

Stakeholder concerns about ethical, legal, and social implications of the genetics of post-traumatic stress disorder (PTSD)

Brandy M. Fox, PhD, MSHCE



What is PTSD?

- Psychiatric condition manifested after exposure to traumatic event(s)
- Symptoms present for > 1 month; include flashbacks, recurring nightmares, intrusive thoughts, hyperarousal, and avoidance and affective numbing
- Significant distress, disruption of normal activities
- 636,120 Ways to have PTSD (Galatzer-Levy & Bryant 2013)
- Prevalence differs by sex:
10-12% incidence for ♀
5-6% incidence for ♂ (Wang et al 2022)

Background

- Approximately 23% of Operation Iraqi Freedom/Operation Enduring Freedom (OIF/OEF) veterans have been diagnosed with PTSD (Fulton et al. 2015).
- Military veterans as a population are very familiar with PTSD with good baseline knowledge about the condition (Williston and Vogt 2022).
- Military personnel and veterans are less likely than civilians to respond to psychotherapies (Haagen et al. 2015).
- Certain genetic markers can make it more likely for a person to get PTSD after exposure to a traumatic event (Duncan et al. 2018).
- PTSD is polygenic: many genetic risk loci are involved. There is not a "PTSD gene." (Campbell-Sills et al. 2023)
- These risk loci can be added together to get a Polygenic Risk Score (PRS) for a person.
- Heritability of PTSD: 30-40% (Banerjee et al 2017)
- Genetic risk factors discovered in primarily civilian samples are not consistently replicated in military samples, and vice-versa (Huckins et al 2020).

Research Questions

What are the ethical and social concerns, including perceived harms and benefits, of polygenic risk score (PRS) testing for PTSD among different stakeholder groups?

Where do the concerns of these three groups intersect, overlap, diverge?

Methodology

- Semi-structured qualitative interviews
- 3 stakeholder groups:
 - Veterans/military members with PTSD
 - Clinicians who treat military veterans/military members with PTSD
 - Genetics researchers who work on PTSD
- Data collection: August 2023-June 2024

Current Enrollment	22
Vets/military	6
Clinicians	8
Researchers	8

Preliminary Themes

Combatting stigma

...if I can prove that genetics play a role in these mental health disorders that it will actually be a proof that those are real and driven by genetic factors.

Participant R1

Oh I think everyone gets it...I think it's...handled at different levels, or accepted, or denied, or blacked out...but I think everyone has a level of PTSD.

Participant V9, Navy

Preliminary Themes

Anti-determinism

Participant C35, Psychologist

I would make sure, abundantly clear, to state that this is not prescriptive, this is not going to say that you get it, right. So there are many people who...score higher than you that still don't develop PTSD...

...having...certain genes is not a guarantee that, you know, you're going to go down that disease pathway.

Participant V5, Air Force

Uses for PRS: Benefits

Providing additional screening, providing support, refining a diagnosis

Participant R24

...it's like in intelligence you got pattern analysis...you start seeing certain patterns and you start helping people before it gets out of hand. That's the key.

...full informed consent... "Hey, just so you know, you have this percent risk of developing PTSD, are you sure you still want to join?"

Participant V1, Marine Corps

Participant C34, Psychologist

Uses for PRS: Risks

I am concerned that...we would go, "You didn't have the genetic precursor, maybe you're faking it, I'm going to...make you jump through the hoop ten more times before we acknowledge...that you're disabled."

Participant C40, Nurse Practitioner

Participant V13, Army

...if I had that gene, now they're going to take away my disability because it was a preexisting condition before I joined the military.

I don't think it should be used for making decision about who is getting hired, who is getting benefits...

Participant R24

Preliminary Conclusions

- Different stakeholder groups all agree that there should be less stigma around PTSD. However, the reasoning is different for each group:
 - Many veterans think that everyone is impacted by service trauma; if everyone has it, no one should be ashamed.
 - Clinicians tended to think there shouldn't be a stigma because it's a treatable condition.
 - Several researchers were eager to pinpoint a biological basis for the disorder, making it "real" for those who do not believe mental illnesses are physical diseases.
- Anti-determinism: All groups were worried about how others might interpret a high PRS.
- PRS uses/benefits: Could signal the need to have support systems/psychological help in place before engaging in dangerous activities (i.e. military deployment); help make lifestyle choices/ better informed decisions; be proactive about responding to trauma; guide or prioritize treatment for individuals.
- PRS risks/harms: Discrimination, esp with regard to employment in the military and health insurance; potential excuse to deny medical/disability claims; genetic determinism (participants worried that others might feel PTSD is inevitable; majority of the interviewees stated that just because someone has a high risk score, shouldn't stop them from doing something they really want to do).

References

- Banerjee, S. B., Morrison, F. G., & Ressler, K. J. (2017). Genetic approaches for the study of PTSD: Advances and challenges. *Neuroscience letters*, 649, 139-146.
- Campbell-Sills, L. et al (2023). Associations of polygenic risk scores with posttraumatic stress symptom trajectories following combat deployment. *Psychological Medicine* 1-10. <https://doi.org/10.1017/S0033291723000211>.
- Duncan, L. E., Cooper, B. N., & Shen, H. (2018). Robust findings from 25 years of PTSD genetics research. *Current psychiatry reports*, 20, 1-9.
- Fulton, J. J., Calhoun, P. S., Wagner, H. R., Schry, A. R., Hair, L. P., Feeling, N., ... & Beckham, J. C. (2015). The prevalence of posttraumatic stress disorder in Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) veterans: A meta-analysis. *Journal of anxiety disorders*, 31, 98-107.
- Galatzer-Levy, I. R., & Bryant, R. A. (2013). 636,120 ways to have posttraumatic stress disorder. *Perspectives on psychological science*, 8(6), 651-662.
- Haagen, J. F., Smid, G. E., Knipscheer, J. W., & Kleber, R. J. (2015). The efficacy of recommended treatments for veterans with PTSD: A meta-regression analysis. *Clinical psychology review*, 40, 184-194.
- Huckins, L. M., Chatzinakos, C., Breen, M. S., Hartmann, J., Klengel, T., da Silva Almeida, A. C., Dobbyn, A., Girdhar, K., Hoffman, G. E., Klengel, C., Logue, M. W., Lori, A., Maihofer, A. X., Morrison, F. G., Nguyen, H. T., Park, Y., Ruderfer, D., Sloboffman, L. G., van Rooij, S. J. H., PTSD Working Group of Psychiatric Genomics Consortium, ... Daskalakis, N. P. (2020). Analysis of Genetically Regulated Gene Expression Identifies a Prefrontal PTSD Gene, SNRPB35, Specific to Military Cohorts. *Cell reports*, 31(9), 107716. <https://doi.org/10.1016/j.celrep.2020.107716>
- Wang, J., Zhao, H., & Gergent, M. J. (2022). Posttraumatic stress disorder brain transcriptomics: convergent genomic signatures across biological sex. *Biological psychiatry*, 91(1), 6-13.

