The Genetics PTSD:

New findings from the Psychiatric Genomics Consortium

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Why study the genetics of PTSD?
The idea that constitutional factors – those within the individual – influence response to trauma is not new.
ACUTE

By William Sargant
psychiatric

Eliot Slater, M.
clinical director

The acute cases of war demonstrated that men may break down if they are put under too much strain.

usual symptoms of the acute cases are terrifying bad dreams, tendency to be startled at the sound of an aeroplane going overhead or any sound resembling it. The noise of a train going past outside would make the patient jump perceptibly. In many cases there was an amnesia, more or less extensive, for the worst part of the past experiences. Individual cases
“There was evidence that the terrifying stresses of war tended to provoke anxiety states to a significantly preferential extent, but they did so far from regularly. A more important determinant of the type of response was the constitution of the individual, as shown by his family history, previous life, and personality.”

Eliot Slater, 1944
PTSD is heritable.
Twin studies rely on a natural experiment to assess heritability

Monozygotic twins: share 100% of their genes

Dizygotic twins: share 50% of their genes
PTSD heritability from twin studies is similar to other psychiatric disorders

Genetics provides foundational insights into biology that may eventually impact clinical care.
PTSD psychopharmacology: Progress needed

- The only FDA approved drugs for PTSD are the SSRIs: sertraline (Zoloft) and paroxetine (Paxil).
- Overall response rate estimated at about 60% with only 20-30% achieving complete remission

Most therapies developed through traditional approaches fail to have efficacy

Finding the genes and mutations that cause disease is the most reliable means of gaining the insights required

No novel therapies for neuropsych disorders
So how do we find genes for PTSD?
If we knew what the genes were, they’d be easy to find...

- 1991-2015 – the era of the candidate gene association study in PTSD
- Hallmarks: poor statistical practice, optimistic data interpretation, few if any reproducible results
- Outcome: little durable knowledge
Initial attempts to identify genes were not successful for complex diseases broadly . . .

Progress required an intellectual shift from Mendelian to complex trait genetics.
Complex trait genetics

- Instead of one gene determining a disease or trait, many genes each exert a small influence.

- None by themselves can “cause” or “explain” the disease or trait fully – but together with environmental influences combine to define an individual outcome.
Progress also required many fundamental paradigm shifts

- Understanding the genome and the fundamental nature of human variation

- Dramatic technological advances in our ability to access genomes
A genomic approach: Compare variation in entire genome in *many thousands* of genomes

- Human genome
  - People with and without disease
  - Define the genetic basis of the disease

- Tumor
  - Cells with and without cancer
  - Define the genetic basis of cancer

- Normal

- Microbial genome
  - Resistant
    - Microbes that do and do not kill
    - Define the genetic basis of virulence
  - Sensitive
Genome-wide association study implicates a novel RNA gene, the lincRNA AC068718.1, as a risk factor for post-traumatic stress disorder in women

Guia Guffanti\textsuperscript{a}, Sandro Galea\textsuperscript{b}, Lulu Yan\textsuperscript{b}, Andrea L. Roberts\textsuperscript{c}, Nadia Solovieff\textsuperscript{d,e,f}, Allison E. Aiello\textsuperscript{g}, Jordan W. Smoller\textsuperscript{d,e,f}, Immaculata De Vivo\textsuperscript{c}, Hardeep Ranu\textsuperscript{h}, Monica Uddin\textsuperscript{i,j}, Derek E. Wildman\textsuperscript{j}, Shaun Purcell\textsuperscript{d,e,f,k}, Karestan C. Koenen\textsuperscript{b,*}

ORIGINAL ARTICLE

A genome-wide association study of post-traumatic stress disorder identifies the retinoid-related orphan receptor alpha (\textit{RORA}) gene as a significant risk locus

MW Logue\textsuperscript{1,2,11}, C Baldwin\textsuperscript{1,3,11}, G Guffanti\textsuperscript{4}, E Melista\textsuperscript{3}, EJ Wolf\textsuperscript{5,6}, AF Reardon\textsuperscript{5}, M Uddin\textsuperscript{7,8}, D Wildman\textsuperscript{7,9}, S Galea\textsuperscript{10}, KC Koenen\textsuperscript{10} and MW Miller\textsuperscript{5,6}

ARCHIVAL REPORT

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Genome-wide Association Study Identifies New Susceptibility Loci for Posttraumatic Stress Disorder

Pingxing Xie, Henry R. Kranzler, Can Yang, Hongyu Zhao, Lindsay A. Farrer, and Joel Gelernter
Consortium approach needed

Patrick Sullivan

Psychiatric Genomics Consortium (and 800+ others)
Sample size accelerates discovery

2009: 2601 cases → 0 hits

2011: 9394 cases → 5 hits

2012: 25K cases → 62 hits

2014: 36K cases → 108 hits

Numbers presented represent samples of European Ancestry
Sample size accelerates discovery (2016)

- 60995 cases, 102860 controls
- 155 genome wide significant sites

Courtesy of Stephan Ripke
Initial molecular parts list for schizophrenia

- C4A
- CACNA1C
- CACNA1D
- CANCA1I
- CACNB2
- GRIA1
- GRIA2
- GRIN2A
- GRIN2B
- GRM3

... 150 genes so far for schizophrenia
Can the PGC provide a road map for PTSD?
PGC PTSD Working Group founded

Karestan Koenen  Kerry Ressler  Israel Liberzon  Caroline Nievergelt

Review Article
The Psychiatric Genomics Consortium Posttraumatic Stress Disorder Workgroup: Posttraumatic Stress Disorder Enters the Age of Large-Scale Genomic Collaboration

PGC PTSD: Data freeze I
PGC PTSD: Data freeze I

Lead Analyst
Laramie Duncan, PhD

Largest GWAS of PTSD ($N = 20070$) yields genetic overlap with schizophrenia and sex differences in heritability

The Psychiatric Genomics Consortium-Posttraumatic Stress Disorder group (PGC-PTSD) combined genome-wide case-control molecular genetic data across 11 multiethnic studies to quantify PTSD heritability, to examine potential shared genetic risk with schizophrenia, bipolar disorder, and major depressive disorder and to identify risk loci for PTSD. Examining 20,730 individuals, we report a molecular genetics-based heritability estimate ($h^2_{SNP}$) for European-American females of 29% that is similar to $h^2_{SNP}$ for schizophrenia and is substantially higher than $h^2_{SNP}$ in European-American males (estimate not distinguishable from zero). We found strong evidence of overlapping genetic risk between PTSD and schizophrenia along with more modest evidence of overlap with bipolar and major depressive disorder. No single-nucleotide polymorphisms (SNPs) exceeded genome-wide significance in the transethnic (overall) meta-analysis and we do not replicate previously reported associations. Still, SNP-level summary statistics made available here afford the best-available molecular genetic index of PTSD—for both European- and African-American individuals—and can be used in polygenic risk prediction and genetic correlation studies of diverse phenotypes. Publication of summary statistics for ~10,000 African Americans contributes to the broader goal of increased ancestral diversity in genomic data resources. In sum, the results demonstrate genetic influences on the development of PTSD, identify shared genetic risk between PTSD and other psychiatric disorders and highlight the importance of multiethnic/racial samples. As has been the case with schizophrenia and other complex genetic disorders, larger sample sizes are needed to identify specific risk loci.

Molecular Psychiatry advance online publication, 25 April 2017; doi:10.1038/mp.2017.77
Trajectories of GWAS discoveries

Freeze 1
EA ~2.4k
Freeze 1
trans-ethnic >5k

Goal: reach inflection point
PGC PTSD: Data freeze 2

- Data Freeze One
  - Pre-Banked Data
  - After CVB/SC RFA
GWAS analysis strategy needs to account for diverse ancestries

### 51 European Ancestry (EUA)
- MRSC
- ONGA
- NHS2
- GSDC
- FSCD
- COGA
- COGB
- SATU
- DEFE
- NHRV
- NSS1
- NSS2
- PPDS
- STRO
- GTPC*
- GMFR
- KSUD
- BOBA
- KMCT
- PORT
- GUTS
- NHSY
- RING
- BRY2

### 30 African Ancestry (AFA)
- MRSC
- SAFR
- DNHS
- GSDC
- FSCD
- COGB
- NSS1
- NSS2
- PPDS
- STRO
- GTPC*

### 6 Latino (AMA)
- MRSC
- NSS1
- NSS2
- PPDS
- STRO
- GTPC*

### Dataset Type
- Freeze 1
- CVB RFA
- GWAS summary data

### Studies analyzed together
- AMA
  - N = 5,703
  - 1,981 cases (34.7%)

### AFA meta-analysis
- N = 15,339
- 4,363 cases (28.4%)

### EUA meta-analysis
- N = 174,659
- 23,212 cases (13.3%)

### Meta-analysis across ancestry groups
- N = 195,701
- 29,556 cases (15.1%)
Three major findings:
1. PTSD is heritable.
PTSD is heritable

Heritability ($h^2$) Proportion of phenotypic variation accounted for by genetic variation.

SNP-chip heritability ($h^2_{SNP}$) Proportion of phenotypic variation accounted for by measured genetic variation.
SNP heritability is lower than twin heritability

<table>
<thead>
<tr>
<th>PGC Group</th>
<th>Cases</th>
<th>Hits</th>
<th>Twin h²</th>
<th>SNP h²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenia</td>
<td>60,995</td>
<td>155</td>
<td>81%</td>
<td>45%</td>
</tr>
<tr>
<td>Major depressive disorder</td>
<td>130,664</td>
<td>44</td>
<td>30%–40%</td>
<td>8.9%</td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>20,352</td>
<td>19</td>
<td>80%</td>
<td>21%</td>
</tr>
<tr>
<td>Attention deficit hyperactivity disorder</td>
<td>20,183</td>
<td>12</td>
<td>70%–80%</td>
<td>22%</td>
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<tr>
<td>Autism spectrum disorder</td>
<td>18,381</td>
<td>3</td>
<td>75%</td>
<td>12%</td>
</tr>
<tr>
<td>Anorexia nervosa</td>
<td>3,495</td>
<td>1</td>
<td>56%</td>
<td>~20%</td>
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<tr>
<td>Substance use disorders</td>
<td>12,798</td>
<td>1</td>
<td>50%</td>
<td>~8%</td>
</tr>
<tr>
<td>Tourette syndrome</td>
<td>4,232</td>
<td>1</td>
<td>60%–80%</td>
<td>58%</td>
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<tr>
<td>Obsessive-compulsive disorder</td>
<td>2,688</td>
<td>0</td>
<td>45%–65%</td>
<td>37%</td>
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<tr>
<td>Posttraumatic stress disorder</td>
<td>5,131</td>
<td>0</td>
<td>30%–40%</td>
<td>5%–35%</td>
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</tbody>
</table>

*Hits: independent associations reaching genome-wide significance. Twin h²: heritability estimated from twin studies. SNP h²: heritability estimated from results of genome-wide association studies (GWAS).*
PTSD is heritable, in the range found for major depression

<table>
<thead>
<tr>
<th>Group</th>
<th>Sample</th>
<th>N Cases</th>
<th>N Controls</th>
<th>$h^2_{snp}$</th>
<th>95% CI</th>
<th>z</th>
<th>p-value</th>
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<tbody>
<tr>
<td>All</td>
<td>PGC2</td>
<td>23,212</td>
<td>151,447</td>
<td>0.05</td>
<td>0.03 - 0.07</td>
<td>5.53</td>
<td>3.18E-08</td>
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<tr>
<td></td>
<td>PGC1.5</td>
<td>12,823</td>
<td>35,648</td>
<td>0.05</td>
<td>0.01 - 0.08</td>
<td>2.54</td>
<td>0.011</td>
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<tr>
<td></td>
<td>UKBB</td>
<td>10,389</td>
<td>115,799</td>
<td>0.17</td>
<td>0.14 - 0.21</td>
<td>8.75</td>
<td>2.06E-18</td>
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<tr>
<td>Men</td>
<td>PGC2</td>
<td>9,908</td>
<td>75,605</td>
<td>0.01</td>
<td>-0.03 - 0.05</td>
<td>0.49</td>
<td>0.63</td>
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<tr>
<td></td>
<td>PGC1.5</td>
<td>6,364</td>
<td>23,905</td>
<td>0.01</td>
<td>-0.05 - 0.07</td>
<td>0.39</td>
<td>0.69</td>
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<tr>
<td></td>
<td>UKBB</td>
<td>3,544</td>
<td>51,700</td>
<td>0.15</td>
<td>0.05 - 0.24</td>
<td>2.99</td>
<td>0.0014</td>
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<td>Women</td>
<td>PGC2</td>
<td>12,973</td>
<td>73,627</td>
<td>0.10</td>
<td>0.07 - 0.13</td>
<td>6.50</td>
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<tr>
<td></td>
<td>PGC1.5</td>
<td>6,128</td>
<td>9,528</td>
<td>0.21</td>
<td>0.11 - 0.31</td>
<td>4.20</td>
<td>2.66E-05</td>
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<tr>
<td></td>
<td>UKBB</td>
<td>6,845</td>
<td>64,099</td>
<td>0.19</td>
<td>0.13 - 0.25</td>
<td>6.36</td>
<td>2.00E-10</td>
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</tbody>
</table>

- Considerable range in SNP heritability
- SNP heritability women > men but not in UK Biobank
- Similar findings in subjects of African ancestry (using GCTA)
- SNP heritability of major depression 8.7% (Wray, 2018, Nature Genetics)
2. PTSD shares genetic risk with other psychiatric disorders, as well as other traits.
Polygenic risk score (PRS)

- A sum of trait-associated alleles across many genetic loci, weighted by effect size estimated from GWAS
- Useful for stratification by level of risk, by sub-phenotypes, for identifying overlap with other traits

Exemplary distribution of PRS
Genetic risk for PTSD is correlated with that for other mental disorders and traits

<table>
<thead>
<tr>
<th>Trait</th>
<th>A) PTSD</th>
<th>B) MDD</th>
<th>C) SCZ</th>
<th>D) BPD</th>
<th>E) ADHD</th>
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<td>ADHD</td>
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<tr>
<td>Autism spectrum disorder</td>
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<td>●</td>
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<tr>
<td>Bipolar disorder</td>
<td>●</td>
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<td>●</td>
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<tr>
<td>Daytime sleepiness</td>
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<td>●</td>
<td>●</td>
<td>●</td>
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<tr>
<td>Depressive symptoms</td>
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<tr>
<td>Insomnia</td>
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<td>PGC cross-disorder analysis</td>
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<td>Tiredness</td>
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Genetic Correlation ($r_g$)

Category
- Psychiatric
- Anthropometric
- Smoking Behaviour
- Reproductive
- Aging
- Education
- Autoimmune
- Cardiometabolic

Nievergelt et al. in prep.
3. PTSD remains underpowered, but the first probable hits are beginning to emerge.
Trajectories of GWAS discoveries

- Freeze 1
  - EA ~2.4k
- Freeze 1
  - trans-ethnic >5k
- Freeze 2
  - European >23.2k

Goal: reach inflection point

Adapted from Gratten et al. 2014
Summary of Freeze 2 Results

Freeze 2: 32K PTSD cases, 174K trauma controls
- 10x increase from Freeze 1

- First genome-wide significant hits
  
  GWAS in European ancestry:
  - N cases: 23,212; N controls: 151,447
  - N studies: 52
  - GWAS hits: 4

  GWAS in African ancestry:
  - N cases: 4,363; N controls: 10,976
  - N studies: 30
  - GWAS hits: 2

- 12 predicted genes
  - EUA: ZDHHC14, PARK2, KAZN, TMRM51-AS1, and ZNF813
  - AFA: LINC02335, MIR5007, TUC338, LINC02571, and HLA-B
  - Gene-based analyses: SH3RF3 and PODXL

Courtesy of Caroline Nievergelt
Summary of Freeze 2 Results

Heritability ($h^2_{SNP}$):
- in women: ~10-20%
- in men: lower

Significant genetic risk scores (PRS):

PGC-PTSD freeze 2 paper: on BioRxiv and in preparation for resubmission to Nature Neuroscience

Million Veteran Program (MVP)
- N = 146,660 EA
- Phenotype:
  - re-experiencing symptoms
- PGC2 GWAS hits:
  - no replication
- LDSC PGC2 vs. MVP:
  - $rg=0.8; p=2.85e-17$
-PRS prediction
  - at $P_T=0.88: p=2.4e-101$
At least three challenges need to be addressed in moving forward . . .
1. PTSD is still underpowered: Continue to increase sample size
Genome-wide association analyses identify 44 risk variants and refine the genetic architecture of major depression

Major depressive disorder (MDD) is a common illness accompanied by considerable morbidity, mortality, costs, and heightened risk of suicide. We conducted a genome-wide association meta-analysis based in 135,458 cases and 344,901 controls and identified 44 independent and significant loci. The genetic findings were associated with clinical features of major depression and implicated brain regions in gene splicing were enrolement with educational at putatively causal, where lesser or greater number and imply that a continu...
2. PTSD is conditional on trauma and heterogeneous: Refine trauma and PTSD phenotypes
Trauma exposure is heritable

Heritability for specific types of traumatic events

- Assaulative Violence: 20%
- Served in Southeast Asia: 50%
- Combat Exposure: 55%
- Awarded a Combat Medal: 60%

Stein et al. (2002) American Journal of Psychiatry
Lyons et al. (1995) American Journal of Medical Genetics
Heritability of childhood trauma

<table>
<thead>
<tr>
<th>Sample</th>
<th>N</th>
<th>$h^2_{\text{pp}}$</th>
<th>SE</th>
<th>z</th>
<th>P-value</th>
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<tbody>
<tr>
<td>UKBB</td>
<td>124,711</td>
<td>0.057</td>
<td>0.005</td>
<td>11.4</td>
<td>1.60E-32</td>
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<tr>
<td>PGC1.5</td>
<td>26,290</td>
<td>0.07</td>
<td>0.02</td>
<td>3.5</td>
<td>5.00E-04</td>
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<tr>
<td>PGC2</td>
<td>151,001</td>
<td>0.051</td>
<td>0.004</td>
<td>12.75</td>
<td>1.46E-43</td>
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</table>

Cross-Cohort Genetic Correlation: UKBB and PGC 1.5
- $rg = 0.62$
- P-value = 1.35e-06

Courtesy of Shareefa Dalvie
PTSD is heterogeneous

<table>
<thead>
<tr>
<th>Criterion*</th>
<th>Description</th>
<th>Specific examples</th>
<th>Requirements</th>
</tr>
</thead>
</table>
| Criterion A | Exposure to stressor | • Direct exposure  
• Witnessing trauma  
• Learning of a trauma  
• Repeat or extreme indirect exposure to aversive details | DSM-5 recognizes that exposure to trauma can occur either by direct or indirect confrontation with extreme trauma |
| Criterion B | Intrusion symptoms | • Recurrent memories  
• Traumatic nightmares  
• Disorientation | At least two of the following examples are required |
| Criterion C | Avoidance | • Efforts to avoid stimuli associated with trauma  
• numbing  
• Avoidance of activities  
• Avoidance of people or places  
• At least two of these six examples are required | |
| Criterion D |Alterations in arousal and reactivity | • Irritable and aggressive behaviour  
• Self-destructive and reckless behaviour  
• Hypervigilance  
• Exaggerated startle  
• Problems concentrating  
• Sleep disturbance | At least two of these six examples are required |

---

**high level of symptom profile heterogeneity**

"636,120 Ways to Have Posttraumatic Stress Disorder"

Galatzer-Levy and Bryant 2013

---

PTSD diagnosis: Crit. A plus 1B, 1C, 1D, 2D, 2E symptoms
Results from the Million Veterans Program CSP575b: GWAS of Reexperiencing in European Americans

N=146,660 European-American

Courtesy of Joel Gelernter, In Press, Nature Neuroscience
3. GWAS hits are not an end in themselves: Translation needed to improve patients’ lives
Genetic findings

Biology

Pathways / “read outs”

Rational drug discovery
Genetic findings inform follow-up studies.
Functional imaging and psychophysiology in the Grady Trauma Project

Amygdala Volume

- T carriers
- CC allele

rs115539978 SNP

Habituation of Startle

- Difference in Startle (μS)

rs115539978 SNP

Torsten Klengel
PCG PTSD Working Group

Complementary phenotypes:

Psychophysiology:
- fear conditioning
- fear extinction
- heart rate variability

Physical health:
- cardio-vascular
- metabolic syndrome

Imaging:
- Enigma consortium data
- structural brain MRI

Core phenotypes:
- PTSD
- trauma exposure
- demographics

Genome-wide genotyping:
- SNPs
- Ancestry inference

GWAS

Complimentary ‘omics’ data:

Copy number variants (CNVs)

Epigenetics
- Genome-wide methylation
  EWAS

Transcriptome
- Gene expression array / RNAseq

Microbiome

Nievergelt et al. Biol. Psychiatry 2018
From the population to clinical medicine

Goal: to provide durable insights into disease biology that ultimately impact clinical care
PGC PTSD Working Group Funding

Magali Haas (Cohen Veterans Bioscience)  
Caroline Nievergelt (Contact PI, NIMH grant)  
Steve Hyman (Stanley Center)
# Acknowledgments: MVP Results

| CSP#575B |
|-------------------|-------------------|-------------------|
| M. Aslan          | J. Gelernter      | S. Pyarajan       |
| D. Beck           | K. Harrington     | R. Quaden         |
| Z. Cheng          | J. Honerlaw       | K. Radhakrishnan  |
| Q. Chen           | G. Huang          | F. Sayward        |
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| K. Cho            | W. Lance          | M. Stein          |
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| P. Crutchfield    | Y. Nunez          | S. Whitbourne     |
| J. Deen           | T. O’Leary        | H. Zhao           |
| J.M. Gaziano      | R. Pietrzak       | R. Polimanti      |
## Acknowledgements: PGC PTSD Freeze 2

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<th>Brisbane twin study (QMR)</th>
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<td>VA Boston-National Center for PTSD Study (NCFT)</td>
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<td>Translational Research Center for TBI and Stress disorders</td>
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<td>Detroit Neighborhood Health Study (DNHS)</td>
<td>Readiness and Resilience in National Guard Soldiers (RINGS)</td>
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<td>Strong Star - Genetic and Environmental Contributions to Combat-Related PTSD</td>
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<td>Yale-Penn Study (Gelernter)</td>
<td>Biomarkers of Anxiety Disorders and Treatment Response – Sydney/Neuroimaging</td>
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<td>Family Study of Cocaine Dependence (FSCD)</td>
<td>CHOICE and OPT: Doubly Randomized Treatment Trials for PTSD (CHOICE and OPT)</td>
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<td>Grady Trauma Project (GTP)</td>
<td>O-cycloserine Iraq RCT (DCS Rothbaum)</td>
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<td>Collaborative Genetic Study of Nicotine Dependence (COGEND)</td>
<td>Neurobiology of Traumatic Dissociation and PTSD (Teicher)</td>
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<td>Injury Vulnerability and Fire studies (Bryant IVS and fire)</td>
<td>Northern Illinois University Trauma Study (NIU)</td>
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<td>Study of Aftereffects of Trauma: Understanding Response in National Guard (SATURN)</td>
<td>National Centre for Mental Health (NCMH Wales)</td>
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<td>Defining Essential Features of Neural Damage (DEFEND)</td>
<td>Genetic Predictors of Acute and Chronic Musculoskeletal Pain after Minor MVC (EA Crash)</td>
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<td>Women and Children's Health Study (WaATCH)</td>
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<td>Army STARRS (NSSI, NSS2, PPDS)</td>
<td>Shared Roots (South Africa)</td>
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<td>Genetics of Posttraumatic Stress Disorder/Substance Use Disorder (Delahanty, KSUD)</td>
<td>Biological Effects of Traumatic Experiences, Treatment and Recovery (BETER)</td>
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<td>Bounce Back Now (BBN)</td>
<td>South East Europe (SEE) - PTSD</td>
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<td>Child Trauma and Neural Systems Underlying Emotion Regulation (McLaughlin, KMCT)</td>
<td>Cohen Veterans Center Study (CVC)</td>
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<td>Estudo Nacional Sobre Saúde e Bem-estar Psicológico - WMH (Portugal)</td>
<td>Fort Campbell study</td>
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<td>Growing Up Today Study (GUTS)</td>
<td>GRACY: Genetic Research and Childbearing Year</td>
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<td>Pregnancy Outcomes, Maternal and Infant Study (PromIS)</td>
<td>A Cross-Sectional, Case-Control Study of the Physical Health Status of Vietnam Veterans with and without Posttraumatic Stress Disorder and Investigation of Genetics of PTSD (GMRF/QUT)</td>
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<td>Vietnam Era Twin Study of Aging (VETSA)</td>
<td>James J. Peters VA Genetic risk for PTSD (Yehuda)</td>
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<tr>
<td>Prospective research in stress-related military operations (PRISMO)</td>
<td>VA San Diego Randomized controlled psychotherapy trial (Risbourough/Norman)</td>
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<td>Mid-Atlantic Mental Illness Research Education and Clinical Center the study of Post-Deployment Mental Health Study (MIRE)</td>
<td>Ralph H Johnson VA Cortical Excitability: Biomarker and Endophenotype in Combat Related PTSD (WANG)</td>
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<td>Injury and Traumatic Stress Clinical Consortium (INTRuST)</td>
<td>UK Biobank</td>
</tr>
<tr>
<td>Danish military study</td>
<td>plus &gt;200 PGC PTSD GWAS collaborators</td>
</tr>
<tr>
<td>Danish i-PSYCH</td>
<td>NIH National Institute of Mental Health</td>
</tr>
<tr>
<td></td>
<td>STANLEY CENTER for Psychiatric Research at Broad Institute</td>
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<td>PGC Psychiatric Genomics Consortium</td>
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**UPCOMING TOPICS**

*SAVE THE DATE: Third Wednesday of the Month from 2-3PM (ET)*

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<tr>
<th>Date</th>
<th>Topic</th>
<th>Speaker</th>
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<tbody>
<tr>
<td>August 21</td>
<td><strong>Focal Brain Stimulation for PTSD</strong></td>
<td>Paul Holtzheimer, MD</td>
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<tr>
<td>September 18</td>
<td><strong>Treating PTSD and Cognitive Impairment from Traumatic Brain Injury</strong></td>
<td>Amy Jak, PhD</td>
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<tr>
<td>October 16</td>
<td><strong>Unconventional Interventions for PTSD: State of the Evidence</strong></td>
<td>Paul Holtzheimer, MD</td>
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<tr>
<td>November 20</td>
<td><strong>Addressing Sleep: A Strategy for Symptom Reduction &amp; Suicide Prevention?</strong></td>
<td>Wilfred Pigeon, PhD</td>
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<tr>
<td>December 18</td>
<td><strong>Treating Comorbid PTSD and Borderline Personality Disorder</strong></td>
<td>Melanie Harned, PhD, ABPP</td>
</tr>
<tr>
<td>January 15</td>
<td><strong>Dissociation, Somatization, and Other Challenging Presentations of PTSD</strong></td>
<td>Abigail Angkaw, PhD</td>
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</table>

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[www.ptsd.va.gov/consult](http://www.ptsd.va.gov/consult)