A. OVERALL COVER PAGE

Project Title: POLYGENIC PREDICTION OF PTSD TRAJECTORIES AND INFLAMMATION IN 9/11 RESPONDERS	
Grant Number: 5U01OH011864-02	**Project/Grant Period:** 07/01/2019 - 06/30/2021
Reporting Period: 07/01/2020 - 06/30/2021	**Requested Budget Period:** 07/01/2020 - 06/30/2021
Report Term Frequency: Final	**Date Submitted:** 01/02/2024
Program Director/Principal Investigator Information: ROMAN I KOTOV , PHD **Phone Number:** 6316327763 **Email:** roman.kotov@stonybrook.edu	**Recipient Organization:** STATE UNIVERSITY NEW YORK STONY BROOK STATE UNIVERSITY NEW YORK STONY BROOK The Office of Sponsored Programs STONY BROOK, NY 117943362 **DUNS:** 804878247 **UEI:** M746VC6XMNH9 **EIN:** 1146013200F7 **RECIPIENT ID:**
Change of Contact PD/PI: NA	
Administrative Official: MICHELE CANTON 100 Nicholls Road W-5510 Frank Melville Jr. Memorial Library Stony Brook, NY 11794 **Phone number:** 6316329029 **Email:** michele.canton@stonybrook.edu	**Signing Official:** MICHELE CANTON 100 Nicholls Road W-5510 Frank Melville Jr. Memorial Library Stony Brook, NY 11794 **Phone number:** 6316329029 **Email:** michele.canton@stonybrook.edu
Human Subjects: NA	**Vertebrate Animals:** NA
hESC: No	**Inventions/Patents:** No

B. OVERALL ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Polygenic risk scores (PRS), an aggregate of individual genetic variants associated with the disorder, can help identify vulnerable individuals and clarify biological mechanisms underpinning PTSD, such as systemic inflammation. However, it remains unclear whether PTSD-PRS is predictive of PTSD in civilians with occupational exposures (e.g. police officers), and whether it predicts the long-term course of PTSD (e.g., resilient, chronic, worsening, and improving trajectories). Furthermore, the nature of association between PTSD and inflammation remains poorly understood. The study involved conducting genotype and inflammatory assays on biobanked blood samples from 8,000 responders to 9/11 disaster from the Long Island WTC Health Program. The level of disaster exposure and an extensive prospective psychiatric and medical history were available for this cohort from electronic medical records collected since 2002.
The specific aims of the grant were:
1. Test whether markers of genetic vulnerability to PTSD are associated with PTSD diagnoses and symptoms
2. Investigate whether markers of genetic vulnerability to PTSD predict 18-year course of PTSD symptoms in responders
3. Study the role of genetic vulnerability in the association between PTSD and inflammation

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File Uploaded : Final Accomplishments_SNPs.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

Not Applicable

Study Findings

Data Generation and Analysis

Genetic Dataset. Genotyping of blood samples (total N= 8,602) was performed in three batches at the Genomics Shared Resource at Roswell Park Cancer Institute, using the Infinium Global Screening Array (Illumina, San Diego, CA, USA), according to protocols of the manufacturer. Genotypes were imputed on the Michigan Imputation Server pipeline v1.2.4, using the Haplotype Reference Consortium reference panel. Before imputation, the genotypes were filtered for ambiguous strand orientation, missingness rate>5% (by marker exclusion, then by individual), Hardy-Weinberg equilibrium violation ($p<10-6$), sex mismatch, and non-European ancestry. After imputation, the SNPs were excluded for imputation $R2<0.5$ and average call rate below 90%. Genotype imputation was performed on 552,230 SNPs, resulting in 25,514,638 SNPs after QC which were used for the final polygenic risk scoring.

PRSs were created using PRSice 2.0 software, based on publically available summary statistics from genome-wide association studies. PRSs were created by aggregating genetic variants up to varying thresholds of significance from a GWAS discovery sample, weighted by the associations in the discovery sample. Our primary analyses used a full list of SNPs after clumping and their corresponding weights from GWAS discovery samples (P-value threshold=1), to incorporate more of the genome Sensitivity analyses at other thresholds were also conducted. All analyses adjusted for the first 10 genetic ancestry principle components (PCs) to account for population stratification.

Immunoassay Dataset. A subset of N=1,000 samples has undergone immunoassay to address Aim 3 of the project. Plasma protein expression was profiled with the Olink Proseek Multiplex Platform. The Olink multiplex immunoassay was designed to provide an ultrasensitive, reproducible, highly multiplexed method for measuring protein expression. The measurement was based on state-of-the-art proximity extension assay technology. We used the Olink Neurology panel consisting of 92 proteins, including markers associated with neurobiological processes and neurological diseases (e.g., neural development, axon guidance, synaptic function, or specific conditions such as Alzheimer's disease), as well as with broader roles in processes such as cellular regulation, immunology, development, and metabolism.

Several internal and external controls were added to the plasma samples for quality control to monitor protein–antibody reactions, the DNA extension step, and the detection quality of the qPCR, in order to estimate the background signal and to calculate the limit of detection for Olink panels. All values below the limit of detection were coded as missing. Proteomics data were converted into normalized protein expression values, Olink Proteomics' arbitrary units on log scale, i.e., a difference of one normalized protein expression unit indicated a doubling of protein concentration.

Clinical Dataset. Clinical datasets combining longitudinal demographic, symptom, diagnosis, and other health variables have been cleaned, assembled, and prepared for analyses. The majority of clinical data came from electronic medical records provided by the WTCHP Data Coordination Center.

Data analysis. The genetic, inflammatory, and clinical datasets were successfully combined to create analytic datasets. All variables were inspected and standardized prior to analyses. The datasets were analyzed to address Aims 1 -3 of the study, resulting in one national scientific conference presentation and one manuscript publication, with more manuscripts under review. Moreover, the generated dataset serves as a parent study to three funded research projects, building on the accomplished resources.

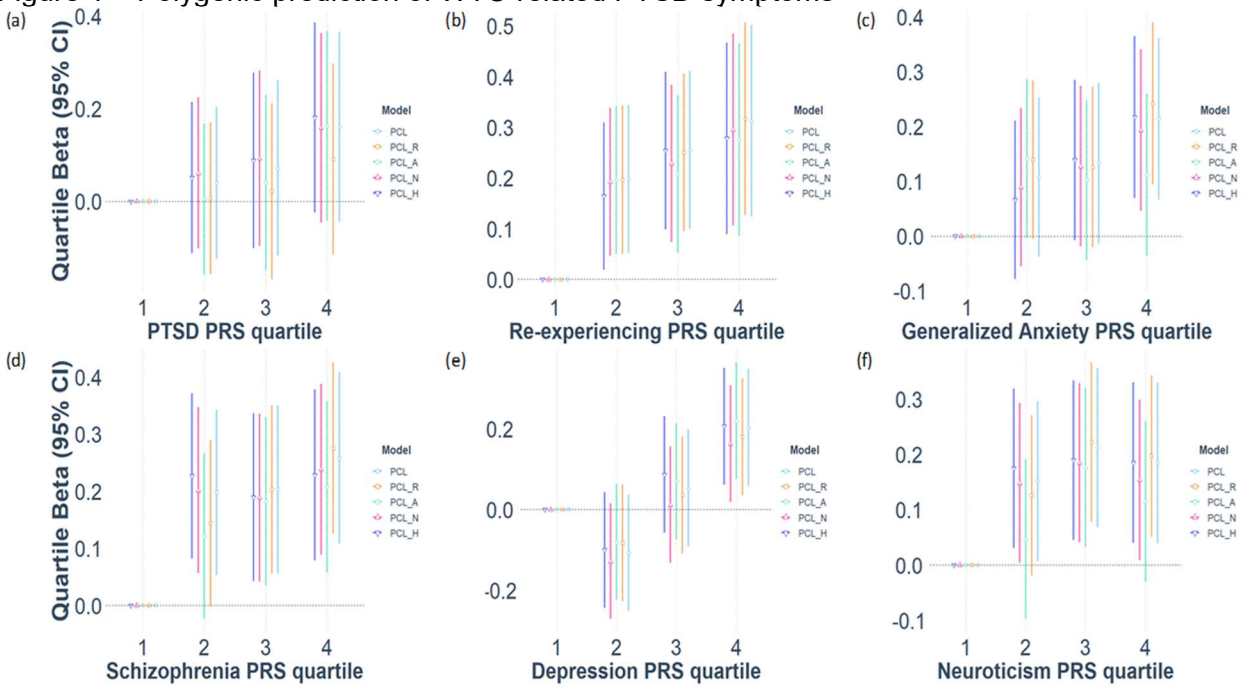
Key scientific findings

1. Polygenic prediction of PTSD severity

Our analyses found that selected psychiatric polygenic biomarkers prospectively predicted WTC-related PTSD symptom severity and diagnosis in responders to 9/11 disaster. Specifically,

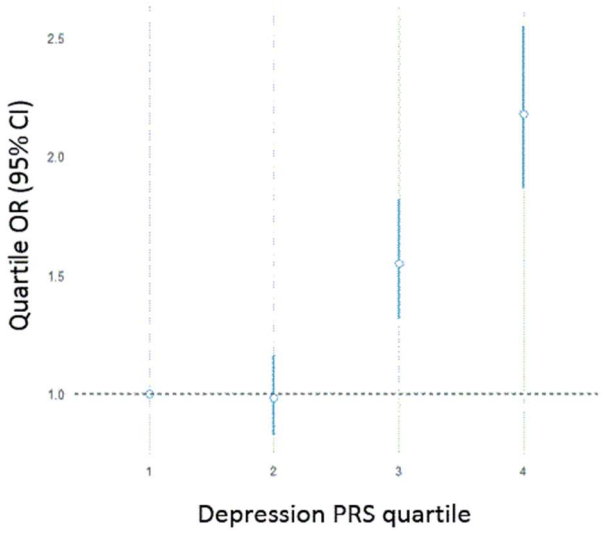
PRSs for Re-experiencing, Generalized Anxiety, Schizophrenia, Depression and Neuroticism predicted WTC-related PTSD symptom severity (Figure 1). Depression-PRS additionally predicted PTSD diagnostic status (Figure 2). The associations were the most prominent when contrasting the lowest and highest genetic risk groups, in line with the view that psychiatric PRSs may be particularly informative at the very high genetic susceptibility scores. This finding is in line with the known genetic overlap between PTSD and depression, as well as with the evidence for common genetic vulnerability to internalizing psychopathology more broadly. Cross-sectional associations with PRSs were comparable across all PTSD symptom clusters, although only three PRSs significantly predicted avoidance symptoms. Overall, the current results show little phenotype-specificity in PRS prediction, and instead support transdiagnostic applications of PRSs in translational studies.

Figure 1 – Polygenic prediction of WTC-related PTSD symptoms



Notes:
R- Re-experiencing, A – Avoidance, N-Numbing, H-Hyperarousal. PRS predictions of PTSD symptoms are reported as standardized regression betas per PRS quartile, relative to the first quartile. For example, participants in the 4th quartile of genetic risk for depression had a significantly higher PTSD symptoms than subjects in the 1st quartile.

Figure 2 – Depression Polygenic Risk Score prediction of WTC-related PTSD diagnosis



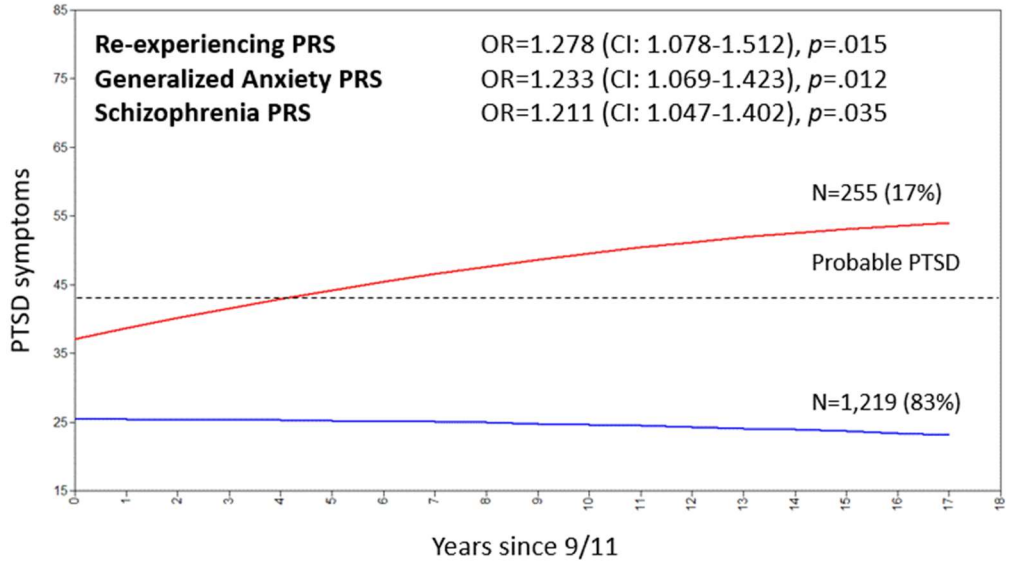
Notes:
Depression-PRS prediction of PTSD diagnosis is illustrated as odds ratios per PRS quartile, relative to the first quartile. For example, responders in the highest 4th quartile of genetic risk for depression had over twice the odds of receiving a PTSD diagnosis than responders in the lowest 1st quartile of genetic risk.

Genetic vulnerability was not correlated with the severity of 9/11 trauma exposure, and instead contributed an independent and larger prediction of PTSD than the exposure severity. Notably, PRSs accounted for approximately four times more variance in PTSD than exposure severity. This novel finding suggests that at the point of trauma exposure, genetic vulnerability to psychopathology may be a better indicator of long-term PTSD outcomes than the severity of trauma. Nonetheless, the trauma exposure is by definition necessary for PTSD onset and an inclusion of both sources of information maximizes prediction. The lack of a significant association between exposure severity and any of the PRSs argues against the gene-environment correlation, i.e. genetic vulnerability to psychopathology contributing to higher levels of trauma exposures.
Finally, there was no association between genetic vulnerability to psychiatric conditions, and employment in law enforcement occupations. Yet in the WTC cohort, police officers show more resilient outcomes than non-traditional responders, in line with findings from other law enforcement samples. The current results suggest that these differences are not due to a lower genetic vulnerability to PTSD or other psychiatric traits in police officers. Instead, this occupational group might report fewer PTSD symptoms due to resilience training and preparedness for disasters, ‘selective survival’ of resilient police officers remaining in the law enforcement, or underreporting due to stigma.

2. Polygenic prediction of PTSD course

Clinical data collected over 18-years of monitoring provided an opportunity to take PTSD genetics beyond the case-control comparisons to longitudinal models, investigating how genetics relate to the trajectory of PTSD after a traumatic event. Growth mixture modeling resulted in a two classes solution. As expected, a majority of responders (83%) were resilient since 9/11 (Figure 3). However, the remaining 17% showed a severe symptom trajectory. The genetic analysis results indicated that Re-experiencing, Generalized Anxiety, and Schizophrenia PRSs were predictive of a severe 18-year PTSD symptom trajectory after 9/11 (Figure 3). The prediction was independent of 9/11 exposure severity. Overall, the current study is the first to demonstrate that existing polygenetic profiles can predict long-term PTSD outcomes in traumatized populations, although the effect sizes are small.

Figure 3- PTSD trajectory classes since 9/11, and prediction of class membership by Polygenic Risk Scores

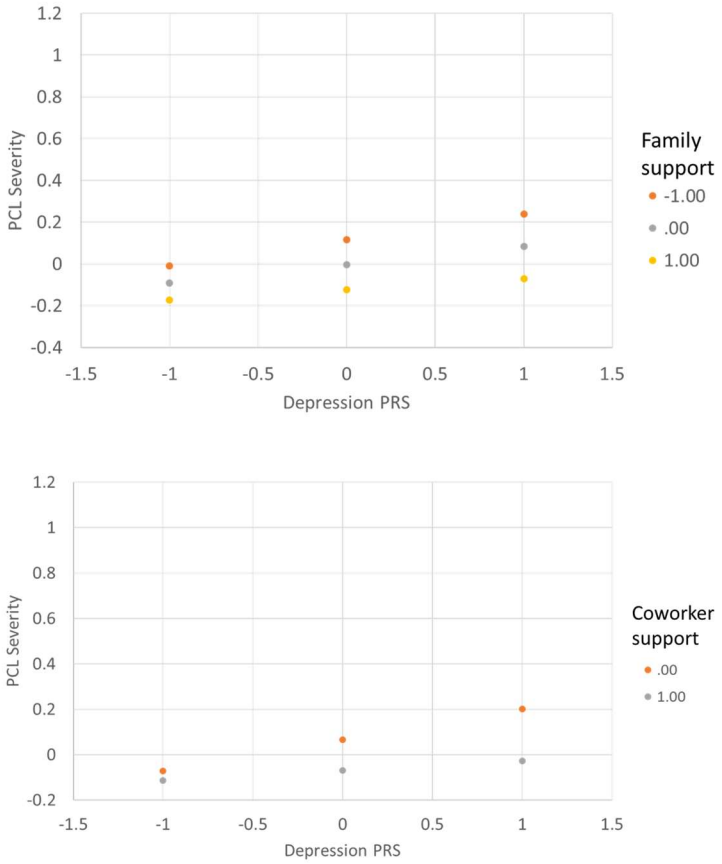


3. Social Support Moderates Polygenic Prediction of PTSD

Various protective factors have been identified for PTSD which might influence disease outcomes. Social support is one such potential protective factor, with previous data indicating that family and well as co-worker support has an inverse relationship with PTSD risk and severity. Although interactions between genetics and environmental factors have been demonstrated in twin studies of PTSD, no studies have explored the interaction between molecular genetic risk scores and social support in PTSD. To address this important gap in the literature, analyses focused on the perceived social support that was assessed during the clinician-administered interview at the first monitoring visit. Participants were asked to report important sources of support (family and work) available to them “while working on the WTC effort”. Familial support included parents, spouse/partner, and children, whereas work support included colleagues and supervisors. As demonstrated in Figure 4, we found that co-worker support significantly moderated the association between Depression PRS and PTSD severity in 9/11 responders (β=-.09, p=.03). Specifically, responders who reported having one or more social support sources at work showed a significantly weaker association between Depression PRS and PTSD severity than responders who did not have any social support at work. A similar pattern was observed for family support, however, the interaction did not reach statistical

significance (*β*=-.05, *p*=.08). All analyses were pre-registered and adjusted for 10 PCs, sex, age, and 9/11 exposure severity.

Figure 4 – Family and co-worker social support buffer the association between depression PRS and PTSD symptoms



4. Immunoassay Signature of PTSD

Proteomics provides an opportunity to develop biomarkers for early detection and monitoring of posttraumatic stress disorder (PTSD). However, research to date has been limited by small sample sizes and a lack of replication. We conducted the largest discovery and replication study of blood-based proteomics in PTSD to date. By analyzing dimensional PTSD symptom severity in over 900 responders to the 9/11 disaster, we replicated findings for seven proteins reported previously in an independent study, identified and replicated two new protein markers associated with PTSD symptom severity, and two associated with PTSD diagnosis. Overall, we report a total of 11 unique replicated proteins associated with PTSD, and their functional roles are summarized in Table 1. These findings suggest that PTSD is characterized by altered expression of several proteins implicated in neurological processes. Replicated associations with TNFRSF21, CLM6, and PVR support the neuroinflammatory signature of PTSD.

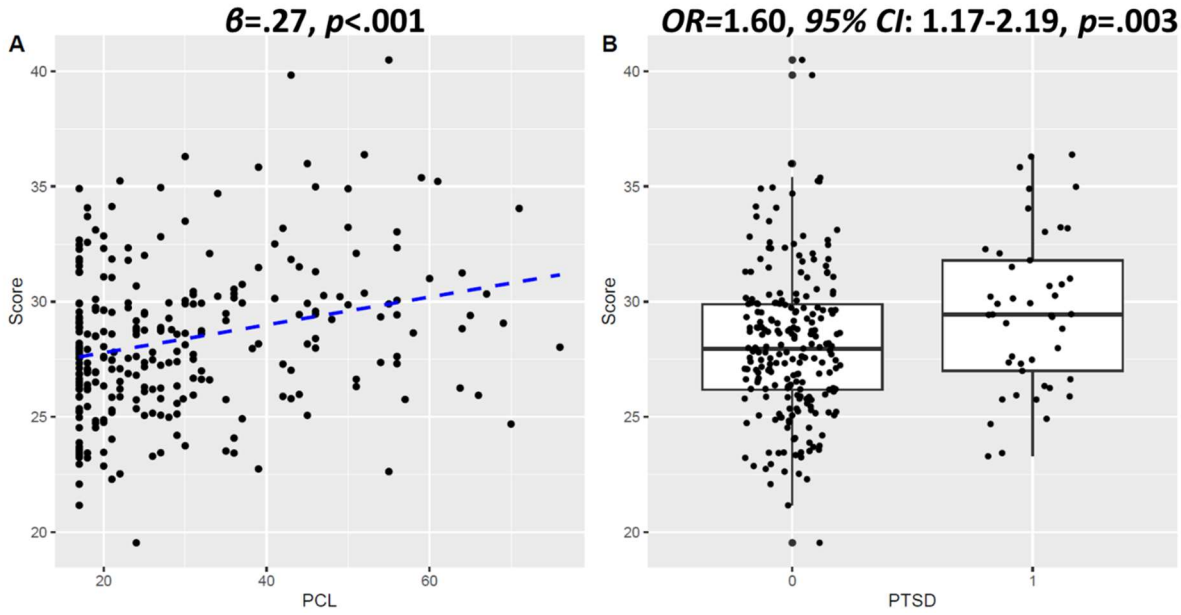
To further investigate the clinical utility of our proteomic findings, we constructed a PTSD composite multiprotein score by aggregating 38 proteins selected in the discovery sample by using machine learning. Our analyses demonstrated that the multiprotein composite score significantly predicted PTSD symptom severity, as well as diagnostic status, in a hold-out sample (Figure 5). Overall, the current immunoassay findings make an important contribution to

the understanding of the pattern of differential protein expression characterizing PTSD. If generalizable to other populations, they may aid in the development of biomarkers for detecting and monitoring PTSD. This opportunity and future research directions for both polygenic risk scores and immunoassay signatures of PTSD were discussed in our recent review.

Table 1 – Functional pathways of 11 replicated immunoassay proteins associated with PTSD

Replicated immunoassay protein	**PTSD definition**	**Functional pathways**
SKR3	Symptom severity and diagnosis	Cell adhesion, cell differentiation, cell growth, cellular metabolic process, signal transduction
NCAN	Symptom severity	Cell adhesion, Cellular metabolic process
BCAN	Symptom severity	Cell adhesion, Cellular metabolic process
MSR1	Symptom severity	Cell differentiation
PVR	Symptom severity	Cell adhesion, immune response
TNFRSF21	Symptom severity	Cell adhesion, cell death, cell differentiation, immune response, neurogenesis, signal transduction
DRAXIN	Symptom severity	Axon development, axon guidance, cell death, cell differentiation, cell growth, neurogenesis, signal transduction
CLM6	Symptom severity	Immune response
SCARB2	Symptom severity	Membrane transportation
CPM	Diagnosis	Cellular metabolic process, Proteolysis
SIGLEC1	Diagnosis	Cell adhesion

Figure 5 - The associations between the multiprotein score and (A) PTSD symptoms, and (B) PTSD diagnosis, in the hold-out subsample.



5. Polygenic Prediction of Comorbid Conditions

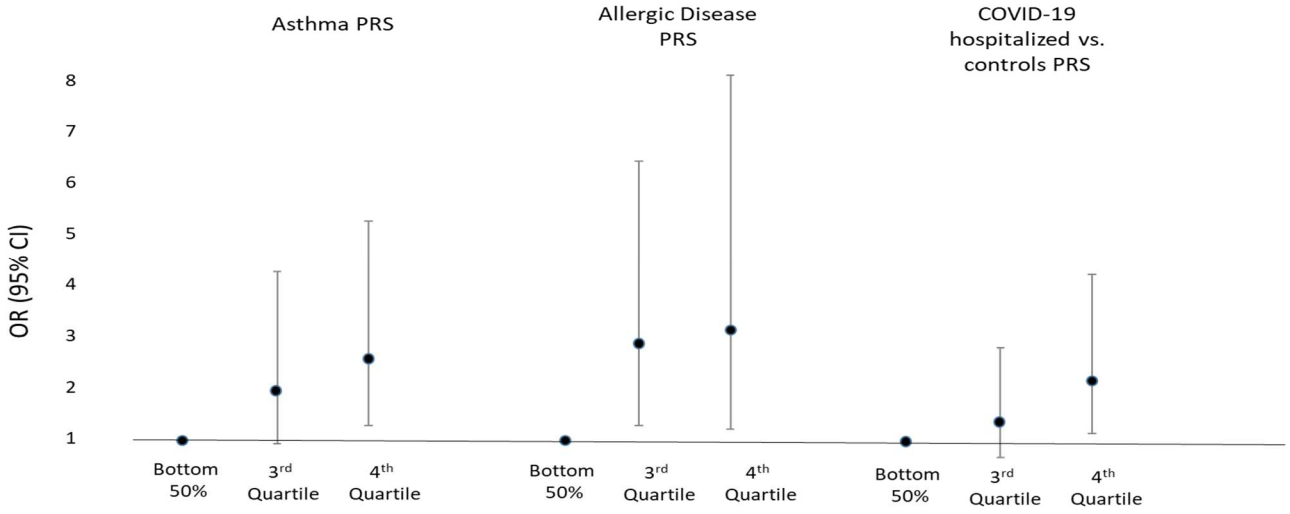
The genetic dataset resource that this project has created has supported three new research projects that use it to further understand the role of genetics in long-term health outcomes of 9/11 responders:

1. *Severity and long-term health effects of COVID-19 among World Trade Center responders* (MPI: Morozova, Luft). CDC/NIOSH. 07/01/2021-06/30/2026. U01OH012275
2. *Trauma Exposure and Cognitive Impairment: Understanding Polygenic Liability and the Causative and Moderating Effects of Exposure, PTSD, and Psychiatric Comorbidity in WTC Responders* (PI: Mann). National Institute of Ageing. 07/01/2021-06/30/2023. R21AG074705
3. *Investigating the association of posttraumatic stress disorder (PTSD) with chronic kidney disease (CKD) in World Trade Center (WTC) responders* (PI: Koraishy). CDC/NIODH. 07/01/2021-06/30/2023. R21OH012237

While these studies are ongoing, we want to highlight recent findings for COVID-19 outcomes in 9/11 responders infected for the first time with SARS-CoV-2. Large-scale, population-based genome-wide association studies demonstrate that genetic factors affect individual differences in COVID-19 disease severity. Genetic variants associated with COVID-19 severity can be aggregated into PRS to capture an individual's overall genetic vulnerability to COVID-19 severity. Likewise, genetic variants associated with physical conditions related to COVID-19 severity: asthma, allergic disease, coronary artery disease, and type II diabetes, can be aggregated into PRS.

We found that the PRS for asthma, allergic diseases, and COVID-19 severity were elevated in infected responders with severe COVID-19, which included hospital admission, supplemental oxygen use, ICU admission, and death. Asthma PRS was also associated with COVID-19 symptomatology across the full spectrum of severity. No significant associations were observed for PRS for coronary artery disease and type II diabetes. Moreover, PRS did not predict post-acute COVID-19 sequelae. These findings add to the growing body of evidence to suggest that existing polygenetic profiles could be informative about the risk for severe COVID-19 presentation, despite the small effect sizes.

Figure 6 – Asthma, Allergic Disease, and COVID-19 Hospitalization Polygenic Risk Score Prediction of COVID-19 Severe Outcome



Notes:

PRS prediction of COVID-19 severe status is illustrated as odds ratios per PRS quartile, relative to the first quartile. For example, responders in the highest 4th quartile of genetic risk for asthma had over twice the odds of having the most severe COVID-19 presentation than infected responders in the lowest 1st quartile of genetic risk.

Dissemination of Findings

The aforementioned findings were reported in the following papers and presentations.

Peer-reviewed publications

Waszczuk, M. A., Docherty, A. R., Shabalin, A. R., Miao, J., Yang, X., Kuan, P.-F., Bromet, E., Kotov, R.*, & Luft, B. J.* (2022). Polygenic prediction of PTSD trajectories in 9/11 responders. *Psychological medicine, 52*(10), 1981-1989.

Waszczuk, M. A. (2022). Insights From Dimensional Phenotypic Definitions of Posttraumatic Stress Disorder and Trauma in Genome-wide Association Studies. *Biological Psychiatry*, 91 (7), 609-611

Waszczuk, M. A., Kuan, P. F., Yang, X., Miao, J., Kotov, R., & Luft, B. J. (2023). Discovery and replication of blood-based proteomic signature of PTSD in 9/11 responders. *Translational Psychiatry*, 13(1), 8.

Waszczuk, M. A., Morozova, O., Lhuillier, E., Docherty, A. R., Shabalin, A. A., Yang, X., ... & Luft, B. J. (2023). Polygenic risk scores for asthma and allergic disease associate with COVID-19 severity in 9/11 responders. *Plos one, 18*(3), e0282271.

Koraishy, F. M., Mann, F. D., Waszczuk, M. A., Kuan, P. F., Jonas, K., Yang, X., ... Kotov, R., & Luft, B. (2022). Polygenic association of glomerular filtration rate decline in world trade center responders. *BMC nephrology*, 23(1), 1-10.

Mann, F. D., Clouston, S. A., Cuevas, A., Waszczuk, M. A., Kuan, P. F., Carr, M. A., ... & Luft, B. J. (2023). Genetic Liability, Exposure Severity, and Post-Traumatic Stress Disorder Predict Cognitive Impairment in World Trade Center Responders. Journal of Alzheimer's Disease, (Preprint), 1-12.

Abi-Dargham, A., Moeller, S. J., Ali, F., DeLorenzo, C., Domschke, K., Horga, G., Jutla, A., Kotov, R., Paulus, M. P., Rubio, J. M., Sanacora, G., Veenstra-VanderWeele, J., & Krystal, J. H. (2023). Candidate biomarkers in psychiatric disorders: state of the field. *World Psychiatry, 22*, 236-262.

Conference Presentations

Polygenic prediction of PTSD trajectories in 9/11 responders. Waszczuk, M. A., Kuan, P-F., Docherty, A., Shabalin, A., Bromet, E., Luft, B. & Kotov, R. Poster presentation at the World Congress of Psychiatric Genetics, October 2019. Los Angeles, California, USA.

Blood-Based Proteomic Signature of Posttraumatic Stress Disorder in 9/11 Responders. Waszczuk, M. A., Kuan, P. F., Yang, X., Miao, J., Kotov, R., Luft, B. J. Oral presentation at the Biomedical Innovation Day, September 2022. North Chicago, Illinois, USA.

C. OVERALL PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

Yes

Publications Reported for this Reporting Period

Public Access Compliance	Citation
N/A: Not NIH Funded	Waszczuk MA, Docherty AR, Shabalin AA, Miao J, Yang X, Kuan PF, Bromet E, Kotov R, Luft BJ. Polygenic prediction of PTSD trajectories in 9/11 responders. Psychological medicine. 2020 October 23:1-9. PubMed PMID: 33092657; PubMed Central PMCID: PMC8186149; DOI: 10.1017/S0033291720003839.
N/A: Not NIH Funded	Waszczuk MA. Insights From Dimensional Phenotypic Definitions of Posttraumatic Stress Disorder and Trauma in Genome-wide Association Studies. Biological psychiatry. 2022 April 1;91(7):609-611. PubMed PMID: 35272767; DOI: 10.1016/j.biopsych.2021.12.012.
N/A: Not NIH Funded	Koraishy FM, Mann FD, Waszczuk MA, Kuan PF, Jonas K, Yang X, Docherty A, Shabalin A, Clouston S, Kotov R, Luft B. Polygenic association of glomerular filtration rate decline in world trade center responders. BMC nephrology. 2022 October 28;23(1):347. PubMed PMID: 36307804; PubMed Central PMCID: PMC9615399; DOI: 10.1186/s12882-022-02967-5.
N/A: Not NIH Funded	Mann FD, Clouston SAP, Cuevas A, Waszczuk MA, Kuan PF, Carr MA, Docherty AR, Shabalin AA, Gandy SE, Luft BJ. Genetic Liability, Exposure Severity, and Post-Traumatic Stress Disorder Predict Cognitive Impairment in World Trade Center Responders. Journal of Alzheimer's disease : JAD. 2023;92(2):701-712. PubMed PMID: 36776056; PubMed Central PMCID: PMC10648279; DOI: 10.3233/JAD-220892.
N/A: Not NIH Funded	Waszczuk MA, Morozova O, Lhuillier E, Docherty AR, Shabalin AA, Yang X, Carr MA, Clouston SAP, Kotov R, Luft BJ. Polygenic risk scores for asthma and allergic disease associate with COVID-19 severity in 9/11 responders. PloS one. 2023;18(3):e0282271. PubMed PMID: 36893177; PubMed Central PMCID: PMC9997960; DOI: 10.1371/journal.pone.0282271.
N/A: Not NIH Funded	Waszczuk MA, Kuan PF, Yang X, Miao J, Kotov R, Luft BJ. Discovery and replication of blood-based proteomic signature of PTSD in 9/11 responders. Translational psychiatry. 2023 January 11;13(1):8. PubMed PMID: 36631443; PubMed Central PMCID: PMC9834302; DOI: 10.1038/s41398-022-02302-4.
N/A: Not NIH Funded	Abi-Dargham A, Moeller SJ, Ali F, DeLorenzo C, Domschke K, Horga G, Jutla A, Kotov R, Paulus MP, Rubio JM, Sanacora G, Veenstra-VanderWeele J, Krystal JH. Candidate biomarkers in psychiatric disorders: state of the field. World psychiatry : official journal of the World Psychiatric Association (WPA). 2023 June;22(2):236-262. PubMed PMID: 37159365; PubMed Central PMCID: PMC10168176; DOI: 10.1002/wps.21078.

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

NOTHING TO REPORT

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization? No

C.5 OTHER PRODUCTS AND RESOURCE SHARING

NOTHING TO REPORT

D. OVERALL PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
BJLUFT	N	LUFT, BENJAMIN J	MD,BA	Co-Investigator	1.2	0.0	0.0			NA
EBROMET	N	BROMET, EVELYN J	PHD,BA,MOTH	Co-Investigator	1.2	0.0	0.0			NA
PFKUAN	N	Kuan, Pei-Fen	PHD	Co-Investigator	0.0	2.3	0.0			NA
WASZCZUKM	Y	Waszczuk, Monika Aldona	PHD	Co-Investigator	10.8	0.0	0.0			NA
RKOTOV	Y	Kotov, Roman I	PHD	PD/PI	1.8	0.0	0.0			NA
	N	Yang, Xiaohua	PhD	Technician	4.2	0.0	0.0			NA

Glossary of acronyms:
S/K - Senior/Key
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RS - Reentry Supplement
DS - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Not Applicable

D.2.b New Senior/Key Personnel

Not Applicable

D.2.c Changes in Other Support

Not Applicable

D.2.d New Other Significant Contributors

Not Applicable

D.2.e Multi-PI (MPI) Leadership Plan

Not Applicable

E. OVERALL IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

G. OVERALL SPECIAL REPORTING REQUIREMENTS SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

NOTHING TO REPORT

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

Not Applicable

G.4.b Inclusion Enrollment Data

File(s) uploaded:
CumulativeInclusionEnrollmentReport.pdf

G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

NOT APPLICABLE

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT No foreign component
G.10 ESTIMATED UNOBLIGATED BALANCE Not Applicable
G.11 PROGRAM INCOME Not Applicable
G.12 F&A COSTS Not Applicable

Cumulative Inclusion Enrollment Report

This report format should NOT be used for collecting data from study participants.

Study Title: POLYGENIC PREDICTION OF PTSD TRAJECTORIES AND INFLAMMATION IN 9/11 RESPONDERS

Comments:

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/ Alaska Native	0	0		0	0		0	0		**0**
Asian	6	58		1	5		1	5		**76**
Native Hawaiian or Other Pacific Islander	0	0		0	0		0	0		**0**
Black or African American	94	192		1	24		8	26		**345**
White	398	4,965		18	173		52	561		**6,167**
More Than One Race	10	20		46	280		2	12		**370**
Unknown or Not Reported	3	11		7	45		113	1,465		**1,644**
Total	**511**	**5,246**	**0**	**73**	**527**	**0**	**176**	**2,069**	**0**	**8,602**

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OMB No. 0925-0001/0002
Cumulative Inclusion Enrollment Report

I. OVERALL OUTCOMES

I.1 What were the outcomes of the award?

The most important outcomes of this project are two major findings. First, we determined that polygenic risk scores for mental disorders predict PTSD trajectories in responders to WTC disaster. Polygenic biomarkers can help to identify people at elevated risk of PTSD and also of more protracted course of this disorder. Second, we identified a protein signature of PTSD in whole blood of responders. This signature may help to detect PTSD and track its worsening and improvement over time (e.g., in response to treatment). Of note, these biomarkers are only modestly related to PTSD, and they are not ready for clinical use at this time. However, further research is expected to improve accuracy of both polygenic and proteomic signatures, and they can become useful clinically.