Common genetic variants associated with personality dimensions in the Heidelberg Cohort Study of the Elderly (HeiDE)

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Abstract

Interindividual differences in personality and their genetic basis have long been of interest to scholars. Here, we present an analysis of data from the HeiDE study, a longitudinal investigation of the inhabitants of Heidelberg, Germany. Using factor scores of previously identified latent personality factors as phenotypes, a genome-wide association study (GWAS; n=2,514) identified a variant on chromosome 5 (rs79136259) to be associated with Emotional Lability. Data from follow-up analyses confirmed differences between allele carriers in both depression scores and lifetime anxiety in social situations. We also determined SNP-based heritability of personality dimensions and found Psychoticism to show a particularly large estimate. These findings should be replicated in independent samples.

Introduction

The HeiDE study is an ongoing longitudinal investigation that started in the beginning of the 1990s. Amongst other variables it assessed an array of personality tests at the first measurement point. As personality traits show substantial heritable components (e.g. Power and Pluess, 2015) and molecular genetic data of participants recently became available, we were interested in common genetic variants underlying individual differences in personality. Previous investigations of this cohort already identified five latent personality dimensions ("The Heidelberg Five"; e.g. Amelang et al., 2004), interpreted as Emotional Lability, Lack of Behavioral Control, Type-A-Behavior, Locus of Control over Disease, and Psychoticism. We ran a GWAS using individual factor scores on latent personality dimensions as phenotypes, calculated SNP-based heritability and validated results using follow-up data.

Methods

Participants Personality questionnaires of N=5,049 (52.2% females, mean age 53.4 years, age range 28-74) participants were re-analyzed using principal components factor analysis (see below). We analyzed genetic data from n=2,514 individuals (post-QC; 52.1% females, mean age 52.0 years, age range 28-69).

Latent personality phenotypes The following personality tests were collected at baseline: *Time Urgency and Perpetual Activation Scale, State-Trait-Anger Expression-Inventory, Hostility, Exaggerated social control, Depression Scale, Sense of Coherence Scale, Optimism, Questionnaire for measuring the locus of control over diseases, Social Support-Scale, Eysenck-Personality-Inventory,* and *Psychoticism*. Original data were re-analyzed using principal components factor analysis with varimax rotation (see Amelang et al., 2004). We used Bartlett's method to calculate individual factor scores.

Genotyping, imputation and analysis of genetic variants Participants were genotyped on the Illumina PsychArray. We imputed common variants (MAF 0.01) using the 1000 Genomes Phase 3 reference panel. Data were analyzed using PLINK 1.07 (http://pngu.mgh.harvard.edu/~purcell/plink/), R (https://www.r-project.org/) and ldsc (Bulik-Sullivan, et al., 2015).

Analyses of HeiDE follow-up data (2013) Answers to lifetime anxiety disorder screening questions from the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I; Wittchen and Fydrich, 1997) and data from the depression questionnaire Allgemeine Depressionsskala (ADS; Hautzinger & Bailer, 1993) were analyzed according to rs79136259 genotype (see below).

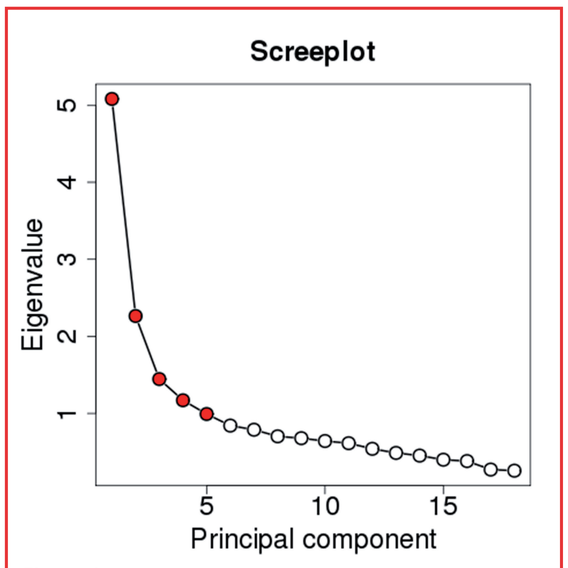

Figure 1
Screeplot from principal component factor analysis of personality scales. Extracted principal components (The Heidelberg Five) are shown in red.

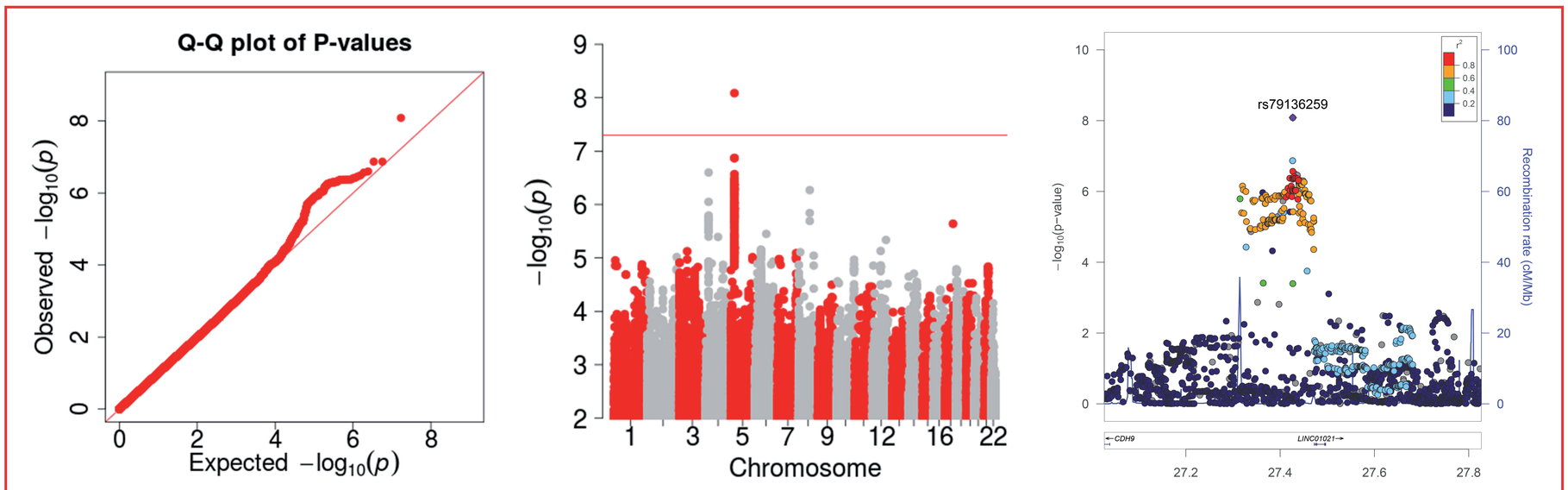

Figure 2
Quantile-Quantile (left) and Manhattan (middle) plots of the GWAS investigating the phenotype Emotional Lability. We observed a genome-wide significant variant ($p=8.2*10^{-9}$) on chromosome 5p, rs79136259 (right).

Phenotype	*h²*	*Standard error*
Emotional Lability	0.0.6	0.18
Lack of Behavioral Control	0.02	0.21
Type-A-Behavior	0.26	0.18
Locus of Control over Disease	0.15	0.17
Psychoticism	0.45	0.20

Table 1 SNP-based heritability of The Heidelberg Five personality phenotypes.

Results

Replication of latent personality dimensions The first ten eigenvalues of the principal components analysis were 5.08-2.26-1.45-1.17-0.99-0.84-0.79-0.70-0.68-0.64 (Figure 1) and are thus in perfect agreement with previously reported analyses (Amelang et al., 2004).

Genetic analyses Controlling for potential population stratification (Figure 2, left), we discovered a genome-wide significant locus for the phenotype Emotional Lability on the short arm of chromosome 5 (rs79136259; Figure 2, middle). This hitherto unknown locus is not associated with a particular gene but lies upstream of the annotated lincRNA LINC01021 (Figure 2, right). Analyses with ldsc revealed varying degrees of SNP-based heritability for the latent phenotypes (Table 1). Here, the personality trait Psychoticism (e.g. Eysenck, 1992) showed a particularly large estimate.

Follow-up analyses Using the non-parametric test nparcomp (Konietschke et al., 2012) we found elevated ADS scores (adjusted for age and sex; TT: -0.34, TG: 0.01, GG: 0.21; overall p=0.014; n=2377) in G risk allele carries. Also, the proportion of participants reporting lifetime anxiety in social situations was higher in risk allele carriers (TT: 6.7%, TG: 9.5%, GG: 12.8%; p<0.01; n=2539), complementing results obtained by GWAS.

Discussion

The HeiDE sample is a unique opportunity to study the association of personality, genetics, and longitudinally defined phenotypes. Replication of the risk locus rs79136259 for Emotional Lability in an independent sample is now required to confirm the association. High heritability of Psychoticism demonstrates biological validity of this personality trait.

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Grants

TGS: DFG Grants HEIDE DFG RI908/8-1, SCHU 1603/5-1 and SCHU 1603/7-1; Lisa-Oehler-Foundation.
MR: BMBF 01ZX1314G, IntegraMent: e:Med Integrierte Untersuchungen von Ursachen und Mechanismen psychiatrischer Störungen. HeiDE: DFG Am 37/12-1 und –2, AM 37/19-1, STU 235/10-2 and HE 2443/8-1.