

A. OVERALL COVER PAGE

Project Title: RDoC Domains Underlying Emotional Health and Trajectories of Psychopathology in Families of WTC First Responders and Evacuees: A Genome-Wide GxE Study	
Grant Number: 5U01OH011327-05	Project/Grant Period: 09/01/2016 - 08/31/2021
Reporting Period: 09/01/2020 - 08/31/2021	Requested Budget Period: 09/01/2020 - 08/31/2021
Report Term Frequency: Final	Date Submitted: 12/05/2022
Program Director/Principal Investigator Information: CHRISTINA W HOVEN , DRPH MPH MS MOTH Phone Number: 646 774 5800 Email: ch42@columbia.edu	Recipient Organization: NEW YORK STATE PSYCHIATRIC INSTITUTE dba RESEARCH FOUNDATION FOR MENTAL HYGIENE, INC 1051 Riverside Drive NEW YORK, NY 100321007 DUNS: 167204994 UEI: TYVNMW8FNQQ3 EIN: 1141410842A2 RECIPIENT ID:
Change of Contact PD/PI: NA	
Administrative Official: JANELLE GREENHILL 1051 RIVERSIDE DRIVE UNIT #33 NEW YORK, NY 10032 Phone number: 646-774-6500 Email: nga@nyspi.columbia.edu	Signing Official: JANELLE GREENHILL 1051 RIVERSIDE DRIVE UNIT #33 NEW YORK, NY 10032 Phone number: 646-774-6500 Email: nga@nyspi.columbia.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?

The World Trade Center Health Registry (WTCHR) – the largest pool of people from which to learn vital lessons of the sequelae of 9/11 – has identified many consequences of WTC-exposure on psychiatric outcomes, especially post-traumatic stress disorder (PTSD). Efforts to minimize dropout and to ensure continued follow-up of exposed adults/children are crucial to examining distal ramifications of WTC-exposure, trajectories of PTSD/other negative outcomes, and the onset of psychopathology with long latency. Despite many important contributions, significant gaps remain in WTCHR studies. In-person, direct assessments, such as those carried out in this study, are critical to obtaining in-depth information and for maintaining the integrity of this longitudinal cohort.

- PROSPECTIVE STUDY OF FAMILIES: DIRECT/INDIRECT WTC-EXPOSURE OF PARENTS/CHILDREN. To date, the strong evidence for untoward consequences from 9/11 exposure, primarily in adults, has not been systematically assessed. The role of familial/parental factors in modulating youth's reactions to terrorism, supported by the literature and by our findings, led the Global Psychiatric Epidemiology Group (GPEG) to obtain a NICHD-funded grant (R01HD046786: PI: Hoven) to understand the impact over time of parental WTC-exposure on their children's psychopathology (Wave 1-2 WTC Family Study) of 855 families (parents + one child) of First Responders, WTC and Residential evacuees (plus non-WTCHR unexposed Control families) recruited between 2007-2012 from the WTCHR. This is a representative sample of WTC-exposed families in the NYC Metropolitan Area, and is the only study that is following WTC-exposed families over time. Capitalizing on the strengths of that innovative family design and its findings, and on other GPEG's epidemiological, behavioral, and genetic findings, this NIOSH study is following up for a 3rd wave of data collection (Wave 3 WTC Family Study), the same families (N=700 youth) and (1200 parents) who participated in the Wave 1-2 WTC Family Study:

OVERALL OBJECTIVE: to understand post-9/11 long-term psychiatric and emotional health outcomes through an examination of associated Research Domain Criteria (RDoC) dimensions and underlying interactions among genome-wide genetic variation and direct/indirect WTC exposure/s.

- RELATIONSHIP BETWEEN WTC-EXPOSURE AND A BROAD SPECTRUM OF PSYCHIATRIC DISORDERS AND INDICATORS OF EMOTIONAL HEALTH: Most WTCHR psychiatric analyses have focused on adult PTSD. There is a need to investigate the links between WTC-exposures and other psychiatric disorders: the Wave 3 WTC Family Study is the only study – among WTCHR enrollees and their families – that has an immediate potential to examine the long-term effects of WTC-exposure on a broad array of psychiatric disorders, and associated outcomes related to emotional health (as indicators of psychological resilience and quality of life):

AIM 1. To Calculate Trajectories of Psychopathology Across Three Waves, Identify their Associated WTC-Exposure/s, and Examine the Relationship Among WTC-Exposure/s, Trajectories of Psychopathology and Emotional Health.

- BEYOND DSM NOSOLOGY: RDOC DIMENSIONS: The underlying validity of DSM disease entities has been questioned, noting that DSM categories do not map well onto emerging findings from genetics, systems neuroscience and behavioral science. As a result, it becomes very difficult to harness the power of new technologies to identify specific etiological process resulting from gene-environment (G×E) interactions, and to translate research findings to individualized treatments or personalized medicine. Fortunately, in an effort to develop an integrative, multi-system precision medicine approach to mental disorders, the NIMH initiated RDoC, a new research classification system based on key dimensional constructs underlying mental function. For the first time, the Wave 3 WTC Family Study will examine DSM disorders, and the effects of direct/indirect WTC-exposure, taking RDoC dimensions of functioning into account: (i) negative valence, (ii) positive valence, (iii) cognitive systems, and (iv) social cognition. This integrative, multi-system examination has the potential to advance translational research in WTC-exposed populations, so that individualized treatments directed at etiologic mechanisms might soon be available to trauma-exposed people:

AIM 2. To Examine how Psychopathology at Wave 3 Maps onto Four Key RDoC Domains of Functioning, and Test Whether RDoC Domains Modulate the Relationship Among Type/Severity of WTC-Exposure/s and Psychopathology.

- HIGH-THROUGHPUT APPROACH TO (G×E) INTERACTIONS: High-throughput technologies have led to a more comprehensive view of G×E interactions underlying observable behaviors. Few studies have examined G×E interactions underlying RDoC domains, and those that exist are almost all on candidate gene studies. G×E interactions in WTCHR enrollees have not been examined. The Wave 3 WTC Family Study would be the first study examining – with genome-wide coverage – G×E interactions underlying RDoC domains and psychiatric outcomes in WTCHR enrollees and their families:

AIM 3. To Identify SNPs, Polygenic Risk, and G×E Interactions Underlying the 4 RDoC Domains and Psychopathology.

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 : Hoven_5U01OH011327_FRw3_final report_2022_FIN.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

**RDoC Domains Underlying Emotional Health and Trajectories of
Psychopathology in Families of WTC First Responders and Evacuees:
A Genome-Wide GxE Study**

TABLE OF CONTENTS

Abstract	3
Significant (Key) Findings.....	4
Translation of Findings	4
Outcomes/Impact	5
Scientific Report	6
1. Background	6
1.1. Prospective Study of Families: Direct/Indirect WTC-Exposure in Parents and Children	6
1.2. Relationship Between WTC-Exposure and a Broad Spectrum of Psychiatric Disorders and Indicators of Emotional Health	6
1.3. Beyond DSM Nosology: RDoC Dimensions	6
1.4. High-Throughput Approach to (G×E) Interactions	7
2. Specific aims.....	7
3. Methodology	7
3.1. Samples	7
3.2. Recruitment	8
3.3. Measures	8
4. Results.....	12
4.1. 9/11 Exposure and Psychiatric Disorders	12
4.2. 9/11 Exposure, Psychiatric Disorders and Emotional Health	14
4.3. RDoC Domains of Functioning, Type/Severity of WTC-exposure/s and Psychopathology	15
4.4. COVID-19 Pandemic	16
5. Discussion	17
5.1. 9/11 Exposure and Psychiatric Disorders	17
5.2. 9/11 Exposure, Psychiatric Disorders and Emotional Health	19
5.3. RDoC Domains of Functioning, Type/Severity of WTC-exposure/s and Psychopathology	19
6. Conclusion	20
Publications	22
References.....	25

**RDoC Domains Underlying Emotional Health and Trajectories of
Psychopathology in Families of WTC First Responders and Evacuees:
A Genome-Wide G×E Study**

PI: Christina W. Hoven, DrPH, MPH

MPI: Franco Lupo Geronazo-Alman, PhD

646-774-6068

Christina.Hoven@nyspi.columbia.edu

Abstract

The role of familial/parental factors in modulating youths' reactions to terrorism is supported by the scientific literature, including our findings from youth assessed six months after the World Trade Center (WTC) attacks of 9/11 (N = 8,236). Those findings led to a NICHD-funded grant (*Wave 1-2 WTC Family Study*) to understand the impact, over time, of parental direct WTC-exposure on their children's psychopathology. For that study, N = 855 families (parents + one child) of WTC First Responders, WTC Evacuees and local Residents were recruited from the WTC Health Registry (WTCHR), as well as 9/11 unexposed Control families.

Since initiation of the *Wave 1-2 WTC Family Study*, NIMH developed the Research Domain Criteria (RDoC) project, a new way to classify mental disorders based on validated behavioral functions. RDoC domains have quickly illuminated the conceptualization of psychopathology by providing a more comprehensive framework of functions/deficits across a spectrum of disorders and the health-illness dimension. Additionally, the explosion of high-throughput technologies has led to a more comprehensive view of the genetic architecture of observable behaviors and of gene-environment interactions (G×E), which may be critical in the development of individualized treatment plans for 9/11 exposed individuals.

To date, there has been no other 9/11 investigation that encompasses families of First Responder, WTC and Residential Evacuee families, the most adversely impacted WTC population. Based on findings from the *Wave 1-2 WTC Family Study*, as well as other epidemiological, behavioral and genetic findings by GPEG regarding these individuals, we assessed these same families for a 3rd wave, to examine how four key **RDoC domains of functioning** (*negative valence; positive valence; cognitive systems; social cognition*) are associated upward with (i) **long-term psychiatric outcomes** (DSM disorders), (ii) **emotional health** (psychological resilience), and (iii) **trajectories of psychopathology**, and downward, with interactions between genetic variation and direct/indirect WTC exposures.

Significant (Key) Findings

Exposure to 9/11 and psychiatric disorders. Mothers directly exposed to 9/11 had higher odds of lifetime substance use disorder (SUD) and past year internalizing psychopathology. Fathers who were directly exposed to 9/11 tended to have higher odds of lifetime Alcohol Use Disorders (AUD).

When analyses were stratified by exposure groups (1-9/11 Evacuee; 2: 9/11 First Responder; 3: 9/11 Residential Evac & Minimally Exposed FR; 4: Non-exposed), mothers who were 9/11 evacuees had higher rates of past year internalizing psychopathology compared to mothers who were minimally exposed or not exposed (Control) on 9/11. Mothers in the 9/11 evacuee and residential evacuee/minimally exposed groups tended to have higher rates of past year agoraphobia compared to mothers in the First Responder and non-exposed groups. 9/11-related PTSD tended instead to be higher among mothers in the First Responders group, compared to the other groups. Compared to fathers who were not exposed to 9/11, lifetime AUD was higher in all exposed groups. PTSD related to 9/11 was highest among evacuees, followed by the First Responders. Children of 9/11 evacuees tended to have higher rates of PTSD compared to other exposure groups.

Exposure to 9/11, psychiatric disorders and emotional health. Among mothers, fathers and youth, internalizing and externalizing psychopathology were associated with decreased general life satisfaction. Among mothers, externalizing psychopathology was associated with decreased general life satisfaction. Among youth, internalizing psychopathology was associated with decreased self-efficacy. Mothers directly exposed to 9/11 and youth indirectly exposed to 9/11 had increased self-efficacy; youth indirectly exposed to 9/11 also had increased general life satisfaction. Youth indirectly exposed to 9/11 had decreased emotional support. Among non-exposed youth, internalizing psychopathology was associated with decreased emotional support and friendship. Externalizing psychopathology was associated with increased self-efficacy among non-exposed youth; among indirectly exposed youth, externalizing psychopathology was instead associated with decreased self-efficacy.

Exposure to 9/11, psychiatric disorders and RDoC dimensions. Mothers, fathers and youth with higher impulsivity and higher trait anxiety showed increased odds of lifetime and past 12 month internalizing psychopathology. Mothers, fathers, and youth with higher negative valence had higher rates of lifetime externalizing psychopathology. Among fathers and youths, lifetime externalizing psychopathology was also associated with higher impulsivity. There was no evidence for modification of 9/11 exposure and psychopathology associations by measures of RDoC domains.

Translation of Findings

The results show that more than 15 years after 9/11, adults who were directly exposed to the attacks still show higher rates of both internalizing and externalizing psychiatric disorders. Interventions to prevent negative outcomes in women exposed to terrorism should focus on the prevention of substance use disorder and internalizing psychopathology, in particular generalized anxiety disorder and agoraphobia. Interventions to prevent negative outcomes in men exposed to terrorism should instead

focus on the prevention of alcohol use disorder and PTSD. Parental exposure to 9/11 does not seem to have significant long-term negative effects on indirectly exposed youth.

In general, in parents and youth, psychiatric disorders were associated with different negative outcomes related to decreased emotional health (as indicators of psychological resilience and quality of life). Additional analyses will determine whether these markers of decreased emotional health are causal risk factors of psychiatric outcomes or consequences of psychiatric outcomes. Answering this causal inferential question has direct relevance for translational research, since intervening on a non-causal factor cannot change the likelihood of an outcome. In indirectly exposed youth, despite evidence of decreased emotional support, increased self-efficacy and general life satisfaction might act as protective factors and, in part, explain the lack of association between parental exposure to 9/11 and psychopathology.

In an effort to develop an integrative, multi-system precision medicine approach to mental disorders the NIMH initiated RDoC, a new research classification system based on key dimensional constructs underlying mental function. In parents and youth, higher trait anxiety and higher negative valence might be specific markers of internalizing and externalizing psychopathology, respectively. In fathers and youth, higher impulsivity may be a transdiagnostic etiologic mechanism underlying both internalizing and externalizing psychopathology. As mentioned above, additional analyses will determine whether higher trait anxiety, negative valence, and impulsivity are mechanisms of psychiatric disorders, and therefore potential targets for interventions, or are instead correlates of psychopathology with no causal role.

Outcomes/Impact

While psychiatric disorders (DSM) are known to be linked to traumatic exposure/s, families play a key role in modulating youth's reaction to terrorism and who may experience greater emotional impact from having a family member exposed than from being directly exposed themselves. Because DSM disorders do not map well onto emerging findings from genetics, systems neuroscience and behavioral science the NIMH initiated the Research Domain Criteria-(RDoC) project, as a new classification system with gene x environment (G×E) interactions with a major role in understanding etiological processes. The RDoC factors have never before been simultaneously taken into account with 9/11-related populations, which has the potential to move forward the field of translational research in WTC-exposed populations, especially within families, so that individualized treatments directed at etiologic mechanisms might soon be available to 9/11 and other trauma-exposed individuals.

Unfortunately, the COVID-19 Pandemic drastically impacted our ability to conduct the required in-home assessments. Eventually, a limited phone-based assessment was initiated resulting in a total lack of physical assessment. Consequently, the important contribution of this investigation was seriously and negatively impacted. It is hoped that future funding will provide for the continuation of this work which has already demonstrated its importance to understanding 9/11 exposure.

Scientific Report

1. Background

The World Trade Center (WTC) Health Registry (WTCHR) – the largest pool of people from which to learn vital lessons of the sequelae of 9/11 – has identified many consequences of WTC-exposure on psychiatric outcomes, especially post-traumatic stress disorder (PTSD).¹⁻¹⁷ Efforts to minimize dropout and to ensure continued follow-up of exposed adults/children are crucial to examining distal ramifications of WTC-exposure, trajectories of PTSD/other negative outcomes, and the onset of psychopathology with long latency.¹⁸ Despite many important contributions, significant gaps remain in WTCHR studies.

1.1. Prospective Study of Families: Direct/Indirect WTC-Exposure in Parents and Children

To date, the strong evidence for untoward consequences from 9/11 exposure, primarily in adults, has not been systematically assessed in families and youth. The role of familial/parental factors in modulating youth's reactions to terrorism, supported by the literature and by our findings, led the Global Psychiatric Epidemiology Group (GPEG) to obtain a NICHD-funded grant (5R01HD046786: PI: Hoven) to understand the impact over time of parental WTC-exposure on their children's psychopathology (*Wave 1-2 WTC Family Study*).¹⁹ 855 families (parents + one child) of First Responders, WTC and Residential evacuees (plus non-WTCHR unexposed Control families) were recruited between 2007-2012 from the WTCHR. This is the only representative sample of WTC-exposed families in the NYC Metropolitan Area,¹⁹ and is the only study that is following WTC-exposed families over time. Capitalizing on the strengths of that innovative family design and its findings, and on other GPEG's epidemiological, behavioral, and genetic findings, the current NOISH study conducted the 3rd wave of data collection (*Wave 3 WTC Family Study*) with the same families who participated in the *Wave 1-2 WTC Family Study*.

1.2. Relationship Between WTC-Exposure and a Broad Spectrum of Psychiatric Disorders and Indicators of Emotional Health

Most WTCHR psychiatric analyses have focused on adult PTSD.¹⁻¹⁷ There is a need to investigate the links between WTC-exposures and other psychiatric disorders: the *Wave 3 WTC Family Study* is the only study – among WTCHR enrollees and their families – that allows the examination of the long-term effects of WTC-exposure on a broad array of psychiatric disorders (not only symptoms), and associated outcomes related to emotional health (as indicators of psychological resilience and quality of life).

1.3. Beyond DSM Nosology: RDoC Dimensions

The underlying validity of DSM disease entities has been questioned, noting that DSM categories do not map well onto emerging findings from genetics, systems neuroscience and behavioral science.²⁰⁻²² Consequently, it is very difficult to harness the power of new technologies to identify specific etiological process resulting from gene-environment (G×E) interactions, and to translate such research findings to individualized treatments or personalized medicine. Fortunately, in an effort to develop an integrative, multi-system precision medicine approach to mental disorders,^{22, 23} the NIMH initiated

RDoC, a new research classification system based on key dimensional constructs underlying mental function.²²⁻²⁴

For the first time, the *Wave 3 WTC Family Study* examined DSM disorders, and the effects of direct/indirect WTC-exposure, taking RDoC dimensions of functioning into account: (i) **negative valence**, (ii) **positive valence**, (iii) **cognitive systems**, and (iv) **social cognition**. This integrative, multi-system examination can advance translational research in WTC-exposed populations, so that individualized treatments directed at etiologic mechanisms might soon be available to trauma-exposed people.

1.4. High-Throughput Approach to (G×E) Interactions

High-throughput technologies have led to a more comprehensive view of G×E interactions underlying observable behaviors. Few studies have examined G×E interactions underlying RDoC domains, and these are all candidate gene studies.²⁵⁻²⁸ G×E interactions in WTCHR enrollees have not been examined. The ***Wave 3 WTC Family Study*** had proposed to examine – with genome-wide coverage – G×E interactions underlying RDoC domains and psychiatric outcomes in WTCHR enrollees and their families.

2. Specific aims

Overall aim: to understand post-9/11 long term psychiatric outcomes and emotional health through an examination of their associated Research Domain Criteria (RDoC) dimensions and underlying interactions among genome-wide genetic variation and direct/indirect WTC exposure/s.

Aim 1: to calculate trajectories of psychopathology across three waves, identify their associated WTC-exposure/s, and examine the relationship between WTC-exposure/s, trajectories of psychopathology and emotional health.

Aim 2: to examine how psychopathology at wave 3 maps onto four key RDoC domains of functioning, and test whether RDoC domains modulate the relationship between type/severity of WTC-exposure/s and psychopathology.

Aim 3: to identify SNPs, polygenic risk, and G×E interactions underlying the 4 RDoC domains and psychopathology.

3. Methodology

3.1. Samples

The *Wave 1-2 WTC Family Study* (R01MH070424 & R01HD046786; PI: Hoven), in collaboration with the WTCHR, recruited a representative sample, and subsequently assessed N = 855 families at Wave 1 and N = 715 at Wave 2 (conducted 12 months after the Wave 1 interview), with an overall 84% retention rate. At Wave 1, 70% of families had 2 parents interviewed, and 65% at Wave 2. Thus, we estimate that 68% of families at Wave 3 will include both parents. Of the N=700 families in Wave 3, 66% (N=642) of the

families have at least one parent with WTC exposure, and 34% (N=238) are non-exposed Control families.

WTC exposed families included a *directly* WTC-exposed parent as well as their spouse and a child, *indirectly* exposed by virtue of parental exposure or Take Home (indirect) Exposure. who was 9-16 years of age at Wave 1 and 10-20 at Wave 2. Exposed parents, as enrollees in the WTCHR, were selected as belonging to three groups: (a) First Responders (FRs): Firefighters (FFs), Police Officers (POs), and Emergency Medical Technicians (EMTs), (b) those who assisted in recovery and relief efforts on/after 9/11, and (c) Evacuees: those who evacuated from the WTC or WFC buildings, the immediate WTC area or their homes. Besides being a member of the WTCHR, families had to be living within 100 mile radius from Ground Zero at the time of interview and had agreed to the WTCHR to being contacted for possible participation in research.¹⁹ In **Control families**, neither parent was present at the WTC area during the attack, nor was registered with the WTCHR. Control children were matched to indirectly exposed children (Take Home Exposed) by geographic location and age. Wave 2 child participants are 51% females, and 68% non-Hispanic Whites. Youth participating in the Wave 3 WTC Family Study were 16-30 years of age at their Wave 3 interview.

3.2. Recruitment

All interviews were conducted in-person by trained interviewers at the participants' residence, or at another agreed upon location, such as a library or the GPEG offices. The Wave 3 WTC Family Study sample recruited families who reside within 100-miles from the WTC. All data was collected on laptop computers. With the consent of adult participants (≥ 18 years of age), and parent consent and child assent if < 18 , a saliva sample was collected at the time of the interview for DNA analysis. In addition to a flat rate reimbursement, participants received a variable sum of money depending on their choices/performance during the three decision paradigms.

3.3. Measures

3.3.1. WTC-Exposure and Psychiatric Disorders: Wave 1-2 WTC Family Study & Wave 3 WTC Family Study (parents/children).

The main exposure and psychiatric variables available from the Wave 1-2 WTC Family Study and measured as part of the **Wave 3 WTC Family Study** are summarized in **Table 1**.

Table 1. Wave 1-2 WTC Family Study and Wave 3 WTC Family Study measures

Informant	Wave 1 and 2	Wave 3
• Psychiatric outcomes		
Parents	PTSD : PTSD checklist, civilian version; ²⁹ major depressive disorder (MDD): Beck Depression Inventory-7 items; ³⁰ alcohol use disorders (AUD) and substance use disorders (SUD): WHO WMH-CIDI. ³¹⁻³³	PTSD, MDD, PD, AGO, AUD/ SUD: WHO WMH-CIDI
Children	PTSD, MDD, panic disorder (PD), agoraphobia (AGO), generalized anxiety disorder (GAD), separation anxiety disorder , AUD/SUD : NIMH DISC-IV; ³⁴ conduct disorder (CD), oppositional defiant disorder (ODD): DISC Predictive Scales (DPS). ^{35, 36}	

• WTC-exposure		
(1) Direct exposure and witnessing (in person) WTC-related events occurring to others.		
Parents	WTC-BOE Survey Questionnaire ^{19, 37, 38} (see note ^a), plus other questions about direct exposure/witnessing (see note ^b).	
Children	WTC-BOE Survey Questionnaire (see note ^a).	
(2) Learning that WTC-related events occurred to a close family member/friend		
Parents	Family member/s and/or friend/s (see note ^c): (a) was/were in the WTC on 9/11 but escaped unhurt, (b) hurt in the attack, and (c) killed in the attack.	
(3) Experiencing repeated or extreme exposure to aversive details of WTC attacks		
Parents	(a) Worked in rescue/relief services at the WTC within 6 months after 9/11; (b) days spent: at Ground Zero, working on the pile, working on the dump in Staten Island, in other activities 9/11-related recovery effort.	
• Exposure to other work-related traumatic events		
Parents	Critical Incident History Questionnaire (CIHQ). ^{39, 40}	CIHQ ^d
• Exposure to life events		
Parents	Life Events Checklist (LEC): ⁴¹ 16 items about potentially traumatic events known to result in PTSD/other posttraumatic difficulties.	LEC (16 items) ⁴¹ (since the time of the last interview)
Children	Modified 26-item LEC: ^{42, 43} youth were asked to report whether each item had happened to them in the previous year and, if so, to categorize the event as "mostly good" or "mostly bad".	
• Other WTC-related factors		
Parents	(a) Grief reactions to a WTC-related loss of a family member/friend/co-worker (5-items on a 3-point scale); (b) peri-traumatic reactions during the attack (8-items on a 5-point scale); (c) WTC-related life disruptions (e.g., home evacuation, home relocation, job loss) because of the attack; (d) changes in family functioning after 9/11 (e.g. changes in family's interactions, economical situation, feelings of closeness/intimacy, etc.); (e) social and mental health support for WTC-related events or job-related stress.	
Children	(a) Youth's awareness of parental exposure to work-related events (CIHQ, ^{39, 40} adapted to ask about parental exposure; (b) PTSD symptoms related to parental exposure to work-related events (DPS ^{35, 36}).	
WHO WMH CIDI: World Health Organization World Mental Health Composite International Diagnostic Interview; NIMH DISC-IV: NIMH Diagnostic Interview Schedule for Children.		
^a The WTC-BOE Survey Questionnaire assessed the following direct exposure events: (a) saw planes crash/towers collapse, (b) in/near the cloud of smoke/dust on 9/11, (c) physically hurt in the attack or during evacuation, (d) had to evacuate/difficulties evacuating.		
^b Any parent who was below Canal Street from the time of the 1 st plane crash and the time the 2 nd tower collapsed was asked: (a) location when plane 1/plane 2 hit (in tower 1/tower 2, including what floor when planes hit; in other WTC buildings; outside in the WTC area; other buildings/areas below Canal street), (b) if entered tower1/tower 2 after planes hit; (c) location when tower 1/tower 2 collapsed (area immediately outside the WTC; within 3 blocks; > 2, < 10 blocks from the WTC; ≥ 10 blocks from the WTC); (d) saw any dead bodies (and how many); (e) saw people jumping from the towers. Participants also reported if they thought they were going to die.		
^c Spouse/partner, fiancé, mother, father, sister/brother, grandparents, aunt/uncle, friend, other family member, co-worker.		
^d The CIHQ will be used with anyone who (since the time of the last interview) has been working as a FR.		

3.3.2. Emotional health (EH): Wave 3 WTC Family Study (parents/children)

Measures are part of the NIH Toolbox emotional battery,⁴⁴⁻⁴⁶ and belong to three subdomains (**Table 2**): (a) **stress/self-efficacy** (S/S-E), (b) **psychological well-being** (PW-B), and (c) **social relationships** (SR). There are individual scores provided for each measure.

Table 2. National Institute of Health Toolbox Emotional battery. Measure (temporal frame): content

S/S-E	Perceived stress (past month): coping resources, and how unpredictable/uncontrollable/overloading participants find their lives. Self-efficacy (In general): sense of global self-efficacy, defined as persons' belief in their capacity to manage their functioning and have control over meaningful events.
PW-B	General life satisfaction (In general): global feelings and attitudes about life experiences; whether respondents like their lives or not. It includes both general (e.g., my life is going well) and domain-specific (e.g., I am satisfied with my family life) aspects. Meaning and purpose (In general): extent to which people feel their life matters or makes sense. Positive affect (past 7 days): 'activated' (e.g., happiness, joy) as well as 'unactivated' (e.g., serenity, peace) aspects of feelings that reflect a level of pleasurable engagement with the environment.
SR	Emotional support (past month): perception that people in one's social network are available to listen to one's problems with empathy, caring and understanding. Instrumental support (past month): perception that people in one's social network are available to material or functional aid in completing daily tasks (such as making meals or providing transportation) if needed. Friendship (past month): perception of the availability of friends or companions with whom to interact or affiliate. Loneliness (past month): perceptions of being alone, lonely or socially isolated from others.

3.3.3. RDoC measures: Wave 3 WTC Family Study (parents/children)

We will measure 10 RDoC constructs/sub-constructs, across 4 domains. Domains, constructs/sub-constructs and their corresponding measures are summarized in **Table 3**. Self-reports are described in **Table 3**; paradigms are described below.

Table 3. RDoC domains, constructs, sub-constructs and units of analysis: Wave 3 WTC Family Study (parents and children)

RDoC domains, constructs, and sub-constructs			Units of analysis	
Domains	Constructs	Sub-constructs	Self-Reports	Paradigms
Negative valence	Acute threat (fear)		STAI ⁴⁷ FQ ⁴⁸	Visual-probe
	Potential threat (anxiety)		Harm Avoidance from TCI-R ⁴⁹⁻⁵⁴	
	Loss		BHS ⁵⁵	
Positive valence systems	Approach motivation	Reward valuation Action selection/preference-based decision making	Consummatory subscale of the TEPS ⁵⁶⁻⁵⁸ BIS/BAS ⁵⁹ Reward Dependence and Novelty Seeking (TCI-R ⁴⁹⁻⁵⁴)	Intertemporal Choice Task; Columbia Card Task
	Initial responsiveness to reward attainment			
	Sustained/longer-term responsiveness to reward attainment			
Cognitive systems	Cognitive control	Response selection; Inhibition/suppression	Effortful Control (ATQ-SF ⁶⁰⁻⁶²); BIS-11 ^{63, 64}	
Social cognition	Perception/understanding of self	Self-knowledge	SRIS ^{65**} TAS ⁶⁶⁻⁶⁸	
	Perception/understanding of others	Understanding mental state	TEQ ⁶⁹	

State-Trait Anxiety Inventory (STAI)⁴⁷ Differentiates between the temporary condition of state anxiety and the more general and long-standing qualities of trait anxiety: 40 items on a 4-point scale. **Fear Questionnaire (FQ)**⁴⁸ How much participants would currently avoid 23 situations because of fear or other unpleasant feelings: 23 items on a 9-point scale. **Beck Hopelessness Scale (BHS)**⁵⁵ Three factors measuring negative attitudes about the future (future, loss of motivation, future expectations): 20 true-false items. **Behavioral**

inhibition/activation scales (BIS/BAS).⁵⁹ Sensitivity of two general motivational systems: *behavioral approach system* (regulation of appetitive motives: the goal is to move toward something desired); *behavioral avoidance (or inhibition) system* (regulation of aversive motives: the goal is to move away from something unpleasant); the BAS scale is divided into 3 sub-domains: drive, fun seeking, and reward responsiveness: 24 items on a 4-point scale. **Temporal Experience of Pleasure Scales (TEPS).**⁵⁶⁻⁵⁸ Feelings of pleasure felt in the moment of goal attainment (*consummatory pleasure*); feelings of desire related to the motivated approach of goals (*anticipatory pleasure*): 18 items on a 6-point scale; past week. **Temperament and Character Inventory-Revised (TCI).**⁴⁹⁻⁵⁴ 3 dimensions of temperament: *harm avoidance* (subscales: worry & pessimism, fear of uncertainty, shyness with strangers, fatigability & asthenia); *novelty seeking* (subscales: exploratory excitability, impulsiveness, extravagance, disorderliness); *reward dependence* (subscales: sentimentality, attachment, dependence); items are scored on a 5-point scale. **Adult Temperament Questionnaire, short form (ATQ-SF).**⁶⁰⁻⁶² Effortful control factor of the ATQ, composed of three scales: *activation control* (the capacity to perform an action when there is a strong tendency to avoid it), *attentional control* (the capacity to focus attention as well as to shift attention when desired), and *inhibitory control* (the capacity to plan, and to suppress inappropriate responses). *Effortful control*: ATQ 19 items on a 5-point scale. **Barratt Impulsiveness Scale (BIS-11).**^{63, 64} It measures three 2nd order factors of impulsivity: *attentional* (1st order factors: attention, cognitive instability), *motor* (1st order factors: motor, perseverance), and *non-planning* (1st order factors: self-control, cognitive complexity) impulsivity; 30 items on a 4-point scale. **Self-Reflection and Insight Scale (SRIS).**⁶⁵ Private self-consciousness (the inner feelings and beliefs one has toward oneself): *engagement in/need for self-reflection* (e.g., “I don’t often think about my thoughts”; “I am not really interested in analyzing my behavior”); *insight* (e.g., “I usually know why I feel the way I do”): 20 items on a 5-point scale. **Toronto Alexithymia Scale (TAS).**⁶⁶⁻⁶⁸ Alexithymia: trouble identifying and describing emotions; tendency to minimize emotional experience and focus attention externally: 3 subscales: *difficulty describing feelings*; *difficulty identifying feelings*; *externally-oriented thinking* (tendency to focus attention externally: 20 items on a 5-point scale. **Toronto Empathy Questionnaire (TEQ).**⁶⁹ A single unidimensional empathy factor: 16 items on a 5-point scale.

- **RdoC Paradigms.** Three paradigms, outlined below, have been used.

1. Visual-probe (V-P) Paradigm: Threat Bias. Ample evidence indicates that attention is biased toward threatening stimuli/threat-related information in the environment (during the early, automatic stages of information processing^{70, 71}) in disorders associated with negative-valence states: anxiety disorders,^{70, 71} depression,^{70, 72-76} and PTSD.⁷⁷⁻⁸¹ These results indicate that threat bias may be a nonspecific trans-diagnostic marker of negative affectivity in a number of clinical conditions. The threat bias is also associated with increased vulnerability to stress (e.g., refs^{82, 83}), suggesting that this cognitive bias likely contributes to both the development and maintenance of internalizing disorders.⁸⁴ Participants will complete a V-P paradigm identical to the one previously used by our group,⁷⁹ and used widely in research on pediatric and adult PTSD, anxiety, depression and other psychopathologies (e.g., refs^{70, 85-90}). For emotional face trials, there are two conditions: congruent and incongruent, in which the probe replaces the emotional face (i.e., threat or happy), or the neutral face, respectively.^{70, 91} The *outcomes of interest* are the threat bias and the happy bias.

2. Delay Discounting: Intertemporal Choice Task (ICT).⁹²⁻⁹⁶ Intertemporal choice (or delay discounting) tasks quantify an individual’s propensity toward seeking immediate rewards, even if later rewards are larger.⁹⁷ Disruptions in reward and self-control circuits involved in processes favoring the choice of rewards fulfilling immediate needs (*now* processes) vs. processes favoring behaviors designed to attain longer-term goals (*later* processes) contribute to diverse pathologies, including SUD.⁹⁷⁻¹⁰⁴ Examination of self-control in intertemporal choices is the “linchpin of universal prevention”, since deficits in

self-control have been suggested to represent a “trans-disease process” (Volkow,⁹⁷ page 348). In the ICT, developed by our collaborator Dr. Figner,^{92, 95, 105} participants – like in a standard delay-discounting task – choose between a smaller-sooner (SS) or a larger-later (LL) amount of money.¹⁰⁵ The ICT differs from standard delay discounting paradigms since it allows examining (a) *framing* (DELAY vs. ACCELERATE) and (b) *immediacy* (NOW or NOT-NOW) effects, based on evidence showing that (a) healthy subjects are more patient when the default option is a LL and they can switch to a SS (ACCELERATE frame), than when the default option is a SS and they can choose a LL (DELAY frame) (asymmetric discounting),¹⁰⁵ and that (b) this asymmetry in discounting is more evident when the SS is available immediately (NOW) than when it is available at a later time (in 2 weeks; NOT-NOW).⁹² Participants are told to choose the option they truly prefer because they will be paid according to their choice on one of the trials (selected randomly). There are two main *outcomes of interest*: (1) log-transformed discount rates for each participant, calculated as in Decker et al.;⁹⁶ lower log-transformed discount rates indicate less steep discounting (less impatience/impulsive decision making), i.e., a preference for LL over SS options. (2) Proportion of LL vs. SS choices; the larger the percentage, the more patient the subject is making intertemporal choices, i.e., more able to delay reward (gratification).

3. Columbia Card Task (CCT). Risk-taking, which involves voluntary choices for behaviors where outcomes remain uncertain is thought to be a trans-diagnostic marker of many behaviors characterized by deficits in action selection/preference-based decision making, initial/sustained responsiveness to reward attainment, such as AU/SU, and ultimately AUD/SUD.¹⁰⁶⁻¹⁰⁹ Unlike other risk-taking tasks, the CCT (also developed by Dr. Figner) measures risk-taking in conditions of higher vs. lower affective arousal,¹¹⁰ and has been shown to track the developmental course of adolescents’ risk-taking behaviors (inverted U-shaped trajectory).^{107, 110} In each trial, 32 cards are shown face down, each containing a gain or loss amount when turned over. Cards can be turned over and each gain card adds a specified amount to the payoff, which the participant can claim by stopping the trial. If, however, a loss card is encountered, the pot is lost. The ‘hot’ version involves step-by-step decisions to turn over another card or to stop and collect, and offers immediate feedback for each choice. In the ‘cold’ version, participants indicate the total number of cards they wish to turn over, which are then turned simultaneously, giving this version more of the character of a ‘cold’ judgment task. The *outcome of interest* is the participants’ number of cards chosen (more cards indicate more risk-taking).

4. Results

4.1. 9/11 Exposure and Psychiatric Disorders

To examine the association of WTC exposure with psychopathology, we fit a linear or logistic regression model for each outcome adjusting for demographic characteristics (participant gender, age, and race/ethnicity). The mental health measures included: past year or lifetime agoraphobia, generalized anxiety disorder, major depressive episode, panic disorder, post-traumatic stress disorder and alcohol or substance abuse or dependence. Dysthymia and minor depressive disorder were also assessed over past year only, and aggregate measures of any internalizing and externalizing disorders over

the past 12 months or the lifetime were examined. Externalizing psychopathology combined alcohol or substance abuse or dependence, internalizing psychopathology includes past year or lifetime agoraphobia, generalized anxiety disorder, major depressive episode, panic disorder and post-traumatic stress disorder. **Table 4** shows results from logistic regression models for a subset of outcomes.

Table 4. Logistic regression models for 9/11 exposure association with mental health outcomes at wave 3.

Outcome	Maternal direct 9/11 exposure				Paternal direct 9/11 exposure				Youth indirect exposure			
	OR	LCL	UCL	p-value	OR	LCL	UCL	p-value	OR	LCL	UCL	p-value
Lifetime												
Internalizing psychop.	1.02	0.78	1.33	0.89	1.00	0.74	1.36	0.99	0.91	0.73	1.13	0.39
Externalizing psychop.	1.27	0.92	1.76	0.15	1.24	0.95	1.61	0.11	1.02	0.82	1.29	0.81
AUD	1.04	0.68	1.59	0.85	1.30	0.98	1.71	0.06	1.11	0.86	1.44	0.44
SUD	1.64	1.09	2.47	0.02	1.21	0.87	1.68	0.25	0.89	0.68	1.15	0.36
Past 12 months												
Internalizing psychop.	1.49	1.05	2.12	0.03	1.02	0.60	1.73	0.93	0.95	0.73	1.22	0.67
Agoraphobia	1.84	0.81	4.20	0.15	288.9	0.00	>999	0.96	0.75	0.42	1.36	0.35

Adjusted for gender and race/ethnicity. AUD=alcohol use disorder; SUD=substance use disorder; psychop. = psychopathology.

We found that among mothers, direct 9/11 exposure was associated with significantly increased odds of lifetime SUD (OR=1.6; p=0.02) and past year internalizing psychopathology (OR=1.5; p=0.03). Among specific internalizing disorders, agoraphobia showed a close to 2-fold (p=0.15) increase. Among fathers, the odds of AUD (OR=1.3; p=0.06) and of lifetime Externalizing psychopathology (OR=1.2; p=0.11) showed trends towards being increased among the groups with direct exposure to the WTC attack. Youth indirect exposure, however, was not associated with significant differences in psychopathology at wave 3.

We further examined the association of 9/11 direct and indirect exposure with psychopathology by comparing the prevalence of different psychopathology outcomes by different types of exposure groups. A selected set of comparisons, including any with significant differences between groups (p<0.05) are shown in **Table 5**. Specifically, among mothers, past year internalizing psychopathology was more prevalent (28%) among 9/11 evacuees than among minimally exposed (10%) and non-exposed (10%) groups (the 9/11 First Responder category among mothers had small N).

Among mothers, generalized anxiety disorder (GAD) was highest over the lifetime (29%) and over the past 12 months (9%) among 9/11 evacuees; in each case, this was over 3 times as high as in the next highest prevalence group. Past year agoraphobia was also elevated in maternal evacuees and residential evacuees/minimally exposed, and PTSD related to 9/11 was highest among first responders, though numbers were limited.

Among fathers, alcohol abuse/dependence was elevated in all exposed groups (ranging from 34-51%) versus 27% prevalence in the non-exposed group, and PTSD related to 9/11 was highest among evacuees (10%), followed by first responders (6%). Youth showed marginal ($p < 0.1$) differences by parental exposure group in their prevalence of PTSD, with the highest proportion affected among those of parents who were 9/11 evacuees (16%). Youth also showed differences in prevalence of dysthymia; however the frequency of outcomes was low for this disorder so test statistics should be interpreted with caution.

Table 5. Prevalence of psychopathology outcomes by exposure groups (shown for respondent-outcome combinations with $p < 0.05$ for comparison of prevalence across groups only).

Outcomes	9/11 Evacuee (%)	9/11 First Responder (%)	9/11 Residential Evac & Minimally Exposed FR (%)	Non-exposed (%)	p-value*
Mothers (N=369)					
Internalizing psychopathology, lifetime	37.0	12.5	38.1	34.3	0.57
Internalizing psychopathology, past year	27.8	0.0	9.5	9.8	0.002
GAD, lifetime	28.6	0.0	4.8	8.4	0.07
GAD, past year	9.3	0.0	0.0	2.5	0.05
Agoraphobia, past year	5.6	0.0	4.8	1.1	0.11
Dysthymia, past year	3.7	0.0	0.0	0.35	0.09
PTSD related to 9/11	3.8	12.5	0.0	1.4	0.095
Fathers (N=322)					
Alcohol abuse/dependence	34.0	39.1	51.4	27.2	0.06
PTSD related to 9/11	9.5	5.5	0.0	0.0	0.01
Youth (N=505)					
PTSD	15.9	8.6	5.1	10.1	0.08
Dysthymia	0.0	4.2	5.0	1.3	0.03

*Chi square p-value. For youth, p-values for all disorders were > 0.05 .

4.2. 9/11 Exposure, Psychiatric Disorders and Emotional Health

To examine the association between WTC exposure, psychopathology, and measures of emotional health, we used linear regression models for emotional health measures (self-efficacy, general life satisfaction, emotional support, friendship), with 9/11 exposure, internalizing or externalizing psychopathology, and 9/11 exposure $\times$ psychopathology interaction as independent variables. Models were also adjusted for demographic factors and were conducted separately in each group (mothers, fathers, youth).

The results are summarized in **Table 6**. 9/11 exposure (direct) was associated with increased self-efficacy among mothers, but the strongest evidence for association was among youth (indirect exposure). Youth indirectly exposed to 9/11 had increased self-efficacy and general life satisfaction, but decreased emotional support, relative to those who were unexposed. Internalizing psychopathology was consistently associated with decreased general life satisfaction, and among youth was associated with decreased self-efficacy; and with decreased emotional support and friendship, but only among those

without indirect exposure to 9/11. Finally, externalizing psychopathology was associated with decreased general life satisfaction among mothers and among indirectly 9/11 exposed youth; among youth, externalizing psychopathology was associated with increased self-efficacy among 9/11 non-exposed but decreased self-efficacy among 9/11 exposed.

Table 6. Summary of the evidence for association of 9/11 direct/indirect exposure and psychopathology and their interaction on Emotional Health.

Emotional health measure	Exposure	Mothers (N=324)	Fathers (N=281)	Youth (N=436)
Self-efficacy	9/11	Λ		Λ
	Internalizing psychop.			▼
	Externalizing psychop.			Λ (9/11 non-exposed); ▼ (9/11 exposed)
General life satisfaction	9/11			Λ
	Internalizing psychop.	▼	▼	▼
	Externalizing psychop.	▼		▼ (9/11 exposed)
Emotional support	9/11			▼
	Internalizing psychopathology			▼ (9/11 non-exposed)
	Externalizing psychop.			
Friendship	9/11			
	Internalizing psychop.			▼ (9/11 non-exposed)
	Externalizing psychop.			

Λ, emotional health measure is increased; ▼, emotional health measure is decreased. Empty cell indicates $p > 0.05$ for corresponding association. Psychop. = psychopathology.

4.3. RDoC Domains of Functioning, Type/Severity of WTC-exposure/s and Psychopathology

To test the association between measures assessing RDoC domains and psychopathology at wave 3, we used logistic regression models with psychiatric diagnoses as the dependent variable, and measures assessing key RDoC domains (BIS-11, cognitive systems; STAI trait anxiety, negative valence; Toronto Empathy Questionnaire, TEQ, social cognition) as independent variables. Models adjusted for demographics, and were examined separately in mothers, fathers, and now adult children. We found (see **Table 7**) that higher impulsiveness (BIS-11, cognitive systems) and higher trait anxiety (negative valence) were significantly associated with increased odds of past 12 month internalizing psychopathology among mothers, fathers, and now adult children; the pattern of association was similar for lifetime internalizing psychopathology, however the associations were stronger when considering the past 12 months. Social cognition was not associated with internalizing psychopathology or externalizing psychopathology. Negative valence was positively associated with lifetime externalizing psychopathology in mothers, fathers and children; whereas impulsiveness was positively associated with lifetime externalizing psychopathology in fathers and children, but not mothers.

To test the hypothesis that RDoC domain measures modulate the association between 9/11 exposure and psychopathology, terms for 9/11 direct or indirect exposure and for

interaction between 9/11 direct or indirect exposure and RDoC domain measures were added to the logistic regression models above for psychopathology outcomes. Statistical significance of evidence for effect modification was assessed as $p < 0.05$ for product interaction terms. Based on this criterion, we did not find evidence for modification of 9/11 exposure and psychopathology associations by measures of RDoC domains.

Table 7. Association between RDoC domain measures and psychopathology

Outcome	RDoC Domain	Mothers				Fathers				Now adult children			
		OR	LCL	UCL	p-value	OR	LCL	UCL	p-value	OR	LCL	UCL	p-value
Past 12 month internalizing psychop.	Cognitive systems	1.99	1.08	3.68	0.03	2.12	1.03	4.35	0.04	3.60	2.20	5.90	<.0001
	Negative valence	1.10	1.07	1.14	<.0001	1.10	1.05	1.15	<.0001	1.09	1.07	1.12	<.0001
	Social cognition	1.01	0.96	1.06	0.82	1.01	0.95	1.07	0.82	0.99	0.95	1.02	0.41
Lifetime internalizing psychop.	Cognitive systems	1.41	0.91	2.17	0.12	1.43	0.92	2.23	0.11	2.61	1.75	3.89	<.0001
	Negative valence	1.06	1.04	1.09	<.0001	1.08	1.05	1.11	<.0001	1.08	1.06	1.11	<.0001
	Social cognition	1.02	0.98	1.05	0.33	1.01	0.97	1.05	0.56	1.01	0.98	1.04	0.63
Lifetime externalizing psychop.	Cognitive systems	1.36	0.78	2.37	0.27	1.82	1.20	2.77	0.00	2.29	1.57	3.34	<.0001
	Negative valence	1.02	1.00	1.05	0.08	1.04	1.02	1.07	0.00	1.02	1.00	1.04	0.05
	Social cognition	0.98	0.94	1.02	0.38	0.99	0.96	1.02	0.52	0.99	0.96	1.02	0.40

4.4. COVID-19 Pandemic

While unable to conduct the in-home, in-person interviews, we conducted a longitudinal telephone survey over 3 waves during the COVID-19 pandemic (Wave 1: March-August 2020, Wave 2: September 2020-February 2021, Wave 3: March-August 2021), in part to check-in on the cohort. Participants included a random selection of WTC Family participant families, including young adults and parents of young adults from the same family. Questions related to mental health and well-being during the pandemic and characterization of participants' pandemic exposure experience. The mental health and substance use and COVID-related exposures of S&W youth and parent participants over 3 waves of this telephone survey are shown in **Table 8**. Overall, depression, GAD, and increased alcohol or smoking/vaping among those who used alcohol or cigarettes were highest among both groups in wave 1 (early pandemic) and declined on average over time. Prevalence of perceived discrimination and of testing positive for COVID-19 increased across waves. Recent exposure to COVID-19 persisted in the range of 20-30% across waves, while the feeling of safety from COVID-19 increased over time

Table 8. Prevalence of mental health and COVID-related exposures among youth and parent WTC Family participants over 3 waves of the COVID-19 pandemic

	Youth (N=159)			Parents (N=309)		
	Wave 1	Wave 2	Wave 3	Wave 1	Wave 2	Wave 3
	%	%	%	%	%	%
Mental health and substance use						
Depression	15.9	9.4	12.0	17.4	8.6	6.1
GAD	15.3	9.4	6.5	21.4	12.3	8.8
Increased alcohol use*	30.6	8.9	9.6	29.6	3.5	3.3
Increased smoking/vaping*	21.1	22.6	17.2	45.5	35.7	23.8
COVID-related exposures						
Perceived discrimination	1.3	3.1	6.5	2.0	6.1	8.5
Tested positive for COVID-19	0.6	4.7	7.4	2.6	4.1	7.4
Loss of family or friends due to COVID-19	4.4	10.1	9.4	5.5	17.2	18.4
Recent exposure to COVID-19	22.6	30.8	27.7	27.5	33.7	28.2
Concern about being victim of violent crime	1.9	0.8	0.9	2.3	1.6	2.3
	<i>Mean</i>	<i>Mean</i>	<i>Mean</i>	<i>Mean</i>	<i>Mean</i>	<i>Mean</i>
Household financial impact of COVID-19 (none=0 to 2=a lot)	0.79	0.62	0.69	0.81	0.62	0.60
Current feeling of safety from COVID-19 (none=0 to 2=a lot)	1.29	1.31	1.57	1.16	1.18	1.56

*Among those who use the respective substance

5. Discussion

5.1. 9/11 Exposure and Psychiatric Disorders

In general, the results show that more than 15 years after 9/11, adults exposed to the attacks still showed higher rates of psychopathology compared to non-exposed adults.

Mothers directly exposed to 9/11 had higher rates of lifetime substance use disorder (SUD). Similarly, fathers who were directly exposed to 9/11 tended to have higher odds of lifetime Alcohol Use Disorders (AUD). Mothers directly exposed to 9/11 had also higher rates of past year internalizing psychopathology; in particular, agoraphobia showed an almost 2-fold increase among mothers directly exposed to 9/11. Higher rates of internalizing psychopathology were not observed among fathers directly exposed to 9/11.

When the analyses were stratified by four exposure groups, mothers who were 9/11 evacuees had much higher rates internalizing psychopathology in the most recent year before assessment compared to mothers who were minimally exposed or not exposed on 9/11; in particular, rates of lifetime generalized anxiety disorder (GAD) and of GAD in the most recent year before assessment were especially high among mothers who were 9/11 evacuees. Mothers in the 9/11 evacuees and residential evacuees/minimally exposed groups also tended to have higher rates of past year agoraphobia compared to mothers in the First Responder and non-exposed groups. 9/11-related PTSD tended instead to be higher among mothers in the First Responders group, compared to the other groups. Unlike mothers, fathers did not show differences in the rates of internalizing psychopathology across the four exposure groups. Compared to fathers who were not exposed to 9/11, lifetime AUD was higher in all exposed groups.

PTSD related to 9/11 was highest among evacuees, followed by the First Responders group.

These results show the long-term associations between 9/11 exposure and a broad range of psychiatric outcomes, including both internalizing and externalizing disorders. This is important, since most WTCR psychiatric studies focused on PTSD, with few exceptions.^{10, 11, 111} Thus, there is a need to further investigate the links between WTC-exposures and other psychiatric disorders, such as major depressive disorder, anxiety disorders and alcohol/substance use disorders. This is true not only for the WTCR but also for the 9/11-related literature in general.¹⁸ Furthermore, the association – in mothers – between 9/11 exposure and both internalizing and externalizing psychiatric disorders indicate the critical importance of developing a better understanding of comorbidity among 9/11-related psychiatric outcomes,¹⁸ examined to date by only two WTCR studies,^{10, 11} and our own study including risk factors for comorbidity.^{112, 113}

In general, among youth, there was no evidence of a significant long-term relationship between parental exposure to 9/11 and their children's mental health. To the best of our knowledge, no study to date has examined the long-term relationship between indirect exposure to 9/11 (due to parental exposure) and psychopathology. Recent reviews^{114, 115} have shown that almost none of the published 9/11-related studies of pre-natal samples (e.g., refs^{116, 117}), and of preschoolers (e.g., ref^{118, 119}), school age (e.g., refs^{38, 120, 121}), and adolescents/young adults (e.g., refs¹²²⁻¹²⁶) have followed participants over an extended period of time. Thus, it is difficult to discuss the current findings in light of findings from the literature. Our findings from the *NYC Department of Education (NYC-DOE) Study* (N = 8236 NYC public school students assessed 6 months post-9/11; ages 8-21)³⁸ showed that PTSD was more strongly associated with family exposure than direct exposure.^{38, 127-129} For example, among 4th graders who were exposed to less than two stressors, those who knew anyone who was at the WTC during the attack were more likely than those who did not to screen positive for PTSD (27% vs. 11%); among children in grades 5-12, the first and second strongest predictors of PTSD were, respectively, having a friend/family member who died in the attack (16% vs. 7%), and a friend/family member who was at the WTC at the time of the attack and survived (10% vs. 6%).¹³⁰ Furthermore, in the *NYC-DOE Study*,¹³¹ children with EMT family members had a high prevalence of PTSD (19%), compared to children who had POs or no FRs in their family (11 and 10%, respectively), and especially to children with FFs family members (6%). Despite the small sample size (EMT: N=288; FFs: N=83), differences in rates of PTSD in EMTs' vs. FFs' children were still significant after controlling for different WTC-exposures, and were still marginally significant after controlling for demographic characteristics. Finally, in the *NYC-DOE Study*, 9/11-related life disruptions in the family (a family member lost her/his job; parents restricted youth' post-attack travel) were associated with youth's elevated rates of PTSD and other anxiety disorders.¹³²

In sum, results from the *NYC-DOE Study* indicated that in children and adolescents assessed 6 months after 9/11, the effects of different kind of parental and familial exposure on youths' mental health were significant. Thus, while indirect exposure to 9/11 might still exert significant effects 6 months after 9/11 (when the *NYC-DOE Study* was conducted), the long-term consequences of parental exposure to 9/11 might diminish over

time and become negligible more than 15 years after 9/11 (when much of the current study was conducted).

5.2. 9/11 Exposure, Psychiatric Disorders and Emotional Health

To the best of our knowledge, the current study is the only study – among WTCRR enrollees and their families – that examined the long-term effects of WTC-exposure on a broad array of psychiatric disorders and associated outcomes related to emotional health, as indicators of psychological resilience and quality of life.

Among mothers, fathers and youth, psychiatric disorders were generally associated with decreased emotional health. More specifically, among mothers, fathers, and youths, internalizing and externalizing psychopathology were associated with decreased general life satisfaction. Among mothers, also externalizing psychopathology was associated with decreased general life satisfaction. Among youth, internalizing psychopathology was associated with decreased self-efficacy.

Some unexpected results were observed when examining the association between exposure to 9/11 and emotional health. Surprisingly, among mothers only, direct 9/11 exposure was associated with increased self-efficacy. Due to the associations between different measures of exposure to 9/11 and maternal psychopathology, it is likely that maternal self-efficacy does not constitute a buffer against the long-term negative effects of exposure to 9/11. However, this hypothesis still needs to be tested; furthermore, increased self-efficacy among mothers exposed to 9/11 might be a protective factor for specific psychiatric disorders and not for others; this hypothesis also needs to be tested. In agreement with findings reported among mothers, youth indirectly exposed to 9/11, relative to those who were unexposed, had increased self-efficacy; youth indirectly exposed to 9/11 also had increased general life satisfaction. Due to the lack of a significant association between parental exposure and psychopathology in youth, self-efficacy and general life satisfaction might constitute indicators of psychological resilience against the long-term effects of indirect exposure. This result suggests that emotional health can buffer stress and enhance psychological and physical health among youth indirectly exposed to 9/11. We still need to understand differential impact.

5.3. RDoC Domains of Functioning, Type/Severity of WTC-exposure/s and Psychopathology

Some of the problems associated with the use of DSM psychiatry nosology in neurobiological research include excessive comorbidity of disorders and the marked heterogeneity of clinical entities and underlying mechanisms (i.e., grouping of heterogeneous syndromes with different pathophysiological mechanisms into one diagnostic entity).^{22, 24} In particular, the underlying validity of the disease entities has been questioned, in that DSM categories do not map well onto emerging findings from genetics, systems neuroscience and behavioral science.²⁰⁻²² As a result, it becomes very difficult to translate research from basic studies to a systematic understanding of pathology or to systematic treatments directed at mechanisms.²² In other areas of medicine (e.g., ref¹³³) there has been a realization that disease entities that appear to be a single disorder actually have distinct genetic precursors and pathophysiology: these approaches move us toward individualized treatment ('precision medicine'), that can harness the power of

new technologies to identify and intervene on specific etiological process that result from genetic and environmental causes, represent the forefront of medical science.^{22, 134}

Fortunately, since the establishment of the WTCHR in 2002, the NIMH has initiated the RDoC project, intended as a new research classification system based on key dimensional constructs underlying mental function across multiple units of analysis, from genes to observable behaviors.²²⁻²⁴ The RDoC project is NIMH's effort to develop an integrative, multi-system precision medicine approach to mental disorders.^{22, 23}

For the *Wave 3 WTC Family Study*, we examined ten constructs/sub-constructs across four RDoC domains of functioning, which are highly pertinent to the etiology and treatment of numerous psychiatric conditions, including PTSD, anxiety disorders, MDD, and AUD/SUD:^{25-28, 135} (i) negative valence, (ii) positive valence, (iii) cognitive systems, and (iv) social cognition. RDoC domains have five main characteristics that are relevant for the proposed study: (a) they have been conceived by NIMH to represent valid behavioral entities mapping onto specific brain circuits;^{22, 136} (b) they incorporate an explicitly dimensional approach to psychopathology,^{22, 24, 137} in which dimensionality is not exclusively intended as a function of symptom severity, as in most studies, but also as examination of the full range of variation, from normal to abnormal; (c) they might show a nonlinear relationship with symptom severity (a critical area of research is to determine the location of 'tipping points' that mark transition to more severe pathology, and how they are affected by various risk/resilience factors); (d) they cut across traditional diagnostic boundaries;¹³⁷ and (e) they vary across development and are influenced by environmental factors.¹³⁸ Applying the RDoC classification to WTC-exposed families will allow examining how psychiatric disorders maps onto RDoC domains.

Mothers, fathers and youth with higher impulsivity and higher trait anxiety showed increased odds of lifetime and past 12 month internalizing psychopathology. Mothers, fathers, and youth with higher negative valence had higher rates of lifetime externalizing psychopathology. Among fathers and youths, lifetime externalizing psychopathology was also associated with higher impulsivity. Thus, these results suggest that – in mothers, fathers and youth – higher trait anxiety and higher negative valence might be specific markers of internalizing and externalizing psychopathology, respectively. In fathers and youth, higher impulsivity may be a transdiagnostic etiologic mechanism underlying both internalizing and externalizing psychopathology.

6. Conclusion

In adults, different types of exposure to 9/11 have long-term effects on mental health. More than 15 years after 9/11, risk of both internalizing and externalizing disorders is elevated in adults exposed to 9/11. In youths, the long-term consequences of parental exposure to 9/11 might instead diminish over time; our preliminary results indicate that there is no evidence of an association between parental exposure to 9/11 and youths' psychopathology at wave 3.

Among mothers, fathers and youth, psychiatric disorders were generally associated with decreased emotional health. Among mothers only, direct 9/11 exposure was associated with increased self-efficacy. Given the association between exposure to

9/11 and maternal psychopathology, self-efficacy might not constitute a protective factor against the long-term effects of exposure to 9/11. Youth indirectly exposed to 9/11, relative to those who were unexposed, had increased self-efficacy and increased general life satisfaction. In youth these measure of emotional health might be markers psychological resilience against the long-term effects of indirect exposure, resulting in a lack of association between indirect exposure and psychopathology at wave 3.

For the first time, the *Wave 3 WTC Family Study* examined DSM disorders and the effects of direct/indirect WTC-exposure taking RDoC dimensions of functioning into account, in agreement with the NIMH goal of creating a framework for research on mechanisms of psychopathology, which ultimately will inform future classification systems, and prevention/treatment of mental illness. The RDoC project is NIMH's effort to develop a precision medicine approach to mental disorders. In mothers, fathers and youth, higher trait anxiety and higher negative valence might be specific markers of internalizing and externalizing psychopathology, respectively. In fathers and youth, higher impulsivity may be a transdiagnostic etiologic mechanism underlying both internalizing and externalizing psychopathology. This integrative, multi-system examination of RDoC domains, has the potential to move forward the field of translational research in WTC-exposed populations, so that individualized treatments directed at etiologic mechanisms might soon be available to trauma-exposed individuals.

Although much of the scientific impact of this investigation was mitigated due to the COVID-19 Pandemic, the findings are important and should be expended and deepened in future longitudinal investigation of this only 9/11 family cohort.

**RDoC Domains Underlying Emotional Health and Trajectories of
Psychopathology in Families of WTC First Responders and Evacuees:
A Genome-Wide G×E Study**

WTC-Family Study Wave 3

Grant/Cooperative Agreement # 5U01OH011327

Grant/Cooperative Agreement Project Period: 9/1/2016-8/31/2022

Publications

- Guffanti* G, Geronazzo-Alman* L, Fan B, Duarte CS, Musa GJ, Hoven CW. Homogeneity of Severe Posttraumatic Stress Disorder Symptom Profiles in Children and Adolescents Across Gender, Age, and Traumatic Experiences Related to 9/11. *Journal of Traumatic Stress*. 2016;29(5):430-439. *Both authors contributed equally to this work and should be considered as co-first authors.
- Geronazzo-Alman L. RDoC Domains Underlying Emotional Health and trajectories of Psychopathology in Families of WTC First Responders and Evacuees: A Genome-Wide G×E study. Scholarly Breakfast & Division Meeting, New York State Psychiatric Institute - Columbia University Medical center. New York, NY, March 22, 2017.
- Geronazzo-Alman L, Eisenberg R, Shen S, Duarte CS, Musa GJ, Wicks J, Fan B, Doan T, Guffanti G, Bresnahan M, Hoven CW, Cumulative Exposure to Work-Related Traumatic Events and Current Post-Traumatic Stress Disorder in New York City's First Responders. *Compr Psychiatry*. 2017, 74:134-143. PMID: 28161583. doi: 10.1016/j.comppsy.2016.12.003
- Duarte C, Eisenberg R, Musa GJ, Addolorato A, Shen S, Hoven CW. Children's Knowledge about Parental Exposure to Trauma. *J Child Adol Trauma*, 2017 [Epub ahead of print]. doi: 10.1007/s40653-017-0159
- Greene T, Gross R, Amsel L, Hoven CW. (2017). The Mental Health of Children and Adolescents Exposed to 9/11: Lessons Learned and Still to be Learned. In A Szema (Ed.), *World Trade Center Pulmonary Diseases and Multi-Organ System Manifestations*. New York: Springer.
- Geronazzo-Alman L, Eisenberg R, Bresnahan M, Wicks J, Duarte CS, Fan B, Hoven CW, Musa GJ, Guffanti G. Comorbidity Classes and Associated Impairment, Demographics and 9/11-Exposures in 8,236 Children and Adolescents. *Journal of Psychiatric Research* 2018, 96: 171–177. PMID: 29078153. doi: 10.1016/j.jpsychires.2017.10.012

- Hoven CW (2019) Are there Long-Term Physical/Psychological Consequences for Children Exposed to 9/11? 7th Annual NYC MRC Symposium: Disaster Mental Health: Effects of Disasters on Adult Survivors, Child Survivors & Responders New York City Medical Reserve Corps. April 28, 2019. New York, NY
- Geronazzo-Alman L, Fan B, Duarte CS, Layne CM, Wicks J, Guffanti G, Musa GJ, Hoven CW. The Distinctiveness of Grief, Depression, and Posttraumatic Stress. Lessons From Children After 9/11. *Journal of the American Academy of Child & Adolescent Psychiatry*. 58:10. 2019. 971-982. Referenced in Melhem NM, Brent D. Editorial: Grief in Children: Phenomenology and Beyond. *Journal of the American Academy of Child & Adolescent Psychiatry*. 58:10. 2019. pii: E1698. PMID: 30096890 doi: 10.3390/ijerph15081698
- Li Y, Hou Y, Musa G, Fan B, Hoven CW. "Posttraumatic Stress Disorder in Children and Adolescents: Some Recent Research Findings" In E Ovuga (Ed.) *Post-Traumatic Stress Disorders - Current Advances*. 2019, London. IntechOpen.
- Hoven CW (2019) Reflections on PTSD, Other Psychopathologies and Co-Morbidities Post-Disaster: What We Have Learned? 37th Brazilian Congress of Psychiatry. October, 11 2019. Rio de Janeiro
- Hoven CW, Amsel L, Herman H, Tyano S (2019) A National Suicide Study with Potential to Increase Understanding of the Protective Roles of Spirituality and Religion. 4th Global Meeting in Spirituality and Mental Health. December 3, 2019 Jerusalem, Israel
- Amsel L, Hoven CW, Tyano S (2019) The Role of Religion and Spirituality for Children's Mental Health in Disasters. 4th Global Meeting in Spirituality and Mental Health. December 3, 2019 Jerusalem, Israel
- Hoven CW (2020) How to Assess Long-Term Impact of Trauma Exposure on Children? UNA Partnership Meeting. January 14, 2020, Kiev, Ukraine
- Kishon R, Geronazzo-Alman L, Teichman M, Teichman Y, Cheslack-Postava K, Fan B, Duarte CS, Wicks J, Musa GJ, Djalovski A, Tadmor B, Moreno DR, Cycowicz Y, Amsel L, Bresnahan M, Hoven CW. Parental Occupational Exposure is Associated with Their Children's Psychopathology: A Study of Families of Israeli First Responders. *J Occup Environ Med*. 2020 Nov;62(11):904-915.
- Goodwin, RD, Cheslack-Postava K, Musa GJ, Eisenberg R, Bresnahan M, Wicks J, Weinberger AH, Fan B, Hoven CW. Exposure to Mass Disaster and Probable Panic Disorder among Children in New York City. *Journal of Psychiatric Research*. 2021.
- Cheslack-Postava K, Bresnahan M, Ryan M, Musa GJ, Forthal S, Sun X, Skokauskas N, Svob C, Lin S, Goodwin R, Wicks J, Hoven CW. Racial/Ethnic Variation in Mental Health During the COVID-9 Pandemic in a Diverse Urban Population. Oral presentation at the meeting of the National Institute of Health –Social, Behavioral, and Economic (NIH-SBE) Health Impacts of COVID-19 webinar, April 27-28, 2022.

- Svob, C, Lin, S X, Cheslack-Postava, K, Bresnahan, M, Goodwin, R D, Skokauskas, N, Musa, G J, Hankerson, S H, Dreher, D R, Ryan, M, Hsu, Y, & Hoven, CW. Religiosity and Substance Use among Black and Hispanic Americans During the COVID-19 Pandemic in New York City. Oral presentation at the meeting of the National Institute of Health – Social, Behavioral, and Economic (NIH-SBE) Health Impacts of COVID-19 webinar, April 27-28, 2022.
- Cheslack-Postava, K, Rafieian, M, Skokauskas, N, & Hoven, CW. Intolerance of Uncertainty and Depression During the COVID-19 Pandemic in New York; Poster Presentation at Aacap, Toronto, Canada, October 21, 2022.
- Ryan, M, Lin, S, Cheslack-Postava, K, Musa, M, Wicks, J, Zemeck, H, & Hoven, C. Food Insecurity and Mental Health Disparities among Women during the COVID-19 Pandemic in an US Based Urban Cohort. Oral presentation at IAWMH 6-9 November 2022, Maastricht, The Netherlands.
- Geronazzo-Alman, L., Ma, S., Kummerfeld, E., Saxe, G., Aliferis, C., Kishon, R., Hoven, C. W. A Machine Learning Causal Structure Discovery and Predictive Modeling Study of Psychiatric Disorders in Children of First Responders. Guyana Mental Health & Well-being Conference. Georgetown, Guyana, November 8-12.
- Geronazzo-Alman, L., Ma, S., Kummerfeld, E., Aliferis, C., Saxe, G., Kishon, R., . . . Hoven, C. W. (In Review). Psychopathology in Children of First Responders: Identifying Causes, Intervention Targets and Predictors Using Machine Learning. Psychological Trauma: Theory, Research, Practice, and Policy.
- Geronazzo-Alman L, Kishon R, Teichman M, Teichman Y, Cheslack-Postava K, Fan B, Duarte CS, Wicks J, Musa G, Djalovsky A, Tadmor B, Moreno D, Cycowicz Y, Amsel L, Bresnahan M, Hoven CW. Parental Work-Related Factors Are Associated with Their Children's Psychopathology: A Study in Families of Israeli First Responders. (In Review).
- Geronazzo-Alman L, Musa GJ, Fan B, Cheslack-Postava K, Bavely R, Wicks J. Bresnagan M, Amsel L, Fiano E, Saxe G, Kummerfeld E, Ma S, Hoven CW. Neighborhood Characteristics and Psychiatric Disorders in the Aftermath of Mass Trauma: A Representative Study of New York City Public School Students After 9/11. (In Review)

References

1. Farfel M, DiGrande L, Brackbill R, Prann A, Cone J, Friedman S, Walker DJ, Pezeshki G, Thomas P, Galea S, Williamson D, Frieden TR, Thorpe L. An overview of 9/11 experiences and respiratory and mental health conditions among World Trade Center Health Registry enrollees. *J Urban Health*. 2008;85(6):880-909.
2. DiGrande L, Neria Y, Brackbill RM, Pulliam P, Galea S. Long-term posttraumatic stress symptoms among 3,271 civilian survivors of the September 11, 2001, terrorist attacks on the World Trade Center. *Am J Epidemiol*. 2011;173(3):271-281.
3. Perrin MA, DiGrande L, Wheeler K, Thorpe L, Farfel M, Brackbill R. Differences in PTSD prevalence and associated risk factors among World Trade Center disaster rescue and recovery workers. *Am J Psychiatry*. 2007;164(9):1385-1394.
4. Bowler RM, Han H, Gocheva V, Nakagawa S, Alper H, DiGrande L, Cone JE. Gender differences in probable posttraumatic stress disorder among police responders to the 2001 World Trade Center terrorist attack. *Am J Ind Med*. 2010;53(12):1186-1196.
5. Schwarzer R, Bowler RM, Cone JE. Social integration buffers stress in New York police after the 9/11 terrorist attack. *Anxiety Stress Coping*. 2014;27(1):18-26.
6. Bowler RM, Harris M, Li J, Gocheva V, Stellman SD, Wilson K, Alper H, Schwarzer R, Cone JE. Longitudinal mental health impact among police responders to the 9/11 terrorist attack. *Am J Ind Med*. 2012;55(4):297-312.
7. Brackbill RM, Hadler JL, DiGrande L, Ekenga CC, Farfel MR, Friedman S, Perlman SE, Stellman SD, Walker DJ, Wu D, Yu S, Thorpe LE. Asthma and posttraumatic stress symptoms 5 to 6 years following exposure to the World Trade Center terrorist attack. *Jama*. 2009;302(5):502-516.
8. Caramanica K, Brackbill RM, Stellman SD, Farfel MR. Posttraumatic Stress Disorder after Hurricane Sandy among Persons Exposed to the 9/11 Disaster. *Int J Emerg Ment Health*. 2015;17(1):356-362.
9. Maslow CB, Caramanica K, Welch AE, Stellman SD, Brackbill RM, Farfel MR. Trajectories of Scores on a Screening Instrument for PTSD Among World Trade Center Rescue, Recovery, and Clean-Up Workers. *J Trauma Stress*. 2015;28(3):198-205.
10. Caramanica K, Brackbill RM, Liao T, Stellman SD. Comorbidity of 9/11-related PTSD and depression in the World Trade Center Health Registry 10-11 years postdisaster. *J Trauma Stress*. 2014;27(6):680-688.
11. Welch AE, Caramanica K, Maslow CB, Cone JE, Farfel MR, Keyes KM, Stellman SD, Hasin DS. Frequent binge drinking five to six years after exposure to 9/11: findings from the World Trade Center Health Registry. *Drug Alcohol Depend*. 2014;140:1-7.
12. Miller-Archie SA, Jordan HT, Ruff RR, Chamany S, Cone JE, Brackbill RM, Kong J, Ortega F, Stellman SD. Posttraumatic stress disorder and new-onset diabetes among adult survivors of the World Trade Center disaster. *Prev Med*. 2014;66:34-38.

13. Jordan HT, Stellman SD, Morabia A, Miller-Archie SA, Alper H, Laskaris Z, Brackbill RM, Cone JE. Cardiovascular disease hospitalizations in relation to exposure to the September 11, 2001 World Trade Center disaster and posttraumatic stress disorder. *J Am Heart Assoc.* 2013;2(5):e000431.
14. Li J, Brackbill RM, Stellman SD, Farfel MR, Miller-Archie SA, Friedman S, Walker DJ, Thorpe LE, Cone J. Gastroesophageal reflux symptoms and comorbid asthma and posttraumatic stress disorder following the 9/11 terrorist attacks on World Trade Center in New York City. *Am J Gastroenterol.* 2011;106(11):1933-1941.
15. Gargano LM, Caramanica K, Sisco S, Brackbill RM, Stellman SD. Exposure to the World Trade Center Disaster and 9/11-Related Post-Traumatic Stress Disorder and Household Disaster Preparedness. *Disaster Med Public Health Prep.* 2015;9(6):625-633.
16. Brackbill RM, Stellman SD, Perlman SE, Walker DJ, Farfel MR. Mental health of those directly exposed to the World Trade Center disaster: unmet mental health care need, mental health treatment service use, and quality of life. *Soc Sci Med.* 2013;81:110-114.
17. Ghuman SJ, Brackbill RM, Stellman SD, Farfel MR, Cone JE. Unmet mental health care need 10-11 years after the 9/11 terrorist attacks: 2011-2012 results from the World Trade Center Health Registry. *BMC Public Health.* 2014;14:491.
18. Perlman SE, Friedman S, Galea S, Nair HP, Eros-Sarnyai M, Stellman SD, Hon J, Greene CM. Short-term and medium-term health effects of 9/11. *Lancet.* 2011;378(9794):925-934.
19. Hoven CW, Duarte CS, Wu P, Doan T, Singh N, Mandell DJ, Bin F, Teichman Y, Teichman M, Wicks J, Musa G, Cohen P. Parental exposure to mass violence and child mental health: the First Responder and WTC Evacuee Study. *Clin Child Fam Psychol Rev.* 2009;12(2):95-112.
20. Hyman SE. Can neuroscience be integrated into the DSM-V? *Nat Rev Neurosci.* 2007;8(9):725-732.
21. Sanislow CA, Pine DS, Quinn KJ, Kozak MJ, Garvey MA, Heinssen RK, Wang PS, Cuthbert BN. Developing constructs for psychopathology research: research domain criteria. *J Abnorm Psychol.* 2010;119(4):631-639.
22. Cuthbert BN, Insel TR. Toward the future of psychiatric diagnosis: the seven pillars of RDoC. *BMC Med.* 2013;11:126.
23. National Institute of Mental Health. Research Domain Criteria (RDoC). <https://www.nimh.nih.gov/research-priorities/rdoc/index.shtml>.
24. Insel T, Cuthbert B, Garvey M, Heinssen R, Pine DS, Quinn K, Sanislow C, Wang P. Research domain criteria (RDoC): toward a new classification framework for research on mental disorders. *Am J Psychiatry.* 2010;167(7):748-751.
25. Sumner JA, Powers A, Jovanovic T, Koenen KC. Genetic influences on the neural and physiological bases of acute threat: A research domain criteria (RDoC) perspective. *Am J Med Genet B Neuropsychiatr Genet.* 2015.
26. Hess JL, Kawaguchi DM, Wagner KE, Faraone SV, Glatt SJ. The influence of genes on "positive valence systems" constructs: A systematic review. *Am J Med Genet B Neuropsychiatr Genet.* 2015.

27. Gur RC, Gur RE. Social cognition as an RDoC domain. *Am J Med Genet B Neuropsychiatr Genet.* 2016;171(1):132-141.
28. Glahn DC, Knowles EEM, Pearlson GD. Genetics of cognitive control: Implications for NIMH's research domain criteria initiative. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics.* 2016;171(1):111-120.
29. Blanchard EB, Jones-Alexander J, Buckley TC, Forneris CA. Psychometric properties of the PTSD checklist (PCL). *Behaviour Research and Therapy.* 1996;34(8):669-673.
30. Aalto AM, Elovainio M, Kivimäki M, Uutela A, Pirkola S. The Beck Depression Inventory and General Health Questionnaire as measures of depression in the general population: a validation study using the Composite International Diagnostic Interview as the gold standard. *Psychiatry Res.* 2012;197(1-2):163-171.
31. Kessler RC, Abelson J, Demler O, Escobar JI, Gibbon M, Guyer ME, Howes MJ, Jin R, Vega WA, Walters EE, Wang P, Zaslavsky A, Zheng H. Clinical calibration of DSM-IV diagnoses in the World Mental Health (WMH) version of the World Health Organization (WHO) Composite International Diagnostic Interview (WMHCIDI). *Int J Methods Psychiatr Res.* 2004;13(2):122-139.
32. Kessler RC, Ustun TB. The World Mental Health (WMH) Survey Initiative Version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). *Int J Methods Psychiatr Res.* 2004;13(2):93-121.
33. Haro JM, Arbabzadeh-Bouchez S, Brugha TS, de Girolamo G, Guyer ME, Jin R, Lepine JP, Mazzi F, Reneses B, Vilagut G, Sampson NA, Kessler RC. Concordance of the Composite International Diagnostic Interview Version 3.0 (CIDI 3.0) with standardized clinical assessments in the WHO World Mental Health surveys. *Int J Methods Psychiatr Res.* 2006;15(4):167-180.
34. Shaffer D, Fisher P, Lucas CP, Dulcan MK, Schwab-Stone ME. NIMH Diagnostic Interview Schedule for Children Version IV (NIMH DISC-IV): description, differences from previous versions, and reliability of some common diagnoses. *J Am Acad Child Adolesc Psychiatry.* 2000;39(1):28-38.
35. Lucas CP, Zhang H, Fisher PW, Shaffer D, Regier DA, Narrow WE, Bourdon K, Dulcan MK, Canino G, Rubio-Stipec M, Lahey BB, Friman P. The DISC Predictive Scales (DPS): efficiently screening for diagnoses. *J Am Acad Child Adolesc Psychiatry.* 2001;40(4):443-449.
36. Wiesner M, Windle M, Kanouse DE, Elliott MN, Schuster MA. DISC Predictive Scales (DPS): Factor structure and uniform differential item functioning across gender and three racial/ethnic groups for ADHD, conduct disorder, and oppositional defiant disorder symptoms. *Psychol Assess.* 2015;27(4):1324-1336.
37. Hoven CW, Duarte CS, Mandell DJ, Musa G, Wicks J, Wu P. *WTC-NYC Child and Adolescent Questionnaire.* NY: Columbia University-New York State Psychiatric Institute.; 2002.
38. Hoven CW, Duarte CS, Lucas CP, Wu P, Mandell DJ, Goodwin RD, Cohen M, Balaban V, Woodruff BA, Bin F, Musa GJ, Mei L, Cantor PA, Aber JL, Cohen P, Susser E. Psychopathology among New York city public school children 6 months after September 11. *Arch Gen Psychiatry.* 2005;62(5):545-552.

39. Weiss DS, Brunet A, Best SR, Metzler TJ, Liberman A, Pole N, Fagan JA, Marmar CR. Frequency and Severity Approaches to Indexing Exposure to Trauma: The Critical Incident History Questionnaire for Police Officers. *Journal of Traumatic Stress*. 2010;23(6):734-743.
40. Chopko BA, Palmieri PA, Adams RE. Critical incident history questionnaire replication: frequency and severity of trauma exposure among officers from small and midsize police agencies. *J Trauma Stress*. 2015;28(2):157-161.
41. Gray MJ, Litz BT, Hsu JL, Lombardo TW. Psychometric properties of the life events checklist. *Assessment*. 2004;11(4):330-341.
42. Goodman SH, Hoven CW, Narrow WE, Cohen P, Fielding B, Alegria M, Leaf PJ, Kandel D, Horwitz SM, Bravo M, Moore R, Dulcan MK. Measurement of risk for mental disorders and competence in a psychiatric epidemiologic community survey: the National Institute of Mental Health Methods for the Epidemiology of Child and Adolescent Mental Disorders (MECA) Study. *Soc Psychiatry Psychiatr Epidemiol*. 1998;33(4):162-173.
43. Tiet QQ, Bird HR, Hoven CW, Moore R, Wu P, Wicks J, Jensen PS, Goodman S, Cohen P. Relationship between specific adverse life events and psychiatric disorders. *J Abnorm Child Psychol*. 2001;29(2):153-164.
44. Gershon RC, Wagster MV, Hendrie HC, Fox NA, Cook KF, Nowinski CJ. NIH toolbox for assessment of neurological and behavioral function. *Neurology*. 2013;80(11 Suppl 3):S2-6.
45. NIH Toolbox. Emotion.
<http://www.nihtoolbox.org/WhatAndWhy/Emotion/Pages/default.aspx>.
46. NIH Toolbox. Emotion Measures.
<http://www.nihtoolbox.org/WhatAndWhy/Emotion/emotionmeasures/Pages/default.aspx>.
47. Spielberger CD, Gorsuch RL, Lushene R, Vagg PR, Jacobs GA. *Manual for the State-Trait Anxiety Inventory*. Palo Alto, CA: Consulting Psychologists Press.; 1983.
48. Marks IM, Mathews AM. Brief standard self-rating for phobic patients. *Behav Res Ther*. 1979;17(3):263-267.
49. Cloninger CR. A systematic method for clinical description and classification of personality variants. A proposal. *Arch Gen Psychiatry*. 1987;44(6):573-588.
50. Cloninger CR, Svrakic DM, Przybeck TR. A psychobiological model of temperament and character. *Arch Gen Psychiatry*. 1993;50(12):975-990.
51. Cloninger CR. What are the different versions of the TCI?
<http://psychobiology.wustl.edu/what-are-the-different-versions-of-the-tci>.
52. Farmer RF, Goldberg LR. A psychometric evaluation of the revised Temperament and Character Inventory (TCI-R) and the TCI-140. *Psychol Assess*. 2008;20(3):281-291.
53. Cloninger CR. What does the TCI measure?
<http://psychobiology.wustl.edu/what-does-the-tci-measure>.
54. Cloninger CR. *The Temperament and Character Inventory—Revised*. St. Louis, MO: Center for Psychobiology of Personality, Washington University (Available from C. R. Cloninger, Washington University School of Medicine, Department of Psychiatry, PO Box 8134, St. Louis, MO, 63110). 1999.

55. Beck AT, Weissman A, Lester D, Trexler L. The measurement of pessimism: the hopelessness scale. *J Consult Clin Psychol*. 1974;42(6):861-865.
56. Gard D, E. State Version of the Temporal Experience of Pleasure Scale. <http://online.sfsu.edu/dgard/researchprojects.htm>.
57. Gard DE, Gard MG, Kring AM, John OP. Anticipatory and consummatory components of the experience of pleasure: A scale development study. *Journal of Research in Personality*. 2006;40(6):1086-1102.
58. Gard DE, Kring AM, Gard MG, Horan WP, Green MF. Anhedonia in schizophrenia: distinctions between anticipatory and consummatory pleasure. *Schizophr Res*. 2007;93(1-3):253-260.
59. Carver CS, White TL. Behavioral-Inhibition, Behavioral Activation, and Affective Responses to Impending Reward and Punishment - the Bis Bas Scales. *Journal of Personality and Social Psychology*. 1994;67(2):319-333.
60. Rothbart MK. The Adult Temperament Questionnaire (ATQ). <http://www.bowdoin.edu/~sputnam/rothbart-temperament-questionnaires/instrument-descriptions/adult-temperament-questionnaire.html>.
61. Evans DE, Rothbart MK. Development of a model for adult temperament. *Journal of Research in Personality*. 2007;41(4):868-888.
62. Rothbart MK, Ahadi SA, Evans DE. Temperament and personality: origins and outcomes. *J Pers Soc Psychol*. 2000;78(1):122-135.
63. Patton JH, Stanford MS, Barratt ES. Factor structure of the Barratt impulsiveness scale. *J Clin Psychol*. 1995;51(6):768-774.
64. Stanford MS, Mathias CW, Dougherty DM, Lake SL, Anderson NE, Patton JH. Fifty years of the Barratt Impulsiveness Scale: An update and review. *Personality and Individual Differences*. 2009;47(5):385-395.
65. Grant AM, Franklin J, Langford P. The self-reflection and insight scale: A new measure of private self-consciousness. *Social Behavior and Personality*. 2002;30(8):821-835.
66. Bagby RM, Parker JD, Taylor GJ. The twenty-item Toronto Alexithymia Scale--I. Item selection and cross-validation of the factor structure. *J Psychosom Res*. 1994;38(1):23-32.
67. Bagby RM, Taylor GJ, Parker JD. The Twenty-item Toronto Alexithymia Scale--II. Convergent, discriminant, and concurrent validity. *J Psychosom Res*. 1994;38(1):33-40.
68. Parker JD, Taylor GJ, Bagby RM. The 20-Item Toronto Alexithymia Scale. III. Reliability and factorial validity in a community population. *J Psychosom Res*. 2003;55(3):269-275.
69. Spreng RN, McKinnon MC, Mar RA, Levine B. The Toronto Empathy Questionnaire: scale development and initial validation of a factor-analytic solution to multiple empathy measures. *J Pers Assess*. 2009;91(1):62-71.
70. Hommer RE, Meyer A, Stoddard J, Connolly ME, Mogg K, Bradley BP, Pine DS, Leibenluft E, Brotman MA. Attention bias to threat faces in severe mood dysregulation. *Depress Anxiety*. 2014;31(7):559-565.
71. Bar-Haim Y, Lamy D, Pergamin L, Bakermans-Kranenburg MJ, van IMH. Threat-related attentional bias in anxious and nonanxious individuals: a meta-analytic study. *Psychol Bull*. 2007;133(1):1-24.

72. Mogg K, Bradley BP, Williams R. Attentional bias in anxiety and depression: the role of awareness. *Br J Clin Psychol*. 1995;34 (Pt 1):17-36.
73. Mathews A, Ridgeway V, Williamson DA. Evidence for attention to threatening stimuli in depression. *Behav Res Ther*. 1996;34(9):695-705.
74. Hankin BL, Gibb BE, Abela JRZ, Flory K. Selective Attention to Affective Stimuli and Clinical Depression Among Youths: Role of Anxiety and Specificity of Emotion. *Journal of Abnormal Psychology*. 2010;119(3):491-501.
75. Salum GA, Mogg K, Bradley BP, Gadelha A, Pan P, Tamanaha AC, Moriyama T, Graeff-Martins AS, Jarros RB, Polanczyk G, do Rosario MC, Leibenluft E, Rohde LA, Manfro GG, Pine DS. Threat bias in attention orienting: evidence of specificity in a large community-based study. *Psychol Med*. 2013;43(4):733-745.
76. Waters AM, Henry J, Mogg K, Bradley BP, Pine DS. Attentional bias towards angry faces in childhood anxiety disorders. *Journal of Behavior Therapy and Experimental Psychiatry*. 2010;41(2):158-164.
77. Wald I, Degnan KA, Gorodetsky E, Charney DS, Fox NA, Fruchter E, Goldman D, Lubin G, Pine DS, Bar-Haim Y. Attention to threats and combat-related posttraumatic stress symptoms: prospective associations and moderation by the serotonin transporter gene. *JAMA Psychiatry*. 2013;70(4):401-408.
78. Beevers CG, Lee HJ, Wells TT, Ellis AJ, Telch MJ. Association of predeployment gaze bias for emotion stimuli with later symptoms of PTSD and depression in soldiers deployed in Iraq. *Am J Psychiatry*. 2011;168(7):735-741.
79. Lindstrom KM, Mandell DJ, Musa GJ, Britton JC, Sankin LS, Mogg K, Bradley BP, Ernst M, Doan T, Bar-Haim Y, Leibenluft E, Pine DS, Hoven CW. Attention orientation in parents exposed to the 9/11 terrorist attacks and their children. *Psychiatry Res*. 2011;187(1-2):261-266.
80. Iacoviello BM, Wu G, Abend R, Murrough JW, Feder A, Fruchter E, Levinstein Y, Wald I, Bailey CR, Pine DS, Neumeister A, Bar-Haim Y, Charney DS. Attention bias variability and symptoms of posttraumatic stress disorder. *J Trauma Stress*. 2014;27(2):232-239.
81. Naim R, Wald I, Lior A, Pine DS, Fox NA, Sheppes G, Halpern P, Bar-Haim Y. Perturbed threat monitoring following a traumatic event predicts risk for post-traumatic stress disorder. *Psychol Med*. 2014;44(10):2077-2084.
82. Eldar S, Ricon T, Bar-Haim Y. Plasticity in attention: implications for stress response in children. *Behav Res Ther*. 2008;46(4):450-461.
83. MacLeod C, Rutherford E, Campbell L, Ebsworthy G, Holker L. Selective attention and emotional vulnerability: assessing the causal basis of their association through the experimental manipulation of attentional bias. *J Abnorm Psychol*. 2002;111(1):107-123.
84. White LK, Suway JG, Pine DS, Bar-Haim Y, Fox NA. Cascading effects: the influence of attention bias to threat on the interpretation of ambiguous information. *Behav Res Ther*. 2011;49(4):244-251.
85. Waters AM, Mogg K, Bradley BP, Pine DS. Attentional bias for emotional faces in children with generalized anxiety disorder. *J Am Acad Child Adolesc Psychiatry*. 2008;47(4):435-442.

86. Bradley BP, Mogg K, White J, Groom C, de Bono J. Attentional bias for emotional faces in generalized anxiety disorder. *Br J Clin Psychol.* 1999;38 (Pt 3):267-278.
87. Pine DS, Mogg K, Bradley BP, Montgomery L, Monk CS, McClure E, Guyer AE, Ernst M, Charney DS, Kaufman J. Attention bias to threat in maltreated children: implications for vulnerability to stress-related psychopathology. *Am J Psychiatry.* 2005;162(2):291-296.
88. Monk CS, Nelson EE, McClure EB, Mogg K, Bradley BP, Leibenluft E, Blair RJ, Chen G, Charney DS, Ernst M, Pine DS. Ventrolateral prefrontal cortex activation and attentional bias in response to angry faces in adolescents with generalized anxiety disorder. *Am J Psychiatry.* 2006;163(6):1091-1097.
89. Brotman MA, Rich BA, Schmajuk M, Reising M, Monk CS, Dickstein DP, Mogg K, Bradley BP, Pine DS, Leibenluft E. Attention bias to threat faces in children with bipolar disorder and comorbid lifetime anxiety disorders. *Biol Psychiatry.* 2007;61(6):819-821.
90. Peckham AD, McHugh RK, Otto MW. A meta-analysis of the magnitude of biased attention in depression. *Depress Anxiety.* 2010;27(12):1135-1142.
91. Britton JC, Bar-Haim Y, Carver FW, Holroyd T, Norcross MA, Detloff A, Leibenluft E, Ernst M, Pine DS. Isolating neural components of threat bias in pediatric anxiety. *J Child Psychol Psychiatry.* 2012;53(6):678-686.
92. Figner B, Weber, E. U., Steffener, J. , Krosch, A., Wager, T. D., Johnson, E. J. . Framing the future first: Brain mechanisms of increased patience in intertemporal choice. Submitted.
93. Figner B, Knoch D, Johnson EJ, Krosch AR, Lisanby SH, Fehr E, Weber EU. Lateral prefrontal cortex and self-control in intertemporal choice. *Nat Neurosci.* 2010;13(5):538-539.
94. Gianotti LR, Figner, B., Ebstein, R. P., Knoch, D. Why Some People Discount More than Others: Baseline Activation in the Dorsal PFC Mediates the Link between COMT Genotype and Impatient Choice. *Frontiers in Decision Neuroscience.* 2012;6.
95. Figner B, Johnson, E. J., Lai, G., Krosch, A. R., Steffener, J., & Weber, E. U. . Asymmetries in intertemporal discounting. Neural systems and the directional evaluation of immediate vs future rewards. *Meeting of the Society for Neuroeconomics.* Park City, USA.; 2008.
96. Decker JH, Figner B, Steinglass JE. On Weight and Waiting: Delay Discounting in Anorexia Nervosa Pretreatment and Posttreatment. *Biol Psychiatry.* 2015;78(9):606-614.
97. Volkow ND, Baler RD. NOW vs LATER brain circuits: implications for obesity and addiction. *Trends Neurosci.* 2015;38(6):345-352.
98. Volkow ND, Wang GJ, Tomasi D, Baler RD. The addictive dimensionality of obesity. *Biol Psychiatry.* 2013;73(9):811-818.
99. Volkow ND, Wang GJ, Tomasi D, Baler RD. Obesity and addiction: neurobiological overlaps. *Obes Rev.* 2013;14(1):2-18.
100. Story GW, Vlaev I, Seymour B, Darzi A, Dolan RJ. Does temporal discounting explain unhealthy behavior? A systematic review and reinforcement learning perspective. *Frontiers in Behavioral Neuroscience.* 2014;8.

101. Hamilton KR, Potenza MN. Relations among Delay Discounting, Addictions, and Money Mismanagement: Implications and Future Directions. *American Journal of Drug and Alcohol Abuse*. 2012;38(1):30-42.
102. Epstein LH, Salvy SJ, Carr KA, Dearing KK, Bickel WK. Food reinforcement, delay discounting and obesity. *Physiology & Behavior*. 2010;100(5):438-445.
103. MacKillop J. Integrating Behavioral Economics and Behavioral Genetics: Delayed Reward Discounting as an Endophenotype for Addictive Disorders. *Journal of the Experimental Analysis of Behavior*. 2013;99(1):14-31.
104. Reynolds B. A review of delay-discounting research with humans: relations to drug use and gambling. *Behavioural Pharmacology*. 2006;17(8):651-667.
105. Weber EU, Johnson EJ, Milch KF, Chang H, Brodscholl JC, Goldstein DG. Asymmetric discounting in intertemporal choice - A query-theory account. *Psychological Science*. 2007;18(6):516-523.
106. Crone EA, van Duijvenvoorde AC, Peper JS. Annual Research Review: Neural contributions to risk-taking in adolescence - developmental changes and individual differences. *J Child Psychol Psychiatry*. 2016;57(3):353-368.
107. Gladwin TE, Figner B, Crone EA, Wiers RW. Addiction, adolescence, and the integration of control and motivation. *Dev Cogn Neurosci*. 2011;1(4):364-376.
108. Dayan J, Bernard A, Olliac B, Mailhes AS, Kermarrec S. Adolescent brain development, risk-taking and vulnerability to addiction. *J Physiol Paris*. 2010;104(5):279-286.
109. Casey BJ, Jones RM. Neurobiology of the adolescent brain and behavior: implications for substance use disorders. *J Am Acad Child Adolesc Psychiatry*. 2010;49(12):1189-1201; quiz 1285.
110. Figner B, Mackinlay RJ, Wilkening F, Weber EU. Affective and deliberative processes in risky choice: age differences in risk taking in the Columbia Card Task. *J Exp Psychol Learn Mem Cogn*. 2009;35(3):709-730.
111. Brackbill RM, Thorpe LE, DiGrande L, Perrin M, Sapp JH, 2nd, Wu D, Campolucci S, Walker DJ, Cone J, Pulliam P, Thalji L, Farfel MR, Thomas P. Surveillance for World Trade Center disaster health effects among survivors of collapsed and damaged buildings. *MMWR Surveill Summ*. 2006;55(2):1-18.
112. Geronazzo-Alman L, Guffanti G, Fan B, Duarte CS, Musa GJ, Poli M, Hoven CW. Patterns of co-occurrence of internalizing and externalizing symptoms in 6733 New York City students exposed to 9/11. *World Trade Center Health Registry Roundtable*. New York, October 29, 2013.
113. Geronazzo-Alman L, Guffanti G, Fan B, Bresnahan M, Musa GJ, Duarte CS, Hoven CW. Patterns of comorbidity between internalizing and externalizing symptoms in 8236 youth six months after 9/11. In preparation.
114. Rousseau C, Jamil U, Bhui K, Boudjarane M. Consequences of 9/11 and the war on terror on children's and young adult's mental health: a systematic review of the past 10 years. *Clin Child Psychol Psychiatry*. 2015;20(2):173-193.
115. Neria Y, DiGrande L, Adams BG. Posttraumatic stress disorder following the September 11, 2001, terrorist attacks: a review of the literature among highly exposed populations. *Am Psychol*. 2011;66(6):429-446.
116. Endara SM, Ryan MA, Seveck CJ, Conlin AM, Macera CA, Smith TC. Does acute maternal stress in pregnancy affect infant health outcomes? Examination of a

- large cohort of infants born after the terrorist attacks of September 11, 2001. *BMC Public Health*. 2009;9:252.
117. Lauderdale DS. Birth outcomes for Arabic-named women in California before and after September 11. *Demography*. 2006;43(1):185-201.
 118. Bannon W, DeVoe ER, Klein TP, Miranda C. Gender as a Moderator of the Relationship between Child Exposure to the World Trade Centre Disaster and Behavioural Outcomes. *Child and Adolescent Mental Health*. 2009;14(3):121-126.
 119. DeVoe ER, Klein TP, Bannon W, Miranda-Julian C. Young Children in the Aftermath of the World Trade Center Attacks. *Psychological Trauma-Theory Research Practice and Policy*. 2011;3(1):1-7.
 120. Fairbrother G, Stuber J, Galea S, Fleischman AR, Pfefferbaum B. Posttraumatic stress reactions in new York City children after the September 11, 2001, terrorist attacks. *Ambul Pediatr*. 2003;3(6):304-311.
 121. Stein BD, Elliott MN, Jaycox LH, Collins RL, Berry SH, Klein DJ, Schuster MA. A national longitudinal study of the psychological consequences of the September 11, 2001 terrorist attacks: reactions, impairment, and help-seeking. *Psychiatry*. 2004;67(2):105-117.
 122. Calderoni ME, Alderman EM, Silver EJ, Bauman LJ. The mental health impact of 9/11 on inner-city high school students 20 miles north of Ground Zero. *J Adolesc Health*. 2006;39(1):57-65.
 123. Mullett-Hume E, Anshel D, Guevara V, Cloitre M. Cumulative trauma and posttraumatic stress disorder among children exposed to the 9/11 World Trade Center attack. *Am J Orthopsychiatry*. 2008;78(1):103-108.
 124. Wu P, Duarte CS, Mandell DJ, Fan B, Liu X, Fuller CJ, Musa G, Cohen M, Cohen P, Hoven CW. Exposure to the World Trade Center attack and the use of cigarettes and alcohol among New York City public high-school students. *Am J Public Health*. 2006;96(5):804-807.
 125. Chemtob CM, Nomura Y, Josephson L, Adams RE, Sederer L. Substance use and functional impairment among adolescents directly exposed to the 2001 World Trade Center attacks. *Disasters*. 2009;33(3):337-352.
 126. Aber JL, Gershoff ET, Ware A, Kotler JA. Estimating the effects of September 11th and other forms of violence on the mental health and social development of New York City's youth: A matter of context. *Applied Developmental Science*. 2004;8:111-129.
 127. Guffanti G, Geronazzo-Alman L, Fan B, Duarte CS, Musa GJ, Hoven CW. Homogeneity of Severe Posttraumatic Stress Disorder Symptom Profiles in Children and Adolescents Across Gender, Age and 9/11-related Traumatic Experiences. *Journal of Traumatic Stress* in press.
 128. Geronazzo-Alman L, Guffanti G, Fan B, Duarte CS, Wu P, Musa GJ, Cohen P, Poli M, Hoven CW. Latent Class Analysis of PTSD symptoms among 6,733 New York City students exposed to 9/11. *20th European Congress of Psychiatry*. Prague, Czech Republic, 3-6 March, 2012.; 2012.
 129. Geronazzo-Alman L, Guffanti G, Fan B, Duarte CS, Wu P, Musa GJ, Cohen P, Poli M, Hoven CW. Latent Class Analysis of PTSD symptoms among 6,733 New

- York City students exposed to 9/11. *World Trade Center Health Registry Roundable*. New York, October 29, 2013.; 2013.
130. Rosen CS, Cohen M. Subgroups of New York City children at high risk of PTSD after the September 11 attacks: a signal detection analysis. *Psychiatr Serv*. 2010;61(1):64-69.
 131. Duarte CS, Hoven CW, Wu P, Bin F, Cotel S, Mandell DJ, Nagasawa M, Balaban V, Wernikoff L, Markenson D. Posttraumatic stress in children with first responders in their families. *J Trauma Stress*. 2006;19(2):301-306.
 132. Comer JS, Fan B, Duarte CS, Wu P, Musa GJ, Mandell DJ, Albano AM, Hoven CW. Attack-related life disruption and child psychopathology in New York City public schoolchildren 6-months post-9/11. *J Clin Child Adolesc Psychol*. 2010;39(4):460-469.
 133. Mirnezami R, Nicholson J, Darzi A. Preparing for precision medicine. *N Engl J Med*. 2012;366(6):489-491.
 134. National Academy of Sciences. *Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease*. Washington, DC: National Academies Press; 2011.
 135. Montalvo-Ortiz JL, Gelernter J, Hudziak J, Kaufman J. RDoC and translational perspectives on the genetics of trauma-related psychiatric disorders. *Am J Med Genet B Neuropsychiatr Genet*. 2015.
 136. Insel TR, Wang PS. Rethinking mental illness. *Jama*. 2010;303(19):1970-1971.
 137. Etkin A, Cuthbert B. Beyond the DSM: development of a transdiagnostic psychiatric neuroscience course. *Acad Psychiatry*. 2014;38(2):145-150.
 138. Cuthbert BN. The RDoC framework: facilitating transition from ICD/DSM to dimensional approaches that integrate neuroscience and psychopathology. *World Psychiatry*. 2014;13(1):28-35.

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?

No

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
HOVENC	Y	Hoven, Christina W.	MPH,MS,MOTH,DRPH	PD/PI	2.4	0.0	0.0			NA
GERONAZZO	Y	Geronazzo-Alman, Lupo	PHD	PD/PI	4.7	0.0	0.0			NA
MUSAGE	Y	Musa, George Jose	PHD,MA,BA	Co-Investigator	1.4	0.0	0.0			NA
	N	Bresnahan, Michaeline		Faculty	1.2	0.0	0.0			NA
	N	Harp, Derek		Non-Student Research Assistant	4.2	0.0	0.0			NA
	N	Ouyang, Bensheng		Assistant Data Manager	1.9	0.0	0.0			NA
	N	Xiaoxiao, Sun		Non-Student Research Assistant	2.1	0.0	0.0			NA
	N	Lucagan, Diane		Recruitment Coordinator	2.1	0.0	0.0			NA
	N	Cuchacovich, Sharon		Non-Student Research Assistant	3.2	0.0	0.0			NA
	N	Tang, Huilan		Non-Student Research Assistant	2.8	0.0	0.0			NA
	N	Ryan, Megan		Field Director	1.9	0.0	0.0			NA
	N	Keating, William		Non-Student Research Assistant	3.7	0.0	0.0			NA
	N	Cole, Hugh		Non-Student Research Assistant	3.1	0.0	0.0			NA
	N	Wasserman, Camilla		Non-Student Research Assistant	2.4	0.0	0.0			NA
	N	Khan, Aziza		Field Coordinator	3.2	0.0	0.0			NA
	N	Duque-Villa, Yuly		Non-Student Research Assistant	2.6	0.0	0.0			NA
	N	Zemeck, Heather		Non-Student Research Assistant	2.5	0.0	0.0			NA
	N	Bista, Kelsang		Non-Student	7.9	0.0	0.0			NA

				Research Assistant						
	N	Mahan, Janice		Non-Student Research Assistant	2.0	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:

FR_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:

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										
Asian										
Native Hawaiian or Other Pacific Islander										
Black or African American										
White										
More Than One Race										
Unknown or Not Reported										
Total										

I. OVERALL OUTCOMES

I.1 What were the outcomes of the award?

While psychiatric disorders (DSM) are known to be linked to traumatic exposure/s, families play a key role in modulating youth's reaction to terrorism and who may experience greater emotional impact from having a family member exposed than from being directly exposed themselves. Because DSM disorders do not map well onto emerging findings from genetics, systems neuroscience and behavioral science the NIMH initiated the Research Domain Criteria-(RDoC) project, as a new classification system with gene x environment (G×E) interactions with a major role in understanding etiological processes. The RDoC factors have never before been simultaneously taken into account with 9/11-related populations, which has the potential to move forward the field of translational research in WTC-exposed populations, especially within families, so that individualized treatments directed at etiologic mechanisms might soon be available to 9/11 and other trauma-exposed individuals.

Unfortunately, the COVID-19 Pandemic drastically impacted our ability to conduct the required in-home assessments. Eventually, a limited phone-based assessment was initiated resulting in a total lack of physical assessment. Consequently, the important contribution of this investigation was seriously and negatively impacted. It is hoped that future funding will provide for the continuation of this work which has already demonstrated its importance to understanding 9/11 exposure.