Supplemental Appendix SA1: Supplemental Methods Information

SA1a) Sociodemographic characteristics of the EDSP Sample

47.7% of the 996 EDSP respondents were males and 52.3% females aged between 21 and 34 years (median=26) at the time of T3 (third follow-up). 7.8% attended secondary general school, 23.6% intermediate secondary school, and 67.2% grammar school. At T3, 0.6% were still at school, 2.7% made an apprenticeship, 34.9% attended university, 46.8% were employed, and 4.2% unemployed. 19.6% were living with their parents, 27.1% alone, and 42.7% with their partner/spouse. The majority of the respondents were classified as middle (58.7%) or upper middle class (26.7%) reflecting the population of Munich. When comparing the 996 individuals participating in the molecular-genetic project with the rest of the T3-sample (n=1214), we found no difference in the prevalence of mental disorders, adverse events, or sociodemographic factors but one; respondents with a lower educational level were less likely to participate (odds ratio=0.7; 95%CI=0.47-0.91). To exclude a selection bias of our findings, we tested for an association between educational level and 'incident major depressive episode' in the total sample of T3 (N=2210) and found no association (odds ratio=1.1; 95%CI=0.81-1.40).

SA1b) Definition of covariates

The category "anxiety disorder" included the following DSM-IV diagnoses: panic disorder, agoraphobia, specific phobia, phobia NOS, social phobia, generalized anxiety disorder, obsessive compulsive disorder, PTSD). "Substance use disorders" was composed of DSM-IV alcohol abuse/dependence, nicotine dependence and illicit drug abuse/dependence.

SA1c) Kind and frequency of traumatic events

The following 7 traumatic events were assessed: 1) "war" (n=2; 0.2%), 2) "physical threat/violence" (n=49; 5.5%), 3) "rape" (n=7; 0.8%), 4) "sexual abuse as child" (n=12; 1.4%), 5) "natural disaster" (n=4; 0.5%), 6) "serious accident" (n=56; 6.3%), and 7) "being kidnapped" (n=1; 0.1%). "Any trauma" comprises all traumatic events (n=118; 13.4%).

SA1d) Power calculation

Power calculation for the gene-environment interaction analysis was conducted using Quanto Version 1.2.3 (http://hydra.usc.edu/gxe/). Model estimates were derived from the present data set (population disease risk: 0.20; prevalence of adverse events: 0.30; minor allele frequency: 0.3; alpha level of significance: 0.005, 2-sided). Following a log-additive model and assuming genetic and environmental main effects with a relative risk of 1.5 and 2.0, respectively, we calculated a power of 80% to detect gene-environment interaction effects with a relative risk of at least 1.55, which is between the limit of a small (1.22) and medium effect (1.86) according to the classification by Cohen (1).

SA1e) Assessment of maltreatment/trauma and major depressive episodes in the replication samples

Dunedin Study:

Evidence of childhood maltreatment was assessed between ages 3 to 11 years and ascertained from 5 sources including parents' reports of discipline, caregiver changes, observations of mother-child interaction, and self-reported physical and sexual abuse. A cumulative exposure index was derived by counting the number of maltreatment experiences during the first decade of life and then categorized into no maltreatment, some maltreatment (1 indicator), and severe maltreatment (2 or more indicators).

Major depressive episodes were evaluated with the Diagnostic Interview Schedule (2, 3) when study members were ages 18, 21, 26, and 32 years. At ages 18 and 21 years diagnoses followed the then-current DSM-III-R, and at ages 26 and 32 years diagnoses followed DSM-IV.

Environmental Risk Longitudinal Twin Study:

Mothers completed the Childhood Trauma Questionnaire (4) when they were on average 40 years of age. The Childhood Trauma Questionnaire inquires about the history of 5 categories of childhood maltreatment: emotional, physical, and sexual abuse and emotional and physical neglect. We derived a cumulative exposure index for each woman by counting the number of maltreatment categories present, which was categorized into no maltreatment, some maltreatment (1-2 categories), and severe maltreatment (3+ categories).

Major depressive episodes were evaluated with the Diagnostic Interview Schedule (2, 3) following DSM-IV criteria when study members were on average 33, 35, 38, and 40 years of age.

References

1. Cohen J: Statistical Power Analysis for the Behavioral Sciences. Hillsdale, NJ, USA, Lawrence Erlbaum Assoc Inc, 1988
2. Robins LN, Helzer JE, Cottler L, Goldring E: Diagnostic Interview Schedule, Version III-R. St Louis, MO, USA, Washington University School of Medicine, 1989
3. Robins LN, Cottler L, Bucholz KK, Compton W: Diagnostic Interview Schedule for DSM-IV. St Louis, MO, USA, Washington University School of Medicine, 1995
4. Bernstein D, Fink L: Childhood Trauma Questionnaire Manual. San Antonio, TX, USA, Psychological Corp., 1998

Supplemental Appendix SA2: Supplemental Results Information

SA2a) Associations between adverse events and incident major depressive episode

Compared to respondents without baseline adversity, respondents with exposure to any adverse event prior to baseline were more likely to report the first onset of a major depressive episode during follow-up (21.1% vs. 16.4%; odds ratio=1.5; 95%CI=1.01-2.09; p=0.039). Associations with separation events (21.5% vs. 16.8%; odds ratio=1.4; 95%CI=0.97-2.09; p=0.071) and trauma (22.9% vs. 17.2%; odds ratio=1.6; 95%CI=0.96-2.52; p=0.067) were not significant, but severe trauma was associated with major depressive episode onset (26.7% vs. 17.0%; odds ratio=1.9; 95%CI=1.16-3.22; p=0.011) withstanding correction for multiple testing (for two independent event categories; $p_{corrected}$=0.022).