Determining genetic risk for posttraumatic chronic pain and related neuropsychiatric disorders using polygenic risk scores.

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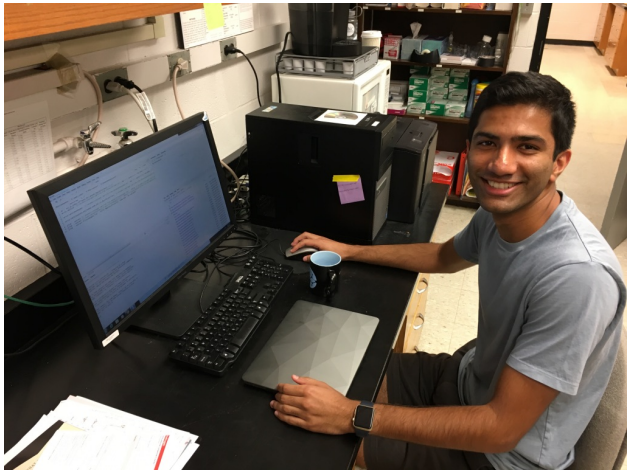

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Overview

Background: Twin and family studies have reported a significant contribution of genetic factors to onset of chronic pain and related psychiatric disorders. Technological advancements now allow for the systematic testing of genetic variants across the genome for association with traits to better understand the cumulative effect of different alleles.

Research Question: Can a polygenic model be used to predict genetic risk for posttraumatic chronic pain and posttraumatic stress symptom development?

Purpose:

Health care providers may use polygenic risk scores as well as nongenetic risk factors to evaluate a patient's risk of chronic pain in order to create an individualized treatment plan.

Methods: Polygenic risk scores were generated using GWAS discovery datasets and the target dataset consisting of European individuals between 18 and 65 years of age who presented to the ED within 24 hours of a motor vehicle collision. Phenotypes tested included pain intensity (scale from 0-10), depression (CESD scale), and PTSD (IESR scale). PRSice, polygenic risk score software, was used to calculate, evaluate, and plot the results of the analyses.

Results: The variance explained by the PRS model for moderate posttraumatic chronic pain (4-10 on pain scale) ranged from 1-3% using polygenic risk scores for back pain (Table 1). As the polygenic risk score increased, the odds ratio for year 1 moderate pain generally increased (Figure 1). Similar results were observed when testing other GWAS discovery datasets and phenotypes (Table 2).

Conclusion: The polygenic risk scores quantify the cumulative effect of genetic variants that play a significant role in the development of posttraumatic chronic pain and related symptoms. Future research may combine these polygenic risk scores with nongenetic risk factors to predict individual susceptibility.

Figure 1. Year 1 Moderate Pain

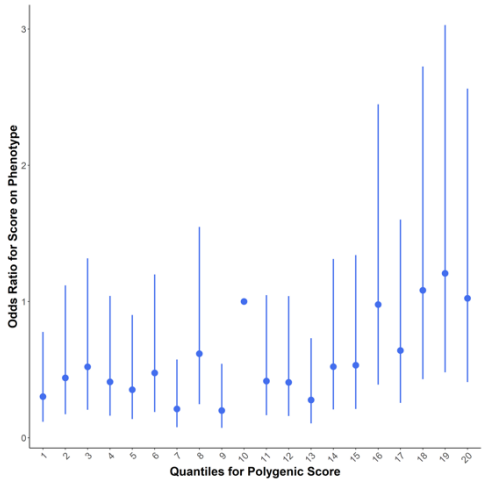

Table 1. Genetic risk for posttraumatic chronic pain using polygenic risk scores for back pain.

	Week 6 Moderate Pain	Month 6 Moderate Pain	Year 1 Moderate Pain
Variance explained by the PRS.	1.24%	1.47%	2.95%
P value of the model fit.	0.00649	0.00357	0.00003
Number of SNPs included.	1,392	1,848	1,205

Table 2. Comparison of variance explained by the PRS model at week 6 using various GWAS discovery datasets.

GWAS	Chronic Pain (Severe 7-10)	Depression (CESD 16)	PTSD (IESR PTSD)
Depression	0.57%	3.12%***	2.81%***
Schizophrenia	1.08%*	2.26%*	1.99%**
Bipolar Disorder	0.67%	1.16%*	1.13%*
PTSD	-	-	-
Multisite Chronic Pain	0.84%*	0.49%	0.72%
Back Pain	1.73%**	1.35%**	1.65%**
Chronic Back Pain	1.72%**	0.79%*	0.61%

* p<0.05 ** p<0.01 *** p<0.001