

Genes Associated with Cardiovascular Risk in Anxiety/Stress Disorders

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Introduction

Relationship to genetics

- ▶ Brain-heart interaction in psychological disorders not studied thoroughly
- ▶ GWAS studies not focused on brain-heart interactions
- ▶ Could be used to identify at-risk individuals

Methods

- ▶ NCBI Phenotype-Genotype integration system (merges NHGRI, dbGaP, OMIM, eQTL, and dbSNP)
- ▶ MeSH term search for phenotype identification: arrhythmia, CAD, depression, anxiety, psychological stress, PTSD
- ▶ significance threshold of $p < 1e-5$ for gene selection
- ▶ script to find overlapping phenotypes and genotypes
- ▶ manual annotation of results

Results

Overview

- ▶ **1095** genes initially identified
- ▶ data included gene location, chromosome, location, and relevant studies
- ▶ identified 41 genes of appropriate phenotype-genotype overlap
- ▶ further annotated results by significance of relationship/overlap and primary literature

BIN1

- ▶ BIN1 (chromosome 2, rs10207628),
- ▶ bridging integrator for synaptic vesicle endocytosis
- ▶ associated with SCD and depression, expressed in brain
- ▶ regulates calcium ion transport, cardiac AP, neuronal differentiation
- ▶ locates to cardiac T-tubules, releases microparticles^{1,2}
- ▶ associated with tau protein in dementia³

PHARCTR1

- ▶ PHARCTR1 (chromosome 6, rs4615376)
- ▶ phosphatase and actin regulator of endothelial cell survival
- ▶ associated with CAD and depression and expressed in the brain and heart
- ▶ migraine pathogenesis⁴ and susceptibility for CAD in type 2 diabetes mellitus⁵

CNNM2

- ▶ CNNM2 (chromosome 10, rs12413409),
- ▶ divalent metal cation transport mediator
- ▶ associated with CAD and depression and expressed in the kidneys
- ▶ magnesium ion homeostasis and transmembrane transport
- ▶ common among major psychiatric disorders⁶
- ▶ susceptibility locus in CAD⁷ and increases the risk of hypertension⁸

PRTFDC1

- ▶ PRTFDC1 (chromosome 10, rs11014306)
- ▶ phosphoribosyl transferase domain protein
- ▶ associated with SCD and anxiety/stress disorders and is expressed in the brain and adrenal glands
- ▶ functions as part of purine salvage pathways
- ▶ cardiometabolic profile in heart failure⁹
- ▶ predictor of combat stress vulnerability in the development of PTSD¹⁰

CDH13

- ▶ CDH13 (chromosome 16, rs8055236)
- ▶ cadherin protein
- ▶ associated with CAD and depression and is expressed in the brain and heart
- ▶ functions in protein signal transduction, endothelial cell migration, and is protective against apoptosis
- ▶ provides resistance to atherosclerosis, and is part of neural differentiation
- ▶ role in the cardioprotective effects of sleep and in incident coronary artery disease¹¹
- ▶ identified in hyperactivity, impulsivity, violent behavior, and extraverted personality traits^{6,12,13}

BMP2

- ▶ BMP2 (chromosome 20, rs6117734)
- ▶ bone morphogenetic transforming growth factor-beta protein
- ▶ associated with CAD and depression and is expressed broadly
- ▶ functions as part of cardiac epithelial transition and cardiomyocyte differentiation
- ▶ associated with depressive traits and stressful life events¹⁴
- ▶ also in cardiac progenitor cell differentiation¹⁵ and atherosclerosis in type 2 diabetes mellitus¹⁶

Additional genes identified I

- ▶ RORA (chromosome 15, rs12912233)
- ▶ GRIN2A (chromosome 16, rs8058295)
- ▶ FAM155A (chromosome 13, rs1509091)
- ▶ ENOX1 (chromosome 13, rs17538444)
- ▶ QKI (chromosome 6, rs7756185)
- ▶ EGFLAM (chromosome 5, rs2561805)
- ▶ SNX7 (chromosome 1, rs11581859)
- ▶ ACVR1 (chromosome 2, rs35806662)
- ▶ MYL10 (chromosome 7, rs1722229)
- ▶ KSR2 (chromosome 12, rs7973260)
- ▶ PARVA (chromosome 11, rs7120489)
- ▶ SNCA (chromosome 4, rs356228)
- ▶ SORCS3 (chromosome 10, rs7074335)
- ▶ MAML3 (chromosome 4, rs1877075)
- ▶ DCLK2 (chromosome 4, rs150175932)
- ▶ LPPR5 (chromosome 1, rs1329461)
- ▶ Pseudogenes: RNA5SP87, RPL26P5, RNA5SP404, HSPE1P20, MTCO3P1, RPL6P18, and MTCL1P1

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