**Supplemental text**

PGC PTSD Study Descriptions

i. Grady Trauma Project (GTP)

See reference for details.1 The modified PTSD Symptom Scale (PSS), a psychometrically valid 17-item self-report scale assessing PTSD symptomatology over the prior 2 weeks, was used to assess PTSD. Consistent with prior literature, the PSS frequency items (0 indicates not at all to 3 indicates ≥5 times a week) to obtain a continuous measure of PTSD symptom severity ranging from 0 to 51. For this sample, the PSS frequency items had standardized α=.90 (mean [SD], 13.81 [11.96]). No clearly established PSS cutoff score for PTSD diagnosis has been established; however, DSM-IV criteria for PTSD can be applied to PSS frequency items to create a proxy variable for PTSD diagnostic status. The Institutional Review Boards of Emory University School of Medicine and Grady Memorial Hospital approved this study.

ii. Detroit Neighborhood Health Study (DNHS)

See reference for details.2 Briefly, participants (264 cases, 817 controls) were assessed for PTSD symptoms using the PTSD checklist (PCL-C), a 17-item self-report measure of Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) symptoms, and additional questions about duration, timing, and impairment or disability due to the symptoms. Participants were initially asked to identify Potentially Traumatic Events that they experienced in the past from a list of 19 events. PTSD symptoms were then assessed by referencing two traumatic events that the respondent may have experienced: one that the participant regarded as the worst and one randomly selected event from the remaining PTEs a respondent may have experienced. Respondents were considered affected by lifetime PTSD if all six DSM-IV criteria were met in reference to either the worst or the random event. The DNHS was approved by the institutional review board at the University of Michigan and University of North Carolina at Chapel Hill.

iii. Yale-Penn Study (previously Genetics of Substance Dependence Study)

See reference for details.3 Sample collection and diagnostic interviews were performed by trained interviewers using the Semi-Structured Assessment for Drug Dependence and Alcoholism (SSADDA; available at https://zork.wustl.edu/nida/study\_descriptions/study\_1/ssaddav11\_2\_ns.pdf) to derive diagnoses for lifetime psychiatric and substance use disorders based on DSM-IV criteria. Twelve types of traumatic events were assessed: experienced direct combat in a war; seriously physically attacked or assaulted; physically abused as a child; seriously neglected as a child; raped; sexually molested or assaulted; threatened with a weapon; held captive or kidnapped; witnessed someone being badly injured or killed; involved in a flood, fire, or other natural disaster; involved in a life-threatening accident; suffered a great shock because one of the above events happened to someone close to you; and other. Participants were asked to list up to three traumatic events and describe the trauma in detail. Those reporting traumatic experiences were then interviewed for potential PTSD symptoms. After the data were scored, PTSD diagnoses were generated based on DSM-IV criteria. The institutional review boards at Yale University School of Medicine, the University of Connecticut Health Center, the University of Pennsylvania School of Medicine, the Medical University of South Carolina, and McLean Hospital approved the study.

iv. Marine Resiliency Study (MRS)

See reference for details.4,5 Participants were recruited from two studies including military personnel: (1) the Marine Resiliency Study, a prospective PTSD study with longitudinal follow-up (pre- and post-exposure to combat stress) of U.S. Marines bound for deployment to Iraq or Afghanistan, and (2) a cross-sectional study involving a cohort of combat-exposed active duty or previously deployed service members (CAVC), including PTSD cases and controls with comparable psychosocial and clinical phenotypes. PTSD was diagnosed up to 3 times, once before deployment and 3 and/or 6 month post deployment. Post-traumatic stress (PTS) symptoms were assessed using a structured diagnostic interview, the Clinician Administered PTSD Scale (CAPS), and PTSD diagnosis followed the DSM-IV criteria. All participants included in this study met the *DSM-IV* criteria A1 event. For participants assessed at multiple timepoints, the timepoint with the highest CAPS score was used. Genomic DNA was prepared from blood leukocytes and genotyping was carried out by Illumina (http://www.illumina.com/) using the HumanOm-niExpressExome (HOEE) array with 951,117 loci and by RUCDR (http://www.rucdr.org) using the HOEE array with 967,537 loci. The study was approved by the University of California – San Diego Institutional Review Board, and all participants pro-vided written informed consent to participate.

v-vi. Family Study of Cocaine Dependence and Collaborative Genetic Study of Nicotine Dependence (FSCD and COG)

See references for details.6,7 A module from the Diagnostic Interview Schedule for DSM-IV (DIS-IV), a structured assessment that evaluated the presence or absence of psychiatric disorders according to the DSM-IV criteria was used to evaluate PTSD in a sample of 471 cases and 3,568 controls. A history of fifteen specific traumatic events were queried including rape or sexual assault, assaultive violence (e.g., shot, stabbed), witnessing trauma to others, and non-violent trauma (e.g., serious accident, sudden death of a loved one). The traumatic events were assessed using closed-ended questions (e.g., Have you ever been raped or sexually assaulted?) with nominal response options (i.e., Yes or No). Participants were asked to select the most distressing event and were subsequently evaluated for symptoms of PTSD. A diagnosis of PTSD was dependent on Criterion A, which required intense fear, helplessness, or horror in association with the most distressing event. Interview data were checked for consistency by a senior editor and entered into a computerized data file. Lifetime psychiatric diagnoses were made by a computer algorithm that analyzed responses to the interview using DSM-IV criteria. The Washington University School of Medicine IRB approved the studies.

vii. Nurses Health Study II (NHS)

See reference for details.8 Participants identified stressful events they had experienced from a list of 25 events used in diagnostic interviews as well as “any other very stressful situation or event”, and PTSD was assessed in relation to the participant’s self-selected worst stressful event. They were asked whether they had ever been bothered by each of the 17 symptoms and rated each symptom on a Likert-style scale (1: ‘not at all’ to 5: ‘extremely’). Additional questions assessed the other three DSM-IV criteria: intense fear, horror, or helplessness in response to the event (criterion A2), symptom duration of at least 1 month (criterion E), and clinically significant impairment in functioning owing to symptoms (criterion F). To meet criteria for the lifetime PTSD diagnosis, respondents must have endorsed experiencing one or more of the five reexperiencing symptoms, three or more of the seven avoidance/numbing symptoms, two or more of the five arousal symptoms, and criteria A2, E, and F as defined above. In addition to the diagnostic phenotype, we analyzed lifetime PTSD symptom severity, which was defined as the sum of the symptom ratings across the 17 questions. The Partners Human Research Committee approved this study.

viii. Drakenstein Child Health Study - South African sample (SAFR)

See reference for details.9-11 The modified PTSD Symptom Scale (PSS) was used to assess PTSD. Specifically, the re-experiencing symptom cluster was considered met if the sum of reported symptoms totaled greater than or equal to 1; the avoidance/emotional numbing reported symptoms were greater than or equal to 3; and increased arousal cluster reported symptoms were greater than or equal to 2. Participants who scored above threshold in each of the clusters and had symptom duration for at least 1 month were classified as PTSD cases. The Faculty of Health Sciences human research ethics committee of the University of Cape Town (UCT) approved this study.

ix. Ohio National Guard (ONG)

See reference for details.12 PTSD symptoms were assessed using a 17-item Structured Interview Scale derived from the PTSD Checklist (PCL) (score range, 17-85) performed as structured telephone interviews by lay interviewers using epidemiological methods (forced choice symptom severity range, 1-5). Reliability of the telephone interview was validated against the criterion standard, in-person Clinician-Administered PTSD Scale interview in a clinical subsample (n = 500), demonstrating high specificity (0.92). Separate PTSD severity assessments were performed for adult lifetime deployment-related and nondeployment-related traumatic exposures. Because the discovery cohort came from a longitudinal study with up to 3 assessments per individual, the highest severity score from any available assessment was used for the highest lifetime PTSD symptom severity. The institutional review boards of Veterans Affairs Ann Arbor Health System, Emory University or Case Western University approved the study.

x. Mid-Atlantic Mental Illness Research Education and Clinical Center the study of Post-Deployment Mental Health Study (MIR6)

See reference for details.13 of the study of Post-Deployment Mental Health (1,308 cases, 1,914 controls). PTSD was diagnosed using the Structured Clinical Interview for DSM-IV Disorders (SCID) administered by trained interviewers. In accordance with the DSM-IV, PTSD consisted of three symptom clusters. These included re-experiencing symptoms (B symptoms), avoidance and numbing symptoms (C symptoms) and hyperarousal symptoms (D symptoms). Total PTSD symptoms and symptom clusters (B, C, or D) were measured using the Davidson Trauma Scale for all veterans, including individuals with current PTSD diagnosis and controls. The research was reviewed and approved by the Institutional Review Boards at the Salisbury, NC VA, Hampton, VA VA, Richmond, VAVA, Durham, NC VA and Duke University Medical Centers.

xi. VA Boston-National Center for PTSD Study (NCPT)

437 white non-Hispanic cases and 215 trauma-exposed controls) is the composite of two datasets. The first from a cohort of white non-Hispanic subjects as described in a previous GWAS14 that passed ancestry filters as performed using SNPweights15 according to PGC-PTSD protocols (300 cases and 165 controls; 305 males and 160 females). The majority of this sample consisted of US veterans, but also included the intimate partners of a subset of the veterans. The second cohort was made up of subjects from the Translational Research Center for TBI and Stress Disorders, a VA RR&D Traumatic Brain Injury Center of Excellence at VA Boston Healthcare System (TRACTS) study of US veterans. From TRACTS, 137 white non-Hispanic cases and 50 controls passed ancestry filters based on SNPweights and were included in the analysis. The TRACTS sample is largely male (170 men and 17 women). The genotyping, quality control, filtering and imputation for these cohorts has been described in detail elsewhere.14,16 Briefly, genotyping was performed using the Illumina HumanOmni2.5-8 microarrays (Illumina, San Diego, CA). Imputation of non-genotyped SNPs was performed using IMPUTE217-20 and 1000 genomes phase 1 reference data.21 Principal components were generated by the program EIGENSTRAT22 based on 100,000 SNPs. For both cohorts, participants were administered the Clinician-administered PTSD scale for DSM-IV (CAPS-IV),23 a 30-item structured diagnostic interview that assesses the frequency and severity of the 17 DSM-IV PTSD symptoms, 5 associated features and functional impairment, and both current and lifetime PTSD symptoms. These studies were performed under the oversight of the appropriate VA health care facilities institutional review boards.

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i. Grady Trauma Project (GTP)

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ii. Detroit Neighborhood Health Study (DNHS)

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iii. Yale-Penn Study (Genetics of Substance Dependence Study)

This study was supported by National Institutes of Health Grants RC2 DA028909, R01 DA12690, R01 DA12849, R01 DA18432, R01 AA11330, and R01 AA017535 and the Veterans Affairs VISN 1 and VISN 4 Mental Illness Research, Educational, and Clinical Centers; and the VA National Center for PTSD Research.

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iv. Marine Resiliency Study (MRS)

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v-vi. Family Study of Cocaine Dependence and Collaborative Genetic Study of Nicotine Dependence (FSCD and COG)

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vii. Nurses Health Study II (NHS)

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viii. Drakenstein Child Health Study - South African sample (SAFR)

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ix. Ohio National Guard (ONG)

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x. Mid-Atlantic Mental Illness Research Education and Clinical Center PTSD Study (MIR6)

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xi. VA Boston-National Center for PTSD Study (NCPT)

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