

Investigation into the heritabilities of some traits in the Human Connectome Project



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1 Introduction

The Human Connectome Project (HCP) provides detailed assessment of a large sample of monozygotic and dizygotic twins and their siblings [1,2]. All HCP data are released to the community, and on the occasion of the HCP-S500 release (Jun/2014), we conducted a heritability analysis of a multitude of imaging (brain structure) and non-imaging measurements. This analysis estimates the proportion of the phenotypic variance explained by genetic (i.e., the heritability, h^2) and by common environmental effects (c^2), after discounting nuisance effects such as age and sex.

2 Method

For this exploratory analysis, we included 390 relevant traits available in the HCP-S500 release (523 subjects). The phenotypic variance was decomposed into genetic (h^2), common environmental (c^2), and unique environmental (e^2) components using maximum likelihood methods [3] as available in the Sequential Oligogenic Linkage Analysis Routines (SOLAR). In this extended twin study, the common environment is a “household” effect, defined here by subjects sharing a common relative. Nuisance variables were age, age-squared, race, ethnicity, and socio-economic status, as well as sex and its interaction with all other variables. The socio-economic status was assessed as income and years of education. The fraction of the variance explained by these variables was also computed, referred to as r^2 . The traits were classified into 11 categories as defined in the HCP Data Public Dictionary [4]. From these, we further examined some of the traits in the category “Cognition”, which showed the largest average common environment effect (results below), deriving new traits for Fluid and Crystallised intelligence following the definition from the NIH Cognition Toolbox [5], and also redefining these traits using principal component analysis (PCA).

3 Results

A summary of the h^2 , c^2 , e^2 and r^2 is shown in Figure 1. In general, nuisance variables accounted for about 15% of the phenotypic variance, although higher for the categories “Motor” and “FreeSurfer” (the last containing morphological brain traits), as these seem to be more strongly influenced by sex and age. Most of the traits (242) were significantly heritable ($pFDR \leq 0.05$), with those representing brain anatomy, as well as most biomarkers (such as those in the category “Health & Family History”) having the highest heritability.

Although most of the “Cognition” traits were also heritable, considerable variance was also explained by common environmental/household factors, as shown in Figure 2. Importantly, within this category, the traits that assess intelligence showed consistently lower heritability estimates (about 0.25) relative to some published values [6, 7, but see 8]. These same traits also showed a substantially higher c^2 . Remarkably, the traits related to the Penn Progressive Matrices test (PMAT) had zero heritability in the HCP sample. The PCA traits derived from the NIH Toolbox that assess Fluid and Crystallised intelligence showed similar pattern of effects on h^2 and c^2 , although most of the common environmental influences collapsed into just the first principal component.

4 Conclusion

Most of the HCP traits are heritable. Differently than the majority of the other traits, the cognitive measurements showed a larger share of the variance explained by common environment, suggesting some other family and/or societal effects that are not otherwise accounted for by our nuisance measures.

Figure 1

Box plots showing the variance partitioning for each of the 11 trait categories. After removing the variance explained by nuisance variables (r^2), the remaining is partitioned into h^2 , c^2 and e^2 .

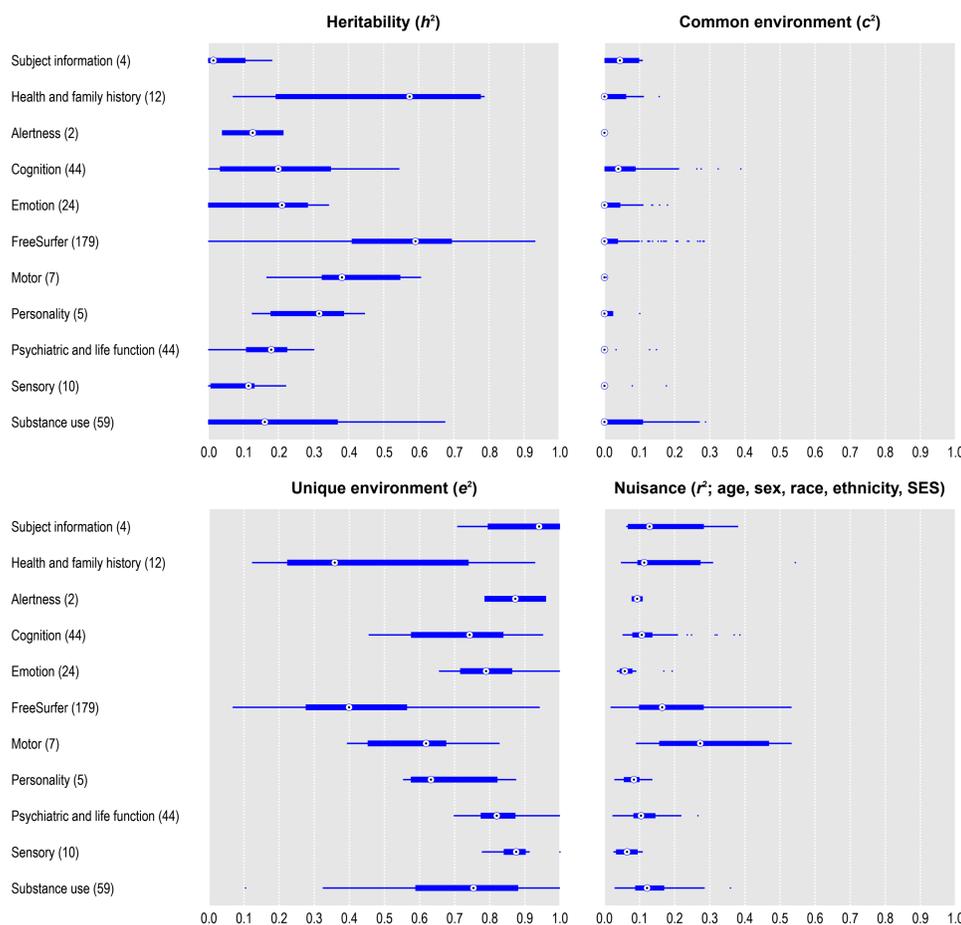


Figure 2

Table showing h^2 , c^2 and r^2 for the “Cognition” traits, which showed generally lower heritability than found in the literature, with a substantial share of the variance explained by common environmental effects. The FDR correction here considers only this same set of traits. After PCA, most of the c^2 collapsed into the first principal component. The traits marked with (F) and (C) are used respectively to derive the Fluid and Crystallised intelligence scores. The background colours are to facilitate viewing; higher values are coded towards yellow, lower values towards red. The font for the p-values is also colour-coded: significant results ($p \leq 0.05$) are shown in red, otherwise in gray.

Trait	h^2	h^2 p	h^2 pFDR	c^2	c^2 p	c^2 pFDR	r^2
CardSort_AgeAdj (F)	0.0848	3.82E-01	4.58E-01	0.2318	6.54E-02	1.31E-01	0.0945
Flanker_AgeAdj (F)	0.1648	3.67E-02	1.32E-01	0.0000	-	-	0.0972
ListSort_AgeAdj (F)	0.5502	4.32E-08	3.89E-07	0.0000	-	-	0.1207
PicSeq_AgeAdj (F)	0.3827	4.77E-02	1.43E-01	0.0513	3.57E-01	5.84E-01	0.1367
ProcSpeed_AgeAdj (F)	0.0000	5.00E-01	5.00E-01	0.2715	5.23E-02	1.31E-01	0.1180
PicVocab_AgeAdj (C)	0.1787	2.00E-01	3.00E-01	0.3149	6.52E-03	3.91E-02	0.3699
ReadEng_AgeAdj (C)	0.2682	1.12E-01	2.02E-01	0.2042	5.70E-02	1.31E-01	0.3144
PMAT24_A_CR	0.0000	5.00E-01	5.00E-01	0.1767	4.47E-02	1.31E-01	0.2486
PMAT24_A_RT	0.0000	5.00E-01	5.00E-01	0.0930	1.49E-01	2.68E-01	0.0994
Fluid	0.2454	1.77E-01	2.90E-01	0.2087	6.57E-02	1.31E-01	0.2026
Crystallised	0.2806	6.99E-02	1.43E-01	0.3196	2.91E-03	2.62E-02	0.3828
Fluid PC1	0.1522	2.88E-01	3.99E-01	0.2401	4.68E-02	1.31E-01	0.1770
Fluid PC2	0.4956	2.40E-08	3.89E-07	0.0000	-	-	0.0576
Fluid PC3	0.3101	4.22E-04	2.53E-03	0.0000	-	-	0.0803
Fluid PC4	0.1546	5.79E-02	1.43E-01	0.0000	-	-	0.0523
Fluid PC5	0.1412	3.16E-01	4.06E-01	0.0368	4.13E-01	6.20E-01	0.0319
Crystallised PC1	0.2785	7.15E-02	1.43E-01	0.3204	2.89E-03	2.62E-02	0.3831
Crystallised PC2	0.2031	1.11E-02	5.00E-02	0.0000	-	-	0.0382

5 References

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