95% CI)* | *p* |
| 1 | REXP-PRS | 1.268 (1.068-1.504) | .007 |
|  | 9/11 exposure severity | 1.185 (1.033-1.359) | .015 |
| 2 | GAD-PRS | 1.230 (1.064-1.422) | .005 |
|  | 9/11 exposure severity | 1.194 (1.041-1.369) | .011 |
| 3 | SZ-PRS | 1.191 (1.028-1.380) | .020 |
|  | 9/11 exposure severity | 1.185 (1.034-1.358) | .015 |

*Notes:*

REXP- Re-experiencing symptoms of PTSD, GAD – Generalized Anxiety, SZ – Schizophrenia

Each regression analysis accounted for the first ten components of population stratification. Each PRS and exposure severity were included together to compare independent prediction of PTSD trajectory class.

**Supplementary References**

Celeux, G., & Soromenho, G. (1996). An entropy criterion for assessing the number of clusters in a mixture model. *Journal of classification, 13*(2), 195-212.

Lo, Y., Mendell, N. R., & Rubin, D. B. (2001). Testing the number of components in a normal mixture. *Biometrika, 88*(3), 767-778.

Wagenmakers, E.-J., & Farrell, S. (2004). AIC model selection using Akaike weights. *Psychonomic bulletin & review, 11*(1), 192-196.