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Common factors across chronic pain conditions in the UK Biobank

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Chronic pain conditions show substantial genetic and phenotypic correlations. Our goal for this study is to find and characterize the shared genetic risk underlying these conditions in the UK Biobank dataset (n = 432,000). We studied 24 chronic conditions marked by persistent pain in different body sites, selected for adequate numbers of cases and heritability. We ran a genome-wide association study (GWAS) on each condition and estimated genetic correlations among them. Factor analysis using genomic structural equation modeling in GenomicSEM[1] revealed evidence for a general factor explaining most of the shared genetic variance across pain conditions and a second factor explaining additional shared variance across musculoskeletal conditions. A GWAS on the general factor revealed 33 independent single nucleotide polymorphisms (SNPs) and 25 genes reaching genome-wide significance. Functional annotation showed that these genes are highly and selectively expressed in brain tissues, particularly midline prefrontal and affective/motivational regions. Significant genes were implicated in a variety of biological pathways, with the top associated gene, *DCC*, associated with axonogenesis. Our results suggest that a common genetic component, representing biological pathways related to brain development and affective/motivational function, may underlie etiologically and anatomically distinct pain conditions. These findings support a conceptualization of chronic pain as a systemic condition involving alteration in neural pathways.

[1]Grotzinger AD, Rhemtulla M, de Vlaming R, Ritchie SJ, Mallard TT, Hill WD, Ip HF, Marioni RE, McIntosh AM, Deary IJ, Koellinger PD. Genomic structural equation modelling provides insights into the multivariate genetic architecture of complex traits. Nature human behaviour. 2019 May;3(5):513-25.