# DOES MACROSCALE GREY MATTER ANATOMY REFLECT PERSONALITY?

Sofie L. Valk[1,2*]; Felix Hoffstaedter[1,2]; Julia A. Camilleri[1,2]; Peter Kochunov[3]; B.T. Thomas Yeo[4,5,6,7]; Simon B. Eickhoff[1,2]

*[1)] Institute of Neuroscience and Medicine (INM-7: Brain and Behaviour), Research Centre Jülich, 52425 Jülich, Germany*
*[2)] Institute of Systems Neuroscience, Heinrich Heine University Düsseldorf, 40225 Düsseldorf, Germany*
*[3)] Maryland Psychiatric Research Center, University of Maryland School of Medicine, Baltimore, Maryland, USA.*
*[4)] Department of Electrical and Computer Engineering, Clinical Imaging Research Centre, Institute for Health and Memory Networks Program, National University of Singapore, Singapore, Singapore.*
*[5)] Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, USA.*
*[6)] Centre for Cognitive Neuroscience, Duke-NUS Medical School, Singapore, Singapore.*
*[7)] NUS Graduate School for Integrative Sciences and Engineering, National University of Singapore, Singapore, Singapore.*

## Significance statement

Personality traits quantify individual differences in goals, cognition, and emotion, that lead to behavior. Evidence from psychology, cognitive neuroscience, and genetics has proposed links between personality and brain structure. In the current study, we used a twin-design to test whether covariance between personality and brain structure is due to shared genetic effects. Indeed, phenotypic correlations between personality traits and cortical thickness were driven by genetic effects, suggesting that associations between personality and cortical thickness have a genetic origin. At the same time, replication analysis indicated that only latent factors underlying personality, rather than personality traits themselves, have a robust relation to brain structure. These observations might inform future studies on the biological basis of individual difference in complex behavior.

**Abstract**

Personality traits are key indices of inter-individual variation. Personality is heritable and associated with brain structure and function. To date, it is unknown whether the relation between personality and brain macrostructure can be explained by shared genetic factors. In a large-scale twin sample, we show that key personality traits, e.g. agreeableness and extraversion, were genetically associated with thickness of specific brain regions. Second, we observed that spatial patterns of phenotypic and genetic correlations between personality and cortical thickness were significantly positive, suggesting a genetic basis for phenotypic associations. However, these findings did not replicate in two large-scale datasets of unrelated individuals. We were able to reconcile this discrepancy by probing the latent relation between personality and cortical thickness using a multivariate approach. Here we could uncover a latent association between personality traits and cortical thickness. This component accounted for 30% of the variance shared between personality traits and cortical thickness. The results of our multivariate analysis indicate that personality is associated with regions supporting lower-order sensory as well as integrative cognitive processes. Our study provides first evidence of a genetic origin of associations between grey matter and personality and highlights robustness of latent personality components in relation to whole-brain spatial patterns, rather than single regions and traits.

"Personality" is an individuals' characteristic set of cognitive, emotional and behavioral patterns. Behavioral science ascertains personality structure using a statistical construct that parcellates the individual variability in goals, cognition, and emotion into independent components (1). The most well-known personality taxonomy is the Big Five Personality inventory (2, 3). The Five-factor personality structure (NEO- Five-Factor-Inventory – NEO-FFI) (4, 5) is a variance portioning approach to derive five orthogonal dimensions or traits of agreeableness (friendly/compassionate vs. challenging/detached), conscientiousness (efficient/organized vs. easy-going/careless), extraversion (outgoing/ energetic vs. solitary/reserved), neuroticism (sensitive/nervous vs. secure/confident), and openness (inventive/curious vs. consistent/cautious). Importantly, personality is related to health, wellbeing, and reproductive success (6, 7). For example personality traits have been linked to the quality of social relationships(8), job performance (9), and risk for mental disorders(10, 11).

Personality has both stable as well as malleable features (12-14) and the strongest predictor of personality across the lifespan is the personality of biological parents. Indeed, personality traits are heritable with about 40% of the variance attributable to additive genetic factors (15-20). Evolutionary causes for variability in personality traits have been suggested to be due to balancing selection, where selection pressures in different directs affected the same traits enabling adaptation to changing environmental demands (14). Indeed, genome-wide association studies (GWAS) have reported several genetic variants associated with personally traits (21-23). However, results point to a large number of genetic variants with individually tiny effects that explain the heritability of personality (22, 24, 25).

Next to these developments in behavioral genetics, the relationship between personality and brain structure has also been investigated using magnetic resonance imaging (MRI) (26-29). While various studies found some phenotypic relationship between brain structure and variations in personality traits, findings have been inconsistent (26-29). For instance,

researchers failed to observe significant relations between personality and various markers of brain structure using the largest sample to date (30). At the same time, using a similarly sized sample with monozychotic and dyzychotic twins, Owens and colleagues (31) report significant phenotypic relationships between personality and cortical structure. Here, they observed associations between agreeableness, conscientiousness, neuroticism, and openness with morphometry of prefrontal cortex.

The phenotypic relationship between personality and brain structure may be due to shared genetic factors. Specifically, phenotypic correlation between two traits can be driven by pleiotropy where a gene exerts phenotypic effects on both traits. However, significant genetic correlations may also be driven by sample biases, such as assortative mating and population stratification (32). On the other hand, phenotypic correlation between brain structure and personality may be also be driven by environmental factors including nutrition, upbringing, stress, and social influences. Genetic correlation analysis can separate between shared additive genetic and environmental factors by using the genetic similarity between individuals (monozychotic twins ~100% and dizychotic twins and siblings ~50% genetic similarity) to calculate the extent to which correlation between two traits varies as a function of genetic proximity.

In the current study we combined structural neuroimaging and behavioral genetics to investigate the shared genetic basis of personality traits and grey mater macrostructure. We captured variations in brain morphometry using an atlas-based approach (33) leading to a biologically meaningful representation of macro-anatomy (34). Here, we first we estimated phenotypic associations between personality and cortical thickness in a twin-based sample. The twin-structure of this sample enabled us to evaluate whether covariance between personality and cortical thickness is due to shared additive genetic effects. Analysis of heritability and co-heritability was performed using maximum likelihood variance-decomposition methods using Sequential Oligogenic Linkage Analysis Routines (www.solar-

eclipse-genetics.org; Solar Eclipse 8.4.0.). Heritability ($h^2$) is the total additive genetic variance, and genetic ($\rho_g$) correlations were estimated using bivariate polygenic analyses. To validate our results, we examined the robustness of the observed relationships between cortical thickness and personality in two additional samples (Genome superstructure project - GSP and enhanced Nathan Kline Institute dataset - eNKI) of consisting unrelated individuals. Lastly, we used a comprehensive multivariate approach (partial least squares (35)) to evaluate whether latent relationships between personality traits and cortical brain structure exist, and assessed its genetic basis.

## Results

*Phenotypical correlation between NEO-FFI and cortical thickness*

To evaluate the relation between personality and macroscale brain structure we first evaluated distribution of behavioral and structural brain measures. All personality traits in full HCP sample (n=1106 including 286 MZ-twins and 170 DZ-twins). were normally distributed (Figure 1A) and in line we previous reports we observed some correlation across personality traits (Figure 1B, Supplementary Table 1). Also, distribution of thickness values summarized in 200 functionally informed parcels (33) was conform previous reports {Cardinale, 2014 #591}, with highest thickness in anterior insula, and relatively low values in occipital regions (Figure 1B). Following, we assessed phenotypic correlation between personality traits and cortical thickness parcels. We observed significant (FDR, corrected for number of parcels) correlations between agreeableness, neuroticism, and openness and local cortical thickness. Specifically, agreeableness related negatively to variations in thickness in left lateral and medial prefrontal cortex (FDRq<0.0125). Neuroticism related positively to thickness in dorsolateral frontal areas and left posterior operculum, and negatively to thickness in posterior mid-temporal cortex and occipital regions (FDRq<0.015). Openness related negatively to thickness in bilateral ventrolateral cortex, and positively to left inferior temporal regions, right temporal pole, and right cuneus (FDRq<0.01) (Supplementary Table 2). Though findings remained similar when controlling for intelligence, agreeableness, conscientiousness, neuroticism and openness all showed significant correlations with total cognition score (Supplementary Table 3) and post-hoc analysis showed that the relation between cortical thickness and personality was partially mediated by intelligence (Supplementary Table 4).

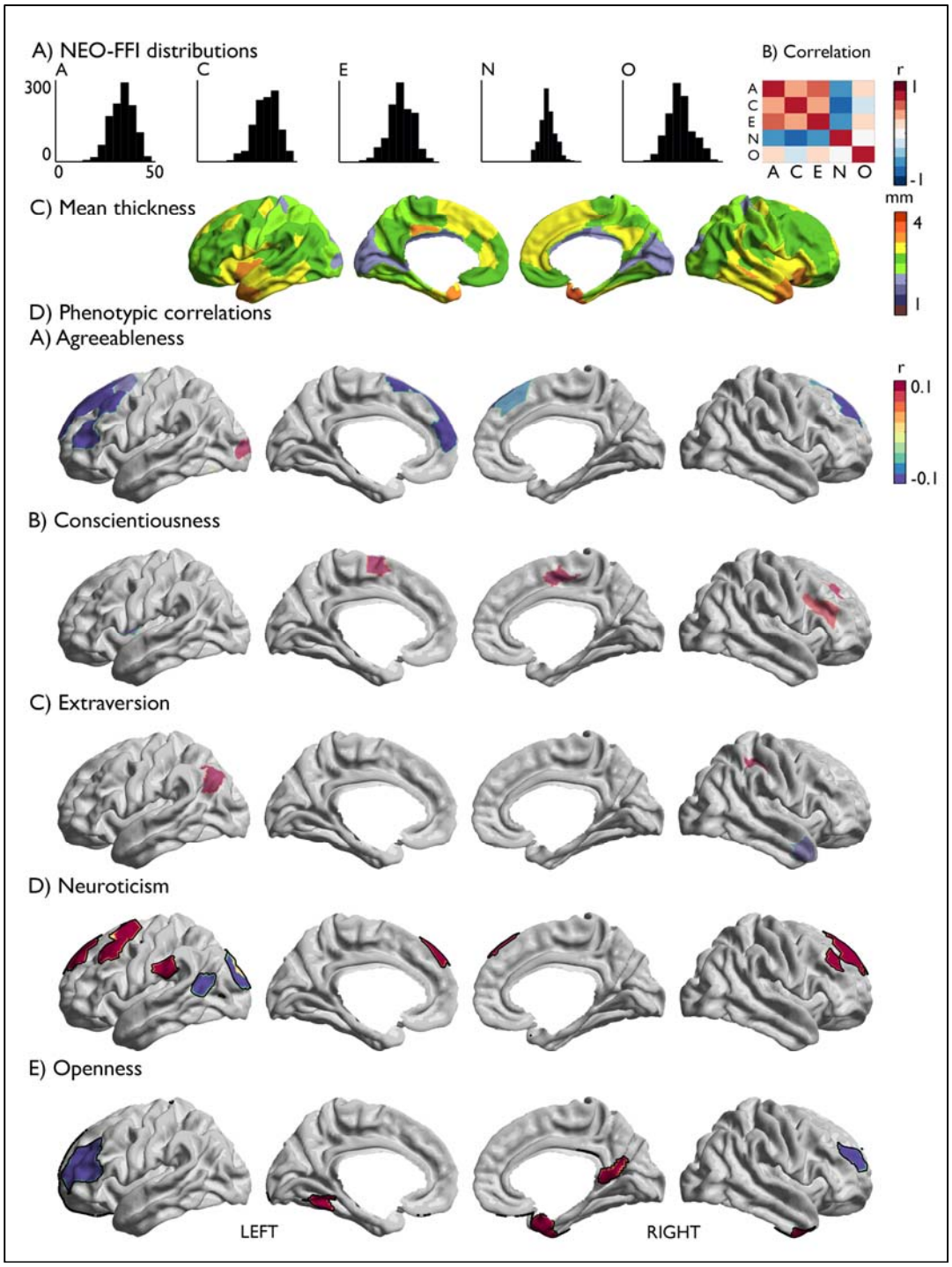



**Figure 1. Significant relation between personality traits and local cortical thickness in the full HCP sample.** Findings in each sample are displayed at $p<0.01$, positive Spearman's $\rho$ is displayed in red, whereas negative spearman's $\rho$ is displayed in blue. Multiple comparisons were accounted for by using FDRq<0.05 correcting for the number of parcels (200).

*Genetic correlation of personality traits and brain structure*

Subsequently, we sought to understand whether the phenotypic correlations observed in the twin-sample might be due to shared genetic effects on grey matter brain structure and personality traits. All personality traits were significantly heritable in our current sample (Figure 2A, Supplementary Table 5), and we next confirmed cortical thickness to be heritable in our parcel-based approach (Figure 2B, Supplementary Table 6). This enabled us to perform genetic correlation analyses between personality traits and cortical structure (Figure 2c). Agreeableness showed genetic correlation (FDR $p<0.05$) with cortical thickness in left posterior superior/mid temporal sulcus ('7Networks_LH_Default_Temp_5') ($\rho=0.03$; $\rho_g = 0.60$, $p<0.0005$; $\rho_e = -0.15$, $p<0.01$), right superior frontal cortex extending to mid cingulate ('7Networks_RH_SalVentAttn_Med_3') ($r=-0.04$; $\rho_g = -0.55$, $p<0.0004$; $\rho_e =0.18$, $p<0.005$), and right dorsolateral frontal cortex ('7Networks_RH_Default_PFCm_6') ($r=-0.02$; $\rho_g = -0.51$, $p<0.0006$; $\rho_e =0.21$, $p<0.0004$). Quantitative functional decoding using the BrainMap database(36) (Supplementary Figure 1) indicated that the left posterior superior-mid temporal sulcus was related to various forms of language processing ($p<0.05$), whereas the left superior frontal / mid cingulate parcel was related to action imagination and execution, as well as cognition and perception, and the dorsolateral prefrontal cortex was found implicated in tasks involving memory and reasoning. Second, we observed a genetic correlation between extraversion and left TPJ thickness ('7Networks_LH_Default_Temp_9') ($\rho=0.1$, $p<0.001$; $\rho_g = 0.49$ $p<0.00005$; $\rho_e = -0.11$, $p<0.05$). Functional decoding linked the TPJ with cognitive and social cognitive processing ($p<0.05$) as well as reasoning and language (Supplementary Figure 1). Lastly, though we observed significant genetic correlation between intelligence (total cognitive score) and agreeableness, conscientiousness, neuroticism, and openness (Supplementary Table 3), genetic correlations between personality and cortical thickness

remained similar when controlling for intelligence (Supplementary Figure 2). We did not observe significant environmental correlations between cortical thickness and personality traits (Supplementary Figure 3).

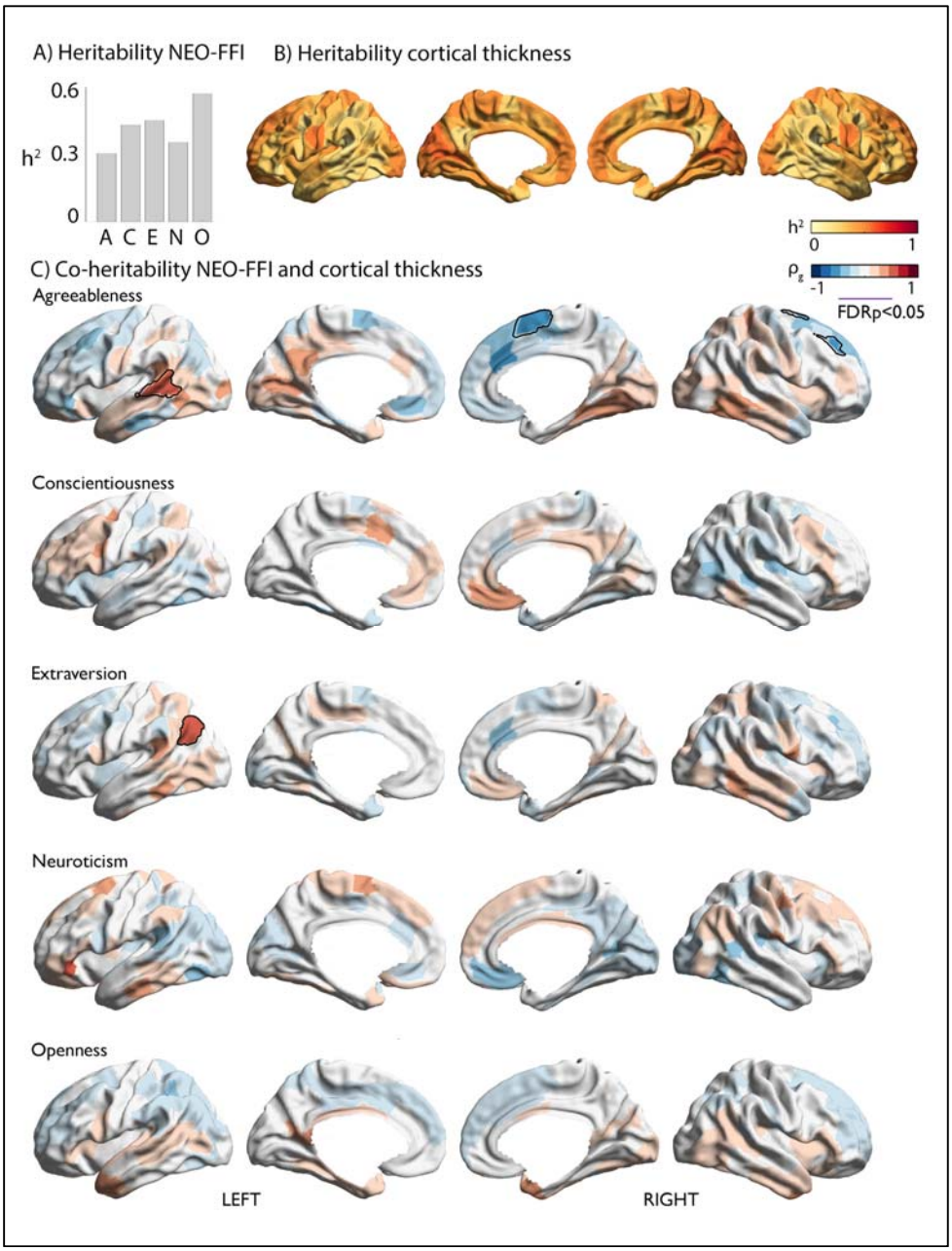



**Figure 2. Genetic correlation between personality traits and cortical thickness.** Upper panel depicts the heritability of A) personality and B) cortical thickness, see supplementary Table 4 and 5 for exact heritability values. Lower panels are genetic correlation between cortical thickness and personality traits, here red values indicate positive associations whereas blue values indicate negative genetic correlation between parcel-wise thickness and personality traits. Findings at FDRq<0.05 are outlined in black.

*Replication of associations between cortical thickness and personality traits.*

Next, we sought to assess whether the phenotypic and genetic correlation observed between personality and cortical thickness in the HCP-based twin sample would be replicated in unrelated samples. For this analysis we selected unrelated individuals from the HCP sample (n=419), as well as GSP sample (n=926), and eNKI sample (n=792). In regions that showed significant associations with personality in the twin HCP dataset, we observed little reliability across samples (Supplementary Table 2). At the same time, spatial distributions of phenotypic correlations showed some consistency across samples (Supplementary Table 7), especially for openness. (See supplementary results for whole brain phenotypic associations between personality traits and cortical thickness in the HCP unrelated sample, as well as GSP and eNKI samples).

Following, we assessed whether we could uncover correspondence between phenotypic and genetic correlations (Cheverud's conjuncture) within the HCP sample, as well as whether genetic correlations related to phenotypic correlations across samples. 11 of 22 previously observed significant (FDRq<0.05) phenotypic correlations in the complete HCP sample also show genetic correlations at p<0.05 (Supplementary Table 8). At the same time, observed significant genetic correlations (based on Figure 2) were not consistently associated with phenotypic correlations, both within the HCP sample as well as in the GSP and eNKI samples (Supplementary Table 9).

Testing whether whole brain distributions of thickness-personality correspondences might be robust, we observed that within the compete HCP sample (and unrelated subsample) whole brain spatial patterns of genetic correlations across the cortex showed strong positive correlations with whole brain spatial patterns of phenotypic correlations (Table 1, Supplementary Figure 8). This suggests that the direction of the phenotypic and genetic relation between personality and cortical thickness was comparable across the cortex.

However, these patterns only extended out of sample for openness, where both phenotypical patterns between openness and cortical thickness in GSP (ρ=0.18 [0.04 0.32]) and eNKI (ρ=0.34 [0.23 0.46]) showed positive correlations with genetic correlation patterns in HCP.

| | **HCP all** | **HCP un** | **GSP** | **eNKI** |
|---|---|---|---|---|
| *Agreeableness* | 0.59 [0.49 0.67] | 0.37 [0.23 0.51] | -0.04 [-0.18 0.10] | -0.14 [-0.27 0.02] |
| *Conscientiousness* | 0.52 [0.38 0.63] | 0.26 [0.13 0.40] | 0.04 [-0.11 0.17] | 0.01 [-0.12 0.16] |
| *Extraversion* | 0.46 [0.32 0.58] | 0.37 [0.26 0.48] | 0.08 [-0.06 0.22] | 0.12 [-0.03 0.25] |
| *Neuroticism* | 0.58 [0.47 0.67] | 0.35 [0.22 0.47] | -0.06 [-0.19 0.09] | -0.03 [-0.15 0.10] |
| *Openness* | 0.71 [0.62 0.78] | 0.43 [0.31 0.54] | 0.18 [0.04 0.32] | 0.34 [0.23 0.46] |

**Table 1. Correlation of phenotypic and genetic correlation across samples.** Spearman's correlation [95% confidence interval] between spatial distribution of genetic correlation based on the HCP related sample, and phenotypic correlation in the HCP complete sample (HCP all), HCP unrelated subsample (HCP un), GSP sample, and eNKI sample. See also Supplementary Figure 8.

**Latent structures between personality traits and cortical thickness.**

As we observed 1. phenotypic (Figure 1) and genetic correlations (Figure 2) between personality traits and brain structure in the twin-based HCP sample, 2. no robust replication of local associations between brain structure and personality traits in unrelated individuals, but 3. significant phenotypic correlation between personality traits, we sought to evaluate whether there would exist latent relationships between personality traits and cortical thickness. First, we replicated phenotypic associations between the various personality traits in both the GSP and eNKI samples (Supplementary Table 10 and 11). In all samples, we observed positive associations between agreeableness, conscientiousness, and extraversion, and negative association between neuroticism and agreeableness, conscientiousness, and extraversion. The relation between openness and the other personality traits was least consistent across samples, suggesting openness was most dissociable from the other personality traits. Moreover, in the HCP sample we observed significant genetic and environmental correlations between personality traits (Supplementary Table 12 and 13). Here extraversion showed a significant

positive genetic correlation with agreeableness and conscientiousness, and agreeableness, conscientiousness and extraversion showed significant environmental correlations.

Next, we utilized a multivariate data-driven approach (partial least squares) to assess whether latent relations between personality and cortical thickness would be robust across samples. Indeed, it has been suggested multiple comparison corrections in mass univariate analysis may result in missing effects and thus inconsistencies in the results and a more comprehensive picture of the associations could be gained by a multivariate approach (37).

To maximize robustness of observations we used the combined unrelated GSP and eNKI sample as discovery dataset, and the full HCP sample as replication sample. This enabled us to assess whether latent relationships between brain and personality, observed in a large sample of unrelated individuals, were driven by genetic effects. We observed that out of five possible components, the second component significantly ($p<0.001$) explained 30% of shared variance between cortical thickness and personality. Post-hoc analysis showed that in both GSP ($r=0.20$), as well as eNKI ($r=0.20$) this component significantly related to brain and behavioral saliencies. The behavioral salience component was significantly related to openness ($r=-0.85$), extraversion ($r=-0.55$), conscientiousness ($r=-0.17$), and agreeableness ($r=-0.12$) (Figure 3). The brain salience component had low loadings (BSR<-2) in occipital and posterior insular regions and high loadings (BSR>2) in frontal and inferior parietal and TPJ regions (Figure 3). Running post-hoc analysis of the spatial distribution, we observed that whereas visual and sensorimotor networks had relatively low saliencies, ventral attention, frontoparietal and default mode regions had relatively high saliencies. This was mirrored by a positive relation ($\rho=0.48$ [0.37 0.58]) between the brain saliency component and principal gradient of functional organization (38), suggesting personality systematically relates to variability in hierarchical organization of grey matter macrostructure. Importantly, the component remained robust when controlling for intelligence. We could replicate the positive association between behavioral salience and brain salience in the HCP sample ($\rho=0.08$ [0.01

0.14]). Indeed, both brain (h2r±se = 0.74± 0.03) and behavioral (0.52±0.05) scores were highly heritable and showed a trending positive genetic correlation ($\rho_g$ = 0.11, p<0.09; $\rho_e$ = 0.02, p>0.5).

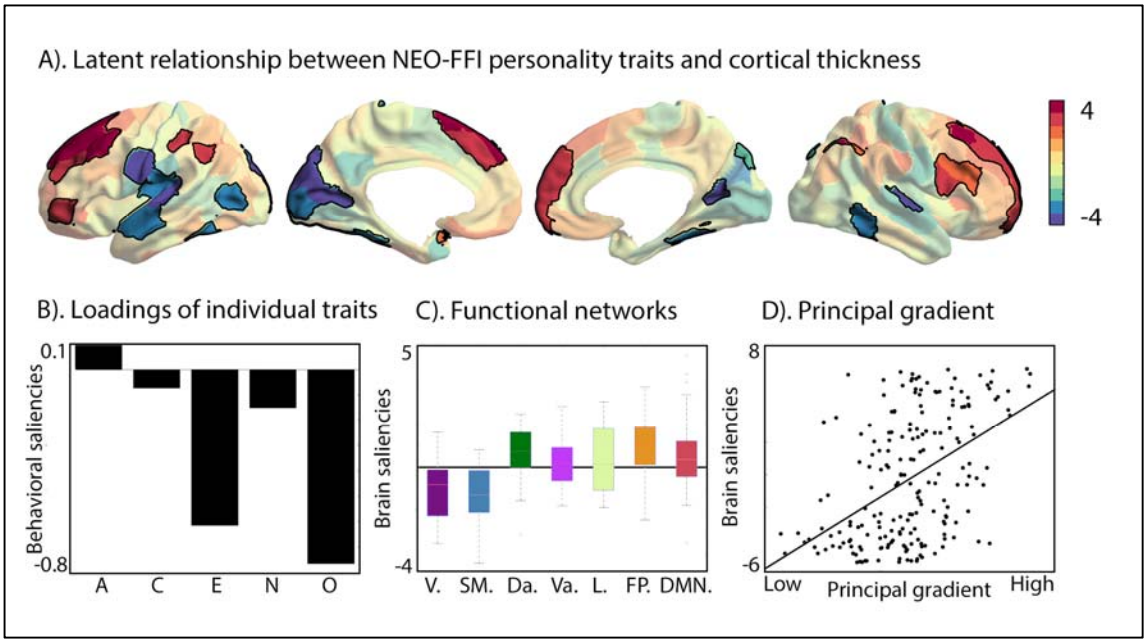



**Figure 3. Latent cortical thickness informed factor of personality traits.** A. Bootstrap ratio of the second brain saliency that showed significant robustness, where parcel-wise saliencies of -2>BSR>2 are highlighted. Red indicates a positive association whereas blue indicates a negative association; B. Loadings of the individual traits; C. Relation to functional networks(39) and D. Relation to functional gradient (38).

## Discussion

Both personality traits and macroscale brain structure are highly heritable, raising the question whether phenotypic relationships between personality and brain structure are driven by shared additive genetic effects. Indeed, in the current study, we observed significant genetic relationships between personality traits and local brain structure in the HCP dataset which included monozychotic and dyzychotic twins. Second, we observed that spatial patterns of phenotypic and genetic correlations between personality and cortical thickness were significantly positive, suggesting a genetic basis for phenotypic associations. At the same time, significant associations between personality traits and local cortical thickness did not consistently reflect phenotypic associations in two, unrelated, independent samples, and we could only observe a robust spatial relationship between openness and cortical thickness. As we observed significant phenotypic correlations between personality traits in all three datasets, we assessed whether robust latent relationships would exist between personality traits and cortical thickness. Using partial least squares analysis, we identified one latent personality component explaining 30% of the shared variance, most strongly related to openness and extraversion. The cortical thickness signature of this component featured a pattern from unimodal to heteromodal association cortices, suggesting a system-level relationship between personality and cortical thickness. The latent relationship between personality and cortical thickness was robust across samples, and observed to be driven by additive genetic effects.

To evaluate the relation between personality and cortical thickness we used compressed surface-based MRI data based on the parcellation scheme of Schaefer et al. Using compressed features of structural MRI has been suggested to both to improve signal-to-noise of brain measures (cf. Eickhoff et al.(34) and Genon et al.(40)), and optimize analysis scalability. The Schaefer parcellation is derived using functional MRI data from ~1500 subjects and integrates

local approaches detecting abrupt transitions in functional connectivity patterns and global approaches that cluster similar functional connectivity patterns (33). Indeed, a combination of within-area micro circuitry, proxied by brain morphometry, and between-area connectivity enables each area to perform a unique set of computations (41). Therefore, a parcellation approach that considers both local and global connectivity might benefit structural image analysis, as it reduces signal-to-noise both within and across individuals and makes control for multiple comparisons more straightforward (40). Based on the findings in our study, we suggest our approach might be a fruitful first exploratory step to investigate the relation between brain structure and behavior, and locate mechanisms of interest. Future studies can subsequently verify these results by exploring more specific mechanisms, as well as neuroanatomical features. For example, in line with our multivariate observations, there is converging evidence that inter-individual differences in topological integrative features of multi-modal areas are more important for higher-order cognitive functions, such as intelligence, than local features only (42).

Though we could establish phenotypic as well as genetic correlations between personality traits and local cortical thickness, associations were weak ($r<0.12$), and did not replicate in two unrelated, independent samples. In the HCP dataset, correspondence between predominantly frontal regions and personality traits of agreeableness, neuroticism, and openness have been previously reported using a non-parcel-based method by Owens and colleagues (31). Indeed, frontal cortices are functionally involved in a number of tasks involving higher cognitive functioning, such as executive functioning, metacognition and social cognition (43-48). At the same time, we observed that intelligence partially mediated these effects. As patterns of phenotypic and genetic correlation between cortical thickness and personality remained similar when controlling for intelligence, it suggests an interplay between intelligence, personality, and macroscale grey matter structure in the HCP sample. In

fact, the relationship between intelligence and personality has been debated in the literature. One the one hand it has been suggested that intelligence and personality relate to two different genetic factors. The former to mutation-selection, and the latter to balancing and frequency dependent selections(49, 50). On the other hand, various studies have shown a genetic relation between general intelligence and personality (51-53), as well as to specific traits such as openness (54) and extraversion (55). In the HCP sample the average intelligence is high (total cognitive score: 122), and all personality traits, except extraversion, show a genetic correlation with intelligence. Given that intelligence is highly heritable, and has been shown to have a genetic correlation with cortical thickness (56, 57) it is possible associations between personality traits and cortical thickness are enhanced in this sample because of its close relation to intelligence. Though we observed significant correlations between intelligence and various personality traits in both the GSP as well as eNKI datasets, intelligence-level in both datasets levels of intelligence was lower (108 and 102, respectively). It is possible that because of this, the interplay between personality traits, intelligence and grey matter structure is altered, resulting lacking robust relationships between personality and brain structure. For example, openness was the only trait that consistently related to general intelligence in all samples, and only in case of openness whole brain spatial patterns correlated across samples. Though these observations are promising, further studies are needed to investigate the interrelation between intelligence, personality, and brain structure in more dept.

We extend previously published phenotypic observations by showing relationships between personality and local cortical thickness are driven by shared additive genetic effects. The strength of genetic correlations is strongly dependent on the heritability of each of the correlated markers. In our sample, between 30 % and 60 % (on average 42 %) of variance in personality traits was explained by additive genetic factors. This is in line with previous

studies using twin and family samples (17) as well as genome-wide approaches (23). A recent meta-analysis (19) confirmed that an average 40 % of the variance in personality traits is of genetic origin. Also, conform previous studies (58-62), we observe high (h2 > 0.4) heritability of cortical thickness, with highest values in primary sensory areas. Heritability patterns follow previously described patterns with relatively strong genetic influence on cortical thickness in unimodal cortices, whereas variance in association cortices is on average less influenced by genetic factors (58-61, 63-65).

By testing the hypothesis that additive genetic effects drive the association between personality traits and local cortical thickness, we could observe a genetic link between agreeableness and extraversion to local brain structure in functionally meaningful regions. Indeed, the genetic relationship between agreeableness and regions involved in higher-order reasoning is in line with theoretical accounts that the ability to reflect on ones actions is essential for being able to be cooperative and prosocial (66). In case of extraversion we observed similar functional specificity. Extraversion was genetically associated with thickness of the temporo-parietal junction (TPJ). Regions in the TPJ have repeatedly been associated with both social cognition and language (67-70). At the same time, these correlations were not consistently mirrored by phenotypic correlations both within sample as well as across two independent samples, questioning the robustness of these local observations. Indeed, regions that showed genetic correlations at FDR-corrected thresholds were outliers, as typical values of genetic correlation ranged between -0.4 and 0.4. Furthermore, we observed that whole brain genetic correlations between personality and cortical thickness significantly related to phenotypic correlations, suggesting that the direction of the phenotypic and genetic relation between personality and cortical thickness was comparable across the cortex. The observed correspondence between phenotypic and genetic correlations within the HCP sample is in line with Cheverud's conjuncture. This assumption asserts the use of phenotypic correlations as proxies for genetic correlations and has been confirmed in other human traits (71). The

observed genetic correlation between cortical thickness and personality in the HCP sample is likely due to mediated pleiotropy (a gene affects A which affects B). Here a genetic process would affect grey matter macrostructure and associated function and, as a consequence, personality. Alternatively, it could be that genetic variation affects brain function which in turn modulates both macroscale structure as well as personality, or a genetic mechanism affects an unknown biological factor which in turn affects personality and brain structure. However, inversely, given that phenotypic correlations between personality and local brain structures are low, the co-heritability between local brain structure and personality traits is likely also low, and contribution of noise, confounding, or environmental factors in potentially high. Comparing genetic correlations with phenotypic correlations out of sample, only the spatial distribution of genetic correlation in openness was robustly related to phenotypic spatial distribution in all three samples. Coincidently openness had highest heritability in the HCP sample (58%), indicating that the largest proportion of variance in openness is not driven by environmental mechanisms or noise.

Assuming that genetic correlation patterns of the personality traits observed in the HCP sample are meaningful, there are various explanations for lack of association between genetic correlation and phenotypic correlation out of sample. First, it could be lack of power. Indeed extraversion, the second-most heritable trait, showed also positive correspondence between genetic correlation and phenotypic correlation out of sample at sub-threshold level. Second, though our samples all were from WEIRD (Western, educated, industrialized, rich, and democratic) populations (72), it is possible that functional processes underlying the responses were not comparable across samples. Indeed, personality is a complex psychological construct where various biological processes could underlie the behavioral phenotype. Thus, multiple functional processes, related to variation in grey matter structure, could underlie a complex trait such as personality. It is possible that due to their genetic similarity power is

increased to observe similar mappings in the twin sample. Also, (part of) variation in personality is due to rare genetic variants (14, 73, 74) which could lead to differences between samples resulting in variable patterns of brain-behavior correspondences. Third, it might be that traits probed are not comparable across samples due to challenges to reliably operationalize personality, and that confounding environmental and noise effects may vary across sample. Indeed, the observed association between intelligence, personality traits and brain structure in the HCP sample highlights the necessity to further study the interaction between personality, general cognitive skills, and brain structure.

Associations between personality traits and brain structure were further evaluated in our multivariate analysis. Indeed, in line with previous studies (19, 23), we observed phenotypic and genetic correlation between personality traits, suggestive that shared biological factors support variance across multiple traits. Using partial least squares, we could identify one multivariate relationship between personality traits on the one hand and cortical thickness on the other. This factor was predominantly driven by both openness and extraversion and showed some overlap with the genetic component of personality identified by Lo et al.(23) where extraversion and openness showed similar loadings. Its corresponding cortical thickness signature followed a pattern from unimodal to transmodal cortices, one of the most stable patterns of genetic, functional and microstructural cortical organization (75). Our observation that personality is related to local alterations in brain regions associated with both external oriented mental operations as well as internally oriented thought suggests that personality traits are not only supported by higher-order cognitive but also sensory processes. Indeed, personality traits have been linked to sensorimotor gating (76) and individual differences in personality relate to variation in cortical developmental processes (78). A different line of research has shown that in ASD, a pervasive neurodevelopmental condition with abnormal behavior, system-level changes in functional connectivity relate to

abnormalities in both sensory as well as higher-cognitive behavioral domains (77). Together, these observations put forward the hypothesis that variance in personality might not be robustly related to distributed effects in local anatomy, but rather integrative multivariate effects encompassing system-level neurobiological variance. Thus, further studies on the neurobiology of personality therefor requires to be conducted with functional and structural connectivity, as well as longitudinal, data enabling more directly analysis of the dynamic relation between system-level connectivity and personality and the role of genes and environment.

In the current study we could, for the first time, show a genetic link between macroscale grey matter anatomy and personality traits. Nevertheless, it is likely not only additive genetic effects, but also environmental and gene-environment interactions shape the relation between personality and cortical thickness (80). Only 40% of personality variance was observed heritable, which indicates that 60% of variance couldn't be attributed to additive genetic effects. Due to limitations in the twin-design, we could not account for these effects. For example, family environment, peer-groups, as well as development shape personality (81, 82). Future studies accounting for environment might be able to uncover environmental effects on covariance between personality and brain structure, and systematically probe sample specific effects. In similar vein, the focus of the current study has been on cortical grey matter macrostructure. Though our latent models indeed suggest that part of the variance in personality traits can be explained by grey matter structure, interindividual differences in personality have been also related to static and dynamic brain functional variations (83, 84). Indeed, recent work has shown genetics underlying structure and function are dissociable in heteromodal association cortices (85). As we observed both univariate as well as multivariate link between heteromodal association cortices and personality traits, future research on the

neurobiological basis of personality therefor requires to integrate differential genetic and environmental effects on brain structure and function.

Our study on the shared genetic basis of personality and brain structure was made possible by the open HCP, GSP, and eNKI neuroimaging repositories. These initiatives offer cognitive neuroimaging communities an unparalleled access to large datasets for the investigation of the brain basis of individual difference. They have also enabled us to highlight variability across samples, and our work involved several statistical corrections as well as validation experiments to verify stability of our observations. Notably, the use of multiple datasets enabled us to test robustness of positive findings, and highlighted lack of consistency in local correspondences between personality and brain structure. Given that reproducibility is increasingly important nowadays, our study illustrates the advantages of open data to increase our understanding of complex traits.

## Materials and methods

HCP sample:

*Participants and study design*

For our analysis we used the publicly available data from the Human Connectome Project S1200 release (HCP; http://www.humanconnectome.org/), which comprised data from 1206 individuals (656 females), 298 MZ twins, 188 DZ twins, and 720 singletons, with mean age 28.8 years (SD = 3.7, range = 22–37). We included for whom the scans and data had been released (humanconnectome.org) after passing the HCP quality control and assurance standards (86). The full set of inclusion and exclusion criteria are described elsewhere(87, 88). After removing individuals with missing structural imaging or behavioral data our sample consisted of 1106 individuals (including 286 MZ-twins and 170 DZ-twins) with mean age of 28.8 years (SD =3.7, range =22-37). See further Table 1 and 2.

*Structural imaging processing*

MRI protocols of the HCP are previously described in(87, 88). The pipeline used to obtain the Freesurfer-segmentation is described in detail in a previous article (87) and is recommended for the HCP-data. The pre-processing steps included co-registration of T1 and T2 scans, B1 (bias field) correction, and segmentation and surface reconstruction using FreeSurfer version 5.3-HCP to estimate cortical thickness.

*Behavioral assessment*

The NEO-FFI personality traits were assessed using the NEO-Five-Factors-Inventory (NEO-FFI)(89). The NEO-FFI is composed of a subset of 60-items extracted from the full-length 240-item NEO-PI-R. For each item, participants reported their level of agreement on a 5-point Likert scale, from strongly disagree to strongly agree. The NEO instruments have been previously validated in USA and several other countries(90). . See further Table 1 and 2.

As a proxy for IQ we used the NIH Toolbox Cognition(91), 'total composite score'. The Cognitive Function Composite score is derived by averaging the normalized scores of each of the Fluid and Crystallized cognition measures, then deriving scale scores based on this new distribution. Higher scores indicate higher levels of cognitive functioning. Participant score is normed to those in the entire NIH Toolbox Normative Sample (18 and older), regardless of age or any other variable, where a score of 100 indicates performance that was at the national average and a score of 115 or 85, indicates performance 1 SD above or below the national average. See further Table 2 and 3.

For post-hoc analysis on the brain saliency we used the behavioral scores as reported in the HCP data dictionary unrestricted variables, for details please see (https://wiki.humanconnectome.org/display/PublicData/HCP+Data+Dictionary+Public-+Updated+for+the+1200+Subject+Release#HCPDataDictionaryPublic-Updatedforthe1200SubjectRelease-Instrument:SocialRelationships).

| **Measure** | **n** | **mean±SD (range)** |
|---|---|---|
| ***Males/Females*** | 506/600 | - |
| ***Age*** | 1106 | 28.8±3.7 (22-36) |
| ***Intelligence (Composite score)*** | 1089 | 121.9±14.6 (84.6-153.4) |
| ***Agreeableness*** | 1106 | 33.5±5.8 |
| ***Conscientiousness*** | 1106 | 34.5±5.9 |
| ***Extraversion*** | 1106 | 30.7±6 |
| ***Neuroticism*** | 1106 | 16.6±7.4 |
| ***Openness*** | 1106 | 28.3±6.2 |

**Table 2. Behavioral characteristics of the full HCP sample.** Behavioral characteristics for gender, age, intelligence as well as the NEO-FFI scores in the HCP sample including twins.

| **Measure** | **n** | **mean±SD (range)** |
|---|---|---|
| ***Males/Females*** | 195/224 | - |
| ***Age*** | 419 | 28.6±3.7 (22-36) |
| ***Intelligence (Composite score)*** | 1089 | 121.6±14.7 (84.6-153.4) |

| | | |
|---|---|---|
| ***Agreeableness*** | 419 | 33.1±5.7 |
| ***Conscientiousness*** | 419 | 34.6±5.8 |
| ***Extraversion*** | 419 | 30.5±6 |
| ***Neuroticism*** | 419 | 17.2±7.8 |
| ***Openness*** | 419 | 28.7±5.9 |

**Table 3. Behavioral characteristics of the unrelated HCP sample.** Behavioral characteristics for gender, age, intelligence as well as the NEO-FFI scores in the HCP sample of unrelated individuals.

GSP sample

*Participants and study design*

To evaluate the cross-sample reproducibility of observations we additionally investigated correspondence between personality and cortical brain structure in the Brain Genomics Superstruct Project (GSP) (92). Participants provided written informed consent in accordance with guidelines established by the Partners Health Care Institutional Review Board and the Harvard University Committee on the Use of Human Subjects in Research (See Supplementary Appendix A in (92)).

*Structural imaging processing*

All imaging data were collected on matched 3T Tim Trio scanners (Siemens Healthcare, Erlangen, Germany) at Harvard University and Massachusetts General Hospital using the vendor-supplied 12-channel phased-array head coil. Structural data included a high-resolution (1.2mm isotropic) multi-echo T1-weighted magnetization-prepared gradient-echo image (multi-echo MPRAGE23, see further: (92)). The low participant burden resulting from the use of multi-echo MPRAGE anatomical scans makes this sequence well suited for high-throughput studies. The morphometric features derived through conventional 6-min 1mm MPRAGE and the 2-min 1.2mm multi-echo MPRAGE are highly consistent (r2>0.9 for most structures)24 suggesting that rapid acquisition multi-echo MPRAGE can be used for many

purposes in place of longer anatomical scans without degradation of the quantitative morphometric estimates. Rapid acquisition is also beneficial because it lessens the opportunity for within-scan motion.

*Behavioral markers.*

The NEO-FFI personality traits were assessed using the NEO-Five-Factors-Inventory (NEO-PI-R)(93), the full-length 240-item NEO-PI-R. For each item, participants reported their level of agreement on a 5-point Likert scale, from strongly disagree to strongly agree. The NEO instruments have been previously validated in USA and several other countries(90). As a proxy for IQ we used the estimated IQ derived through the OPIE3 formula(94). Reported values are in integers and binned. For post-hoc analysis on the partial least squares behavioral saliency we used the behavioral data from (https://static1.squarespace.com/static/5b58b6da7106992fb15f7d50/t/5b68650d8a922db3bb807a90/1533568270847/GSP_README_140630.pdf). See further Table 4.

| **Measure** | **n** | **mean±SD (range)** |
|---|---|---|
| ***Males/Females*** | 536/390 | - |
| ***Age*** | 926 | 21.6±3.9 (19-35) |
| ***Estimated IQ*** | 892 | 108.7±8.1 (77-129) |
| ***Agreeableness*** | 926 | 32.0±6.6 |
| ***Conscientiousness*** | 926 | 31.7±7.2 |
| ***Extraversion*** | 926 | 30.7±6.5 |
| ***Neuroticism*** | 926 | 20.3±8.8 |
| ***Openness*** | 926 | 31.6±6.1 |

**Table 4. Behavioral characteristics of the GSP sample.** Behavioral characteristics for gender, age, intelligence as well as the NEO-FFI scores in the GSP sample.

eNKI sample:

*Participants and study design*

To evaluate the cross-sample reproducibility of observations we additionally investigated correspondence between personality and cortical brain structure in the enhanced Nathan Kline Institute-Rockland Sample (NKI). The sample was made available by the Nathan-Kline Institute (NKY, NY, USA), as part of the '*enhanced NKI-Rockland sample*' (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3472598/). All approvals regarding human subjects' studies were sought following NKI procedures. Scans were acquired from the International Neuroimaging Data Sharing Initiative (INDI) online database http://fcon_1000.projects.nitrc.org/indi/enhanced/studies.html

For our phenotypical analyses, we selected individuals with personality and imaging data. Our sample for phenotypical correlations consisted of 792 (494 females) individuals with mean age of 41.1 years (SD =20.3, range =12-85). Please see Table 5 for demographic characteristics.

| **Measure** | **n** | **mean±SD (range)** |
|---|---|---|
| ***Males/Females*** | 298/494 | - |
| ***Age*** | 792 | 41.1±20.3 (12-85) |
| ***Intelligence (WASI)*** | 792 | 101.9±13.3 (65-141) |
| ***Agreeableness*** | 792 | 34.3±6.0 |
| ***Conscientiousness*** | 792 | 33.9±7.4 |
| ***Extraversion*** | 792 | 30.0±6.4 |
| ***Neuroticism*** | 792 | 18.5±8.1 |
| ***Openness*** | 792 | 31.9±6.3 |

**Table 5. Behavioral characteristics of the eNKI sample**. Behavioral characteristics for gender, age, intelligence as well as the NEO-FFI scores in the eNKI sample.

*Structural imaging processing*

3D magnetization-prepared rapid gradient-echo imaging (3D MP-RAGE) structural scans(95) were acquired using a 3.0 T Siemens Trio scanner with TR=2500 ms, TE=3.5 ms, Bandwidth=190 Hz/Px, field of view=256 × 256 mm, flip angle=8°, voxel size=1.0 × 1.0 × 1.0 mm. More details on image acquisition are available at http://fcon_1000.projects.nitrc.org/indi/enhanced/studies.html. All T1 scans were visually inspected to ensure the absence of gross artefacts and subsequently pre-processed using the Freesurfer software library (http://surfer.nmr.mgh.harvard.edu/) Version 5.3.0(96).

*Behavioral markers.*

The NEO-FFI personality traits were assessed using the NEO-FFI3(89). The NEO-FFI-3 is a 60-item psychological personality inventory that assesses based on the five-factor model: Openness to Experience, Conscientiousness, Extraversion, Agreeableness, and Neuroticism. Participants are asked to select the response that best represents their opinion on a 5-point scale: 0-Strongly Agree, 1-Agree, 2-Neutral, 3-Disagree, 4-Strongly Disagree. The NEO instruments have been previously validated in USA and several other countries(90).

For intelligence we used the Wechsler Abbreviated Scale of Intelligence (WASI-II)(97), full scale IQ. The WASI is a general intelligence, or IQ test designed to assess specific and overall cognitive capabilities and is individually administered to children, adolescents and adults (ages 6-89). It is a battery of four subtests: Vocabulary (31-item), Block Design (13-item), Similarities (24-item) and Matrix Reasoning (30-item). In addition to assessing general, or Full Scale, intelligence, the WASI is also designed to provide estimates of Verbal and Performance intelligence consistent with other Wechsler tests. Specifically, the four subtests comprise the full scale and yield the Full Scale IQ (FSIQ-4), see further Table 5.

*Parcellation approach*

In all three samples, we used a parcellation scheme(33) based on the combination of a local gradient approach and a global similarity approach using a gradient-weighted Markov Random models. The parcellation has been extensively evaluated with regards to stability and convergence with histological mapping and alternative parcellations. In the context of the current study, we focus on the granularity of 200 parcels, as averaging will improve signal-to-noise. 200 parcels are close to granularity used in Enigma (Desikan-atlas, 68 parcels) while at the same time providing more anatomical detail in functionally heterogeneous regions such as parietal and frontal cortex. In order to improve signal-to-noise and improve analysis speed, we opted to average unsmoothed structural data within each parcel. Thus, cortical thickness of each ROI was estimated as the trimmed mean (10 percent trim).

*Reproducibility and phenotypic correlation analysis*.

Between-sample comparison of the cortical thickness estimations are performed using paired t-tests, within each region while controlling for global thickness effects. For our phenotypical analysis between local cortical thickness and personality traits we performed Spearman correlation analysis, controlling for the same variables as in the genetic analysis, namely age, sex, age × sex interaction, $age^2$, $age^2$ × sex interaction, as well as global thickness effects when investigating brain structure. Results were corrected for multiple comparisons using Benjamin-Hochberg FDR(98) at whole-brain analysis, where we corrected for number of analysis within the current step and report FDR thresholds. Bonferroni correction was applied when investigating behavior or in post-hoc brain analysis, here we corrected for number of analysis x ROIs. Post-hoc we also controlled for a proxy for intelligence, total cognitive score(91) or comparable measures in the GSP(94) and eNKI samples.

*Heritability and genetic correlation analysis*

To investigate the heritability and genetic correlation of brain structure and personality traits, we analyzed 200 parcels of cortical thickness, as well as personality trait score of each subject in a twin-based heritability analysis. As in previous studies (99), the quantitative genetic analyses were conducted using Sequential Oligogenic Linkage Analysis Routines (SOLAR) (100). SOLAR uses maximum likelihood variance-decomposition methods to determine the relative importance of familial and environmental influences on a phenotype by modeling the covariance among family members as a function of genetic proximity. This approach can handle pedigrees of arbitrary size and complexity and thus, is optimally efficient with regard to extracting maximal genetic information. To ensure that our traits, behavioral as well as of cortical thickness parcels, conform to the assumptions of normality, an inverse normal transformation was applied for all behavioral and neuroimaging traits(99).

Heritability ($h^2$) represents the portion of the phenotypic variance ($\sigma^2_p$) accounted for by the total additive genetic variance ($\sigma^2_g$), i.e., $h^2 = \sigma^2_g/\sigma^2_p$. Phenotypes exhibiting stronger covariances between genetically more similar individuals than between genetically less similar individuals have higher heritability. Within SOLAR, this is assessed by contrasting the observed covariance matrices for a neuroimaging measure with the structure of the covariance matrix predicted by kinship. Heritability analyses were conducted with simultaneous estimation for the effects of potential covariates. For this study, we included covariates including age, sex, age × sex interaction, age$^2$, age$^2$ × sex interaction. Post-hoc we also controlled for a proxy for intelligence, total cognitive score(91). When investigating cortical thickness, we additionally controlled for global thickness effects (mean cortical thickness).

To determine if variations in personality and brain structure were influenced by the same genetic factors, genetic correlation analyses were conducted. More formally, bivariate polygenic analyses were performed to estimate genetic ($\rho_g$) and environmental ($\rho_e$)

correlations, based on the phenotypical correlation ($\rho_p$), between brain structure and personality with the following formula: $\rho_p = \rho_g\sqrt{(h^2_1 h^2_2)} + \rho_e\sqrt{[(1 - h^2_1)(1 - h^2_2)]}$, where $h^2_1$ and $h^2_2$ are the heritability's of the parcel-based cortical thickness and the various behavioral traits. The significance of these correlations was tested by comparing the log likelihood for two restricted models (with either $\rho_g$ or $\rho_e$ constrained to be equal to 0) against the log likelihood for the model in which these parameters were estimated. A significant genetic correlation (corrected for multiple comparisons using Benjamin-Hochberg FDR(98) in case of whole-brain analysis and Bonferroni correction when investigating behavior or in post-hoc brain analysis) is evidence suggesting that (a proportion of) both phenotypes are influenced by a gene or set of genes(101).

*Functional decoding*

All significant parcels were in a last step functionally characterized using the Behavioral Domain meta-data from the BrainMap database using forward inference (http://www.brainmap.org(102, 103)). To do so, volumetric counterparts of the surface-based parcels were identified. In particular, we identified those meta-data labels (describing the computed contrast [behavioral domain]) that were significantly more likely than chance to result in activation of a given parcel(27, 36, 40). That is, functions were attributed to the identified neurogenetic effects by quantitatively determining which types of experiments are associated with activation in the respective parcellation region. Significance was established using a binomial test ($p < 0.05$, corrected for multiple comparisons using false discovery rate (FDR)).

*Mediation analysis*

In short, mediation analysis is an important tool in the behavioral sciences for investigating the role of intermediate variables that lie in the path between a treatment and an outcome

variable. The influence of the intermediate variable on the outcome is often explored using a linear structural equation model (LSEM), with model coefficients interpreted as possible effects. Here we performed single-level mediation analysis combined with bootstrap-based significant testing using the function 'mediation.m' from the Mediation toolbox download from https://github.com/canlab/MediationToolbox (104, 105). We controlled for effects of global thickness, age and gender, and used ranked variables of personality traits, intelligence and local brain structure.

*Partial least squares*

PLS is a multivariate data-driven statistical technique that aims to maximize the covariance between two matrices by deriving *latent components* (LCs), which are optimal linear combinations of the original matrices (35, 79). We applied PLS to the cortical thickness and personality measures of all participants. Each LC is characterized by a distinct cortical thickness pattern (called brain *saliences*) and a distinct behavioral profile (called behavioral *saliences*). By linearly projecting the brain and behavioral measures of each participant onto their respective saliences, we obtain individual-specific brain and behavioral *composite scores* for each LC. By construction, PLS seeks to find saliences that maximize across-participant covariance between the brain and behavioral composite scores. The number of significant LCs was determined by a permutation (1000 permutations). The p-values (from the permutation test) for the LCs were corrected for multiple comparisons using a false discovery rate (FDR) of $p < 0.05$. To interpret the LCs, we computed Pearson's correlations between behavioral composite scores for each LC and behavioral measures not included in the analysis. A large positive (or negative) correlation for a particular behavioral measure for a given LC indicates greater importance of the behavioral measure for the LC (106).

**Acknowledgements**

We would like to thank the various contributors to the open access databases that our data was downloaded from. Specifically; HCP data were provided by the Human Connectome Project, Washington University, the University of Minnesota, and Oxford University Consortium (Principal Investigators: David Van Essen and Kamil Ugurbil;1U54MH091657) funded by the 16 NIH Institutes and Centers that support the NIH Blueprint for Neuroscience Research; and by the McDonnell Center for Systems Neuroscience at Washington University. GSP data were provided by the Brain Genomics Superstruct Project of Harvard University and the Massachusetts General Hospital, (Principal Investigators: Randy Buckner, Joshua Roffman, and Jordan Smoller), with support from the Center for Brain Science Neuroinformatics Research Group, the Athinoula A. Martinos Center for Biomedical Imaging, and the Center for Human Genetic Research. 20 individual investigators at Harvard and MGH generously contributed data to the overall project.

For enhanced NKI, we would like to thank the principal support for the enhanced NKI-RS project is provided by the NIMH BRAINS R01MH094639-01 (PI Milham). Funding for key personnel was also provided in part by the New York State Office of Mental Health and Research Foundation for Mental Hygiene. Funding for the decompression and augmentation of administrative and phenotypic protocols provided by a grant from the Child Mind Institute (1FDN2012-1). Additional personnel support provided by the Center for the Developing Brain at the Child Mind Institute, as well as NIMH R01MH081218, R01MH083246, and R21MH084126. Project support also provided by the NKI Center for Advanced Brain Imaging (CABI), the Brain Research Foundation (Chicago, IL), and the Stavros Niarchos Foundation. Last, we want to thank L.C.Valk for proofreading the manuscript.

## References


1. W. Mischel, Toward an integrative science of the person. *Annu Rev Psychol* **55**, 1-22 (2004).
2. R. R. McCrae, P. T. Costa, Jr., Personality trait structure as a human universal. *Am Psychol* **52**, 509-516 (1997).
3. O. P. John, S. Srivastava, "The Big Five Trait taxonomy: History, measurement, and theoretical perspectives." in Handbook of Personality: Theory and Research., L. A. Pervin, O. P. John, Eds. (Guilford Press, 1999), pp. 102-138.
4. R. R. McCrae, P. T. Costa, Jr., Updating Norman's "Adequate Taxonomy": intelligence and personality dimensions in natural language and in questionnaires. *J Pers Soc Psychol* **49**, 710-721 (1985).
5. R. R. McCrae, P. T. Costa, Jr., Validation of the five-factor model of personality across instruments and observers. *J Pers Soc Psychol* **52**, 81-90 (1987).
6. J. E. Strickhouser, E. Zell, Z. Krizan, Does personality predict health and well-being? A metasynthesis. *Health Psychol* **36**, 797-810 (2017).
7. A. Alvergne, M. Jokela, V. Lummaa, Personality and reproductive success in a high-fertility human population. *Proc Natl Acad Sci U S A* **107**, 11745-11750 (2010).
8. J. B. Asendorpf, S. Wilpers, Personality effects on social relationships. *Journal of Personality and Social Psychology* **74**, 1531-1544 (1998).
9. S. Rothmann, E. P. Coetzer, The big five personality dimensions and job performance. *SA Journal of Industrial Psychology* **29** (2003).
10. J. D. Miller, D. R. Lynam, T. A. Widiger, C. Leukefeld, Personality disorders as extreme variants of common personality dimensions: can the Five-Factor Model adequately represent psychopathy? *J Pers* **69**, 253-276 (2001).
11. T. J. Trull, Dimensional models of personality: the five-factor model and the DSM-5. *Dialogues Clin Neurosci* **15**, 135-146 (2013).
12. R. I. Damian, M. Spengler, A. Sutu, B. W. Roberts, Sixteen going on sixty-six: A longitudinal study of personality stability and change across 50 years. *J Pers Soc Psychol* **117**, 674-695 (2019).
13. M. A. Harris, C. E. Brett, W. Johnson, I. J. Deary, Personality stability from age 14 to age 77 years. *Psychol Aging* **31**, 862-874 (2016).
14. L. Penke, M. Jokela, The evolutionary genetics of personality revisited. *Current Opinion in Psychology* **7**, 104-109 (2016).
15. T. J. Bouchard, Jr., Genes, environment, and personality. *Science* **264**, 1700-1701 (1994).
16. T. J. Bouchard, Jr., M. McGue, Genetic and environmental influences on human psychological differences. *J Neurobiol* **54**, 4-45 (2003).
17. K. L. Jang, W. J. Livesley, P. A. Vernon, Heritability of the big five personality dimensions and their facets: a twin study. *J Pers* **64**, 577-591 (1996).
18. J. C. Loehlin, R. R. McCrae, P. T. Costa, O. P. John, Heritabilities of Common and Measure-Specific Components of the Big Five Personality Factors. *Journal of Research in Personality* **32**, 431-453 (1998).
19. T. Vukasovic, D. Bratko, Heritability of personality: A meta-analysis of behavior genetic studies. *Psychol Bull* **141**, 769-785 (2015).
20. T. J. Bouchard, Jr., J. C. Loehlin, Genes, evolution, and personality. *Behav Genet* **31**, 243-273 (2001).
21. M. H. de Moor *et al.*, Meta-analysis of genome-wide association studies for personality. *Molecular psychiatry* **17**, 337-349 (2012).

22. S. M. van den Berg *et al.*, Meta-analysis of Genome-Wide Association Studies for Extraversion: Findings from the Genetics of Personality Consortium. *Behav Genet* **46**, 170-182 (2016).
23. M. T. Lo *et al.*, Genome-wide analyses for personality traits identify six genomic loci and show correlations with psychiatric disorders. *Nat Genet* **49**, 152-156 (2017).
24. K. J. Verweij *et al.*, Maintenance of genetic variation in human personality: testing evolutionary models by estimating heritability due to common causal variants and investigating the effect of distant inbreeding. *Evolution* **66**, 3288-3251 (2012).
25. G. o. P. Consortium, Meta-analysis of genome-wide association studies for neuroticism, and the polygenic association with major depressive disorder. *JAMA Psychiatry* (2015).
26. C. G. DeYoung *et al.*, Testing predictions from personality neuroscience. Brain structure and the big five. *Psychol Sci* **21**, 820-828 (2010).
27. A. D. Nostro, V. I. Muller, A. T. Reid, S. B. Eickhoff, Correlations Between Personality and Brain Structure: A Crucial Role of Gender. *Cereb Cortex* **27**, 3698-3712 (2017).
28. R. Riccelli, N. Toschi, S. Nigro, A. Terracciano, L. Passamonti, Surface-based morphometry reveals the neuroanatomical basis of the five-factor model of personality. *Soc Cogn Affect Neurosci* **12**, 671-684 (2017).
29. A. Bjornebekk *et al.*, Neuronal correlates of the five factor model (FFM) of human personality: Multimodal imaging in a large healthy sample. *Neuroimage* **65**, 194-208 (2013).
30. R. Avinun, S. Isreal, A. R. Knodt, A. R. Hariri, No evidence for associations between big five personality traits and variability in brain gray or white matter. (BioArchiv June 4th).
31. M. M. Owens *et al.*, Cortical morphometry of the five-factor model of personality: findings from the Human Connectome Project full sample. *Soc Cogn Affect Neurosci* **14**, 381-395 (2019).
32. N. Solovieff, C. Cotsapas, P. H. Lee, S. M. Purcell, J. W. Smoller, Pleiotropy in complex traits: challenges and strategies. *Nat Rev Genet* **14**, 483-495 (2013).
33. A. Schaefer *et al.*, Local-Global Parcellation of the Human Cerebral Cortex from Intrinsic Functional Connectivity MRI. *Cereb Cortex* **28**, 3095-3114 (2018).
34. S. B. Eickhoff, R. T. Constable, B. T. T. Yeo, Topographic organization of the cerebral cortex and brain cartography. *Neuroimage* **170**, 332-347 (2018).
35. A. R. McIntosh, N. J. Lobaugh, Partial least squares analysis of neuroimaging data: applications and advances. *Neuroimage* **23 Suppl 1**, S250-263 (2004).
36. P. T. Fox, J. L. Lancaster, A. R. Laird, S. B. Eickhoff, Meta-analysis in human neuroimaging: computational modeling of large-scale databases. *Annu Rev Neurosci* **37**, 409-434 (2014).
37. S. Kharabian Masouleh, S. B. Eickhoff, F. Hoffstaedter, S. Genon, I. Alzheimer's Disease Neuroimaging, Empirical examination of the replicability of associations between brain structure and psychological variables. *elife* (2019).
38. D. S. Margulies *et al.*, Situating the default-mode network along a principal gradient of macroscale cortical organization. *Proc Natl Acad Sci U S A* **113**, 12574-12579 (2016).
39. B. T. Yeo *et al.*, The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *J Neurophysiol* **106**, 1125-1165 (2011).
40. S. Genon, A. Reid, R. Langner, K. Amunts, S. B. Eickhoff, How to Characterize the Function of a Brain Region. *Trends Cogn Sci* **22**, 350-364 (2018).
41. D. C. Van Essen, M. F. Glasser, Parcellating Cerebral Cortex: How Invasive Animal Studies Inform Noninvasive Mapmaking in Humans. *Neuron* **99**, 640-663 (2018).

42. J. Seidlitz *et al.*, Morphometric Similarity Networks Detect Microscale Cortical Organization and Predict Inter-Individual Cognitive Variation. *Neuron* **97**, 231-247 e237 (2018).
43. D. M. Amodio, C. D. Frith, Meeting of minds: the medial frontal cortex and social cognition. *Nat Rev Neurosci* **7**, 268-277 (2006).
44. B. Baird, J. Smallwood, K. J. Gorgolewski, D. S. Margulies, Medial and lateral networks in anterior prefrontal cortex support metacognitive ability for memory and perception. *J Neurosci* **33**, 16657-16665 (2013).
45. S. Bludau *et al.*, Cytoarchitecture, probability maps and functions of the human frontal pole. *Neuroimage* **93 Pt 2**, 260-275 (2014).
46. R. L. Buckner, J. R. Andrews-Hanna, D. L. Schacter, The brain's default network: anatomy, function, and relevance to disease. *Ann N Y Acad Sci* **1124**, 1-38 (2008).
47. S. M. Fleming, R. J. Dolan, The neural basis of metacognitive ability. *Philos Trans R Soc Lond B Biol Sci* **367**, 1338-1349 (2012).
48. S. L. Valk, B. C. Bernhardt, A. Bockler, P. Kanske, T. Singer, Substrates of metacognition on perception and metacognition on higher-order cognition relate to different subsystems of the mentalizing network. *Hum Brain Mapp* **37**, 3388-3399 (2016).
49. M. A. Woodley, The cognitive differentiation-integration effect hypothesis: A synthesis between the fitness indicator and life history models of human intelligence. *Review of General Psychology* **15**, 228-245 (2011).
50. J. C. Loehlin *et al.*, Is the a genetic correlation between general factors of intelligence and personality. *Twin Research and Human Genetics* **18**, 234-242 (2015).
51. C. S. Dunkel, T. Cabeza de Baca, M. A. Woodley, H. B. F. Fernandes, The general factor of personality and general intelligence: Testing hypothesis from differential-K, life history theory, and strategic differentiation-integration effort. . *Personality and Individual Differences* **61-62**, 13-17 (2014).
52. C. S. Dunkel, D. van der Linden, K. M. Beaver, M. A. Woodley, Using a prison sample to assess the association between the general intelligence factor of personality and general intelligence. *Intelligence* **47** (2014).
53. A. Kretzschmar, M. Spengler, A. L. Schubert, R. Steinmayr, M. Ziegler, The Relation of Personality and Intelligence-What Can the Brunswik Symmetry Principle Tell Us? *J Intell* **6** (2018).
54. M. Bartels *et al.*, The five factor model of personality and intelligence: A twin study of the relationship between the two constructs. *Personality and Individual Differences* **53**, 368-373 (2012).
55. D. Bratko, A. Butkovic, T. Vukasovic, T. Chamorro-Premuzic, S. von Stumm, Cognitive ability, self-assessed intelligence, and personality: Common genetic but indepedent environmental aetiologies. *Intelligence* **40** (2012).
56. J. E. Schmitt *et al.*, The Dynamic Associations Between Cortical Thickness and General Intelligence are Genetically Mediated. *Cereb Cortex* 10.1093/cercor/bhz007 (2019).
57. T. Ge *et al.*, The Shared Genetic Basis of Educational Attainment and Cerebral Cortical Morphology. *Cereb Cortex* 10.1093/cercor/bhy216 (2018).
58. W. S. Kremen *et al.*, Genetic and environmental influences on the size of specific brain regions in midlife: the VETSA MRI study. *Neuroimage* **49**, 1213-1223 (2010).
59. L. T. Strike *et al.*, Genetic Complexity of Cortical Structure: Differences in Genetic and Environmental Factors Influencing Cortical Surface Area and Thickness. *Cereb Cortex* 10.1093/cercor/bhy002 (2018).

60. L. T. Eyler *et al.*, A comparison of heritability maps of cortical surface area and thickness and the influence of adjustment for whole brain measures: a magnetic resonance imaging twin study. *Twin Res Hum Genet* **15**, 304-314 (2012).
61. M. S. Panizzon *et al.*, Distinct genetic influences on cortical surface area and cortical thickness. *Cereb Cortex* **19**, 2728-2735 (2009).
62. A. M. Winkler *et al.*, Cortical thickness or grey matter volume? The importance of selecting the phenotype for imaging genetics studies. *Neuroimage* **53**, 1135-1146 (2010).
63. J. Teeuw *et al.*, Genetic Influences on the Development of Cerebral Cortical Thickness During Childhood and Adolescence in a Dutch Longitudinal Twin Sample: The Brainscale Study. *Cereb Cortex* 10.1093/cercor/bhy005 (2018).
64. E. Hofer, e. al., Genetic Determinants of Cortical Structure (Thickness, Surface Area and Volumes) among Disease Free Adults in the CHARGE Consortium. *bioRxiv preprint first posted online Sep. 9, 2018; doi: http://dx.doi.org/10.1101/409649*. (2018).
65. A. M. Fjell *et al.*, Development and aging of cortical thickness correspond to genetic organization patterns. *Proc Natl Acad Sci U S A* **112**, 15462-15467 (2015).
66. C. D. Frith, The role of metacognition in human social interactions. *Philos Trans R Soc Lond B Biol Sci* **367**, 2213-2223 (2012).
67. D. Bzdok *et al.*, Left inferior parietal lobe engagement in social cognition and language. *Neurosci Biobehav Rev* **68**, 319-334 (2016).
68. R. A. Mar, The neural bases of social cognition and story comprehension. *Annu Rev Psychol* **62**, 103-134 (2011).
69. P. Kanske, A. Bockler, F. M. Trautwein, T. Singer, Dissecting the social brain: Introducing the EmpaToM to reveal distinct neural networks and brain-behavior relations for empathy and Theory of Mind. *Neuroimage* **122**, 6-19 (2015).
70. S. L. Valk *et al.*, Socio-Cognitive Phenotypes Differentially Modulate Large-Scale Structural Covariance Networks. *Cereb Cortex* 10.1093/cercor/bhv319 (2016).
71. S. M. Sodini, K. E. Kemper, N. R. Wray, M. Trzaskowski, Comparison of Genotypic and Phenotypic Correlations: Cheverud's Conjecture in Humans. *Genetics* **209**, 941-948 (2018).
72. R. Laajaj *et al.*, Challenges to capture the big five personality traits in non-WEIRD populations. *Science Advances* **5** (2019).
73. W. D. Hill *et al.*, Genomic analysis of family data reveals additional genetic effects on intelligence and personality. *Molecular psychiatry* **23**, 2347-2362 (2018).
74. E. A. Boyle, Y. I. Li, J. K. Pritchard, An Expanded View of Complex Traits: From Polygenic to Omnigenic. *Cell* **169**, 1177-1186 (2017).
75. J. M. Huntenburg, P. L. Bazin, D. S. Margulies, Large-Scale Gradients in Human Cortical Organization. *Trends Cogn Sci* **22**, 21-31 (2018).
76. N. R. Swerdlow, D. Filion, M. A. Geyer, D. L. Braff, "Normal" personality correlates of sensorimotor, cognitive, and visuospatial gating. *Biol Psychiatry* **37**, 286-299 (1995).
77. S. J. Hong *et al.*, Atypical functional connectome hierarchy in autism. *Nat Commun* **10**, 1022 (2019).
78. L. Ferschmann *et al.*, Personality Traits Are Associated With Cortical Development Across Adolescence: A Longitudinal Structural MRI Study. *Child Dev* **89**, 811-822 (2018).
79. D. Zoller *et al.*, Disentangling resting-state BOLD variability and PCC functional connectivity in 22q11.2 deletion syndrome. *Neuroimage* **149**, 85-97 (2017).
80. A. Kong *et al.*, The nature of nurture: Effects of parental genotypes. *Science* **359**, 424-428 (2018).

81. C. J. Hopwood *et al.*, Genetic and environmental influences on personality trait stability and growth during the transition to adulthood: a three-wave longitudinal study. *J Pers Soc Psychol* **100**, 545-556 (2011).
82. K. Nakao *et al.*, The influences of family environment on personality traits. *Psychiatry Clin Neurosci* **54**, 91-95 (2000).
83. X. Wu *et al.*, Personality traits are related with dynamic functional connectivity in major depression disorder: A resting-state analysis. *J Affect Disord* **245**, 1032-1042 (2019).
84. J. Dubois, P. Galdi, Y. Han, L. K. Paul, R. Adolphs, Resting-state functional brain connectivity best predicts the personality dimension of openness to experience. *Personal Neurosci* **1** (2018).
85. M. A. Bertolero *et al.*, The network architecture of the human brain is modularly encoded in the genome. (arXiv).
86. D. S. Marcus *et al.*, Human Connectome Project informatics: quality control, database services, and data visualization. *Neuroimage* **80**, 202-219 (2013).
87. M. F. Glasser *et al.*, The minimal preprocessing pipelines for the Human Connectome Project. *Neuroimage* **80**, 105-124 (2013).
88. D. C. Van Essen *et al.*, The WU-Minn Human Connectome Project: an overview. *Neuroimage* **80**, 62-79 (2013).
89. R. R. McCrae, P. T. Costa, A contemplated revision of the NEO Five-Factor Inventory. *Pers Individ Dif.* **36**, 587-596 (2004).
90. R. R. McCrae, A. Terracciano, Personality profiles of cultures: aggregate personality traits. *J Pers Soc Psychol* **89**, 407-425 (2005).
91. S. Weintraub *et al.*, Cognition assessment using the NIH Toolbox. *Neurology* **80**, S54-64 (2013).
92. A. J. Holmes *et al.*, Brain Genomics Superstruct Project initial data release with structural, functional, and behavioral measures. *Sci Data* **2**, 150031 (2015).
93. P. T. Costa, R. R. McCrae, *NEO PI-R Professional Manual* (Psychological Assessment Resources, Inc., 1992).
94. M. R. Schoenberg, J. G. Scott, K. Duff, R. L. Adams, Estimation of WAIS-III intelligence from combined performance and demographic variables: development of the OPIE-3. *Clin Neuropsychol* **16**, 426-437 (2002).
95. J. P. Mugler, 3rd, J. R. Brookeman, Three-dimensional magnetization-prepared rapid gradient-echo imaging (3D MP RAGE). *Magn Reson Med* **15**, 152-157 (1990).
96. B. Fischl, FreeSurfer. *Neuroimage* **62**, 774-781 (2012).
97. D. Wechsler, *Wechsler Abbreviated Scale of Intelligence.* (The Psychological Corporation., San Antonio, TX., 1999).
98. Y. Benjamini, Y. Hochberg, Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. *Journal of the Royal Statistical Society. Series B (Methodological)* **57**, 289-300 (1995).
99. D. C. Glahn *et al.*, Genetic control over the resting brain. *Proc Natl Acad Sci U S A* **107**, 1223-1228 (2010).
100. L. Almasy, J. Blangero, Multipoint quantitative-trait linkage analysis in general pedigrees. *Am J Hum Genet* **62**, 1198-1211 (1998).
101. L. Almasy, T. D. Dyer, J. Blangero, Bivariate quantitative trait linkage analysis: pleiotropy versus co-incident linkages. *Genet Epidemiol* **14**, 953-958 (1997).
102. A. R. Laird *et al.*, The BrainMap strategy for standardization, sharing, and meta-analysis of neuroimaging data. *BMC Res Notes* **4**, 349 (2011).
103. A. R. Laird *et al.*, ALE Meta-Analysis Workflows Via the Brainmap Database: Progress Towards A Probabilistic Functional Brain Atlas. *Front Neuroinform* **3**, 23 (2009).

104. T. D. Wager *et al.*, Brain mediators of cardiovascular responses to social threat: part I: Reciprocal dorsal and ventral sub-regions of the medial prefrontal cortex and heart-rate reactivity. *Neuroimage* **47**, 821-835 (2009).
105. T. D. Wager, M. L. Davidson, B. L. Hughes, M. A. Lindquist, K. N. Ochsner, Prefrontal-subcortical pathways mediating successful emotion regulation. *Neuron* **59**, 1037-1050 (2008).
106. V. Kebets *et al.*, Somatosensory-Motor dysconnectivity spans multiple transdiagnosic dimensions of psychopathology. (BioArchiv).

# - DOES MACROSCALE GREY MATTER ANATOMY REFLECT PERSONALITY?
# - SUPPLEMENTARY MATERIAL -

Sofie L. Valk[1,2*]; Felix Hoffstaedter[1,2]; Julia Camilleri[1,2]; Peter Kochunov[3]; B.T. Thomas Yeo[4,5,6,7]; Simon B. Eickhoff[1,2]

*[1)] Institute of Neuroscience and Medicine (INM-7: Brain and Behaviour), Research Centre Jülich, 52425 Jülich, Germany*
*[2)] Institute of Systems Neuroscience, Heinrich Heine University Düsseldorf, 40225 Düsseldorf, Germany*
*[3)] Maryland Psychiatric Research Center, University of Maryland School of Medicine, Baltimore, Maryland, USA.*
*[4)] Department of Electrical and Computer Engineering, Clinical Imaging Research Centre, Institute for Health and Memory Networks Program, National University of Singapore, Singapore, Singapore.*
*[5)] Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, USA.*
*[6)] Centre for Cognitive Neuroscience, Duke-NUS Medical School, Singapore, Singapore.*
*[7)] NUS Graduate School for Integrative Sciences and Engineering, National University of Singapore, Singapore, Singapore.*

## SUPPLEMENTARY TABLES

| Personality trait | A | C | E | N | O |
|---|---|---|---|---|---|
| *Agreeableness* | 1 | | | | |
| *Conscientiousness* | 0.22 ** | | | | |
| *Extraversion* | 0.29 ** | 0.26 ** | | | |
| *Neuroticism* | -0.33 ** | -0.42 ** | -0.35 ** | | |
| *Openness* | 0.11 ** | -0.10 ** | 0.09 * | 0.00 | |

**Supplementary Table 1. Phenotypic correlation of personality traits in HCP.** Phenotypic correlation across personality traits ** indicates a Bonferroni corrected at p<0.05, controlled for number of analysis (10), whereas * indicates p<0.05.

| Agreeableness | HCP all | HCP unrelated | GSP | eNKI |
|---|---|---|---|---|
| *7Networks_LH_Cont_PFCl_4* | -0.11 | -0.07 | 0.04 | -0.02 |
| *7Networks_LH_Default_PFC_7* | -0.11 | -0.12 * | 0.02 | 0.01 |
| *7Networks_LH_Default_PFC_9* | -0.12 | -0.15 ** | -0.01 | 0.05 |
| *7Networks_LH_Default_PFC_11* | -0.12 | -0.10 * | -0.01 | -0.03 |
| *7Networks_LH_Default_PFC_12* | -0.10 | -0.02 | 0.08 * | 0.01 |
| *7Networks_LH_Default_PFC_13* | -0.11 | -0.14 ** | -0.02 | -0.01 |
| *7Networks_RH_Default_PFCm_5* | -0.11 | -0.08 | -0.06 | 0.04 |

| Neuroticism | HCP all | HCP unrelated | GSP | eNKI |
|---|---|---|---|---|
| *7Networks_LH_Vis_14* | -0.11 | -0.08 | 0.07 * | -0.01 |
| *7Networks_LH_DorsAttn_FEF_2* | 0.10 | 0.09 | 0.07 * | 0.00 |
| *7Networks_LH_SalVentAttn_ParOper_2* | 0.10 | 0.08 | -0.03 | 0.01 |
| *7Networks_LH_Default_Temp_6* | -0.11 | -0.13 * | 0.06 | -0.01 |
| *7Networks_LH_Default_PFC_9* | 0.11 | 0.15 ** | 0.03 | -0.02 |
| *7Networks_LH_Default_PFC_11* | 0.10 | 0.11 * | 0.00 | -0.05 |
| *7Networks_RH_Cont_PFCl_6* | 0.10 | 0.05 | 0.07 * | -0.03 |
| *7Networks_RH_Default_PFCm_5* | 0.12 | 0.11 * | -0.01 | -0.04 |

| Openness | HCP all | HCP unrelated | GSP | eNKI |
|---|---|---|---|---|
| *7Networks_LH_Vis_1* | 0.10 | 0.08 | 0.05 | -0.01 |
| *7Networks_LH_SalVentAttn_PFCl_1* | -0.11 | -0.11 * | 0.02 | -0.06 |
| *7Networks_LH_Cont_PFCl_3* | -0.11 | -0.11 * | 0.01 | -0.07 * |
| *7Networks_LH_Cont_PFCl_4* | -0.12 | -0.12 * | 0.02 | -0.01 |
| *7Networks_RH_Limbic_TempPole_1* | 0.11 | 0.07 | 0.02 | 0.00 |
| *7Networks_RH_Cont_PFCl_5* | -0.10 | -0.09 | 0.05 | -0.09 * |
| *7Networks_RH_Default_PCC_1* | 0.10 | 0.07 | -0.03 | -0.00 |

**Supplementary Table 2. Inconsistent pattern of phenotypic correlations across samples.** Robustness of phenotypical association between parcels that showed significant phenotypic correlation in the related HCP sample and the corresponding personality trait. ** indicates Bonferroni corrected p<0.05 (corrected for number of ROIs per trait), whereas * indicates p<0.05. Nomenclature of the regions is based on the official parcel names of the Schaefer 200 – 7 networks parcel solution.

| Intelligence (h2r=0.75) | r | $\rho_g$ | $\rho_e$ | GSP | eNKI |
|---|---|---|---|---|---|
| *Agreeableness* | 0.10 ** | 0.31(0.09) ** | -0.09(0.07) | 0.04 | 0.02 |
| *Conscientiousness* | -0.11 ** | -0.26(0.07) ** | 0.11(0.07) | -0.01 | -0.09* |
| *Extraversion* | -0.03 | -0.06(0.07) | 0.01(0.07) | -0.08* | -0.10** |
| *Neuroticism* | -0.11 ** | -0.22(0.08) ** | 0.01(0.07) | -0.08* | -0.02 |
| *Openness* | 0.24 ** | 0.37(0.06) ** | -0.002(0.07) | 0.12** | 0.28** |

**Supplementary Table 3. Phenotypic and genetic correlation between personality traits and intelligence.** Phenotypic and genetic correlation between intelligence (total cognitive

score) and personality traits in HCP as well as replication in GSP and eNKI samples. ** indicates a Bonferroni corrected at p<0.05 (controlled for number of analysis), whereas * indicates p<0.05.

| | X > M | M > Y | X > Y unmediated | X > Y | X > Y mediated |
|---|---|---|---|---|---|
| **7Networks_LH_Cont_PFCl_4** | | | | | |
| *mean* | 4,1927 | -0,0728 | -3,95 | -4,2537 | -0,3037 |
| *std* | 1,3378 | 0,0277 | 1,2262 | 1,2307 | 0,1537 |
| *p* | 0,0007 | 0,0071 | 0,0015 | 0,0009 | 0,0162 |
| **7Networks_LH_Default_PFC_7** | | | | | |
| *mean* | 4,1641 | -0,1137 | -3,465 | -3,9369 | -0,4719 |
| *std* | 1,332 | 0,0318 | 1,3845 | 1,3912 | 0,2018 |
| *p* | 0,0023 | 0,0003 | 0,0129 | 0,0041 | 0,005 |
| **7Networks_LH_Default_PFC_9** | | | | | |
| *mean* | 4,1891 | -0,0924 | -3,9936 | -4,38 | -0,3864 |
| *std* | 1,3401 | 0,0312 | 1,374 | 1,3812 | 0,1825 |
| *p* | 0,004 | 0,0029 | 0,0014 | 0,0003 | 0,0131 |
| **7Networks_LH_Default_PFC_11** | | | | | |
| *mean* | 4,1476 | -0,1819 | -4,7158 | -5,4693 | -0,7535 |
| *std* | 1,3647 | 0,0294 | 1,3357 | 1,3523 | 0,2773 |
| *p* | 0,0014 | 0,0003 | 0,0002 | 0,0003 | 0,003 |
| **7Networks_LH_Default_PFC_12** | | | | | |
| *mean* | 4,1476 | -0,0836 | -2,8679 | -3,2146 | -0,3466 |
| *std* | 1,3306 | 0,0282 | 1,3769 | 1,3866 | 0,1653 |
| *p* | 0,002 | 0,0044 | 0,0364 | 0,0227 | 0,0131 |
| **7Networks_LH_Default_PFC_13** | | | | | |
| *mean* | 4,2008 | -0,0715 | -3,95 | -4,2472 | -0,2972 |
| *std* | 1,3327 | 0,0306 | 1,3694 | 1,3723 | 0,1592 |
| *p* | 0,0027 | 0,0205 | 0,0012 | 0,0007 | 0,0432 |
| **7Networks_RH_Default_PFCm_5** | | | | | |
| *mean* | 4,1516 | -0,1474 | -3,2194 | -3,8306 | -0,6112 |
| *std* | 1,3437 | 0,0293 | 1,3178 | 1,3424 | 0,234 |
| *p* | 0,0009 | 0,0003 | 0,0129 | 0,0039 | 0,0021 |

**Supplementary Table 4a. Mediation of phenotypic relationship of agreeableness with cortical thickness by intelligence (total cognitive score).** For each mediation test the relation between personality and intelligence (X > M), intelligence and brain (M > Y), relationship between personality and brain unmediated (residual), relationship between personality > brain, and mediated relationship between personality and brain (X>M * M>Y). Nomenclature of the regions is based on the official parcel names of the Schaefer 200 – 7 networks parcel solution.

| | | | | | |
|---|---|---|---|---|---|
| **7Networks_LH_Vis_14** | | | | | |
| *mean* | -3,4579 | -0,0164 | -3,6376 | -3,5826 | 0,055 |
| *std* | 1,0132 | 0,0308 | 0,9672 | 0,9621 | 0,1111 |
| *p* | 0,0019 | 0,5795 | 0,0002 | 0,0002 | 0,5324 |
| **7Networks_LH_DorsAttn_FEF_2** | | | | | |
| *mean* | -3,4821 | -0,0758 | 2,8688 | 3,1337 | 0,2649 |
| *std* | 1,0069 | 0,031 | 1,0646 | 1,0658 | 0,1376 |
| *p* | 0,0003 | 0,0162 | 0,0074 | 0,0038 | 0,0107 |
| **7Networks_LH_SalVentAttn_ParOper_2** | | | | | |
| *mean* | -3,4836 | 0,0713 | 3,2862 | 3,0383 | -0,2479 |
| *std* | 1,018 | 0,0287 | 1,0193 | 1,0116 | 0,1258 |
| *p* | 0,0003 | 0,0131 | 0,0004 | 0,0028 | 0,0213 |
| **7Networks_LH_Default_Temp_6** | | | | | |
| *mean* | -3,4613 | 0,069 | -2,79 | -3,028 | -0,238 |
| *std* | 1,0095 | 0,0303 | 1,0612 | 1,057 | 0,128 |
| *p* | 0,0017 | 0,0228 | 0,0063 | 0,003 | 0,0412 |
| **7Networks_LH_Default_PFC_9** | | | | | |
| *mean* | -3,4868 | -0,0906 | 3,426 | 3,7433 | 0,3173 |
| *std* | 1,005 | 0,0309 | 1,0523 | 1,0506 | 0,1481 |
| *p* | 0,0008 | 0,0041 | 0,0003 | 0,0003 | 0,0033 |
| **7Networks_LH_Default_PFC_11** | | | | | |
| *mean* | -3,4751 | -0,1853 | 2,2229 | 2,8674 | 0,6445 |
| *std* | 1,0102 | 0,03 | 1,0431 | 1,0576 | 0,2171 |
| *p* | 0,0006 | 0,0004 | 0,0382 | 0,0119 | 0,0005 |
| **7Networks_RH_Cont_PFCl_6** | | | | | |
| *mean* | -3,4729 | -0,087 | 3,1641 | 3,4667 | 0,3026 |
| *std* | 1,0009 | 0,0306 | 1,0333 | 1,0331 | 0,1419 |
| *p* | 0,0003 | 0,0041 | 0,002 | 0,0005 | 0,0025 |
| **7Networks_RH_Default_PFCm_5** | | | | | |
| *mean* | -3,491 | -0,1449 | 3,0807 | 3,5878 | 0,5071 |
| *std* | 1,0269 | 0,0292 | 1,0248 | 1,0284 | 0,1864 |
| *p* | 0,0006 | 0,0003 | 0,0014 | 0,0007 | 0,0004 |

**Supplementary Table 4b. Mediation of phenotypic relationship of neuroticism with cortical thickness by intelligence (total cognitive score).** For each mediation test the relation between personality and intelligence (X > M), intelligence and brain (M > Y), relationship between personality and brain unmediated (residual), relationship between personality > brain, and mediated relationship between personality and brain (X>M * M>Y). Nomenclature of the regions is based on the official parcel names of the Schaefer 200 – 7 networks parcel solution.

| | | | | | |
|---|---|---|---|---|---|
| **7Networks_LH_Vis_1** | | | | | |
| *mean* | 9,5516 | 0,07 | 2,9474 | 3,6178 | 0,6703 |
| *std* | 1,1722 | 0,0328 | 1,4448 | 1,4028 | 0,3298 |
| *p* | 0,0004 | 0,0281 | 0,0451 | 0,014 | 0,024 |
| **7Networks_LH_SalVentAttn_PFCl_1** | | | | | |
| *mean* | 9,555 | -0,1021 | -2,6757 | -3,6512 | -0,9755 |
| *std* | 1,173 | 0,0309 | 1,2662 | 1,2363 | 0,3206 |
| *p* | 0,0005 | 0,001 | 0,0315 | 0,0035 | 0,0013 |
| **7Networks_LH_Cont_PFCl_3** | | | | | |
| *mean* | 9,5113 | -0,0457 | -3,5776 | -4,0116 | -0,4341 |
| *std* | 1,1724 | 0,0295 | 1,3229 | 1,3032 | 0,2865 |
| *p* | 0,0003 | 0,1136 | 0,0083 | 0,0034 | 0,1318 |
| **7Networks_LH_Cont_PFCl_4** | | | | | |
| *mean* | 9,5422 | -0,056 | -4,2244 | -4,757 | -0,5326 |
| *std* | 1,1536 | 0,0276 | 1,1796 | 1,1658 | 0,2702 |
| *p* | 0,0004 | 0,0437 | 0,0003 | 0,0003 | 0,0496 |
| **7Networks_RH_Limbic_TempPole_1** | | | | | |
| *mean* | 9,5439 | 0,0853 | 4,4995 | 5,3135 | 0,814 |
| *std* | 1,1616 | 0,0346 | 1,4554 | 1,4421 | 0,3461 |
| *p* | 0,0004 | 0,0162 | 0,0017 | 0,0004 | 0,0131 |
| **7Networks_RH_Cont_PFCl_5** | | | | | |
| *mean* | 9,5311 | -0,091 | -3,0622 | -3,9291 | -0,8669 |
| *std* | 1,1608 | 0,0314 | 1,2414 | 1,2225 | 0,3194 |
| *p* | 0,0004 | 0,002 | 0,0129 | 0,0015 | 0,0025 |
| **7Networks_RH_Default_PCC_1** | | | | | |
| *mean* | 9,5402 | 0,1268 | 2,448 | 3,657 | 1,2089 |
| *std* | 1,1672 | 0,0333 | 1,4864 | 1,4742 | 0,3505 |
| *p* | 0,0004 | 0,0004 | 0,0954 | 0,014 | 0,0002 |

**Supplementary Table 4c. Mediation of phenotypic relationship of neuroticism with cortical thickness by intelligence (total cognitive score).** For each mediation test the relation between personality and intelligence (X > M), intelligence and brain (M > Y), relationship between personality and brain unmediated (residual), relationship between personality > brain, and mediated relationship between personality and brain (X>M * M>Y). Nomenclature of the regions is based on the official parcel names of the Schaefer 200 – 7 networks parcel solution.

| Personality trait | Heritability | SE | p |
|---|---|---|---|
| *Agreeableness* | 0.29 | 0.07 | 0.0000 |
| *Conscientiousness* | 0.43 | 0.06 | 0.0000 |
| *Extraversion* | 0.43 | 0.05 | 0.0000 |
| *Neuroticism* | 0.37 | 0.06 | 0.0000 |
| *Openness* | 0.58 | 0.05 | 0.0000 |

**Supplementary Table 5. Heritability of personality traits.** Heritability of personality traits computed using Solar 8.4.0. Here we report heritability values, standard error, as well as p-values.

| ROIS | Heritability | SE | p |
|---|---|---|---|
| *'7Networks_LH_Vis_1'* | 0.3960 | 0.0506 | 0.0000 |
| *'7Networks_LH_Vis_2'* | 0.3280 | 0.0555 | 0.0000 |
| *'7Networks_LH_Vis_3'* | 0.1523 | 0.0586 | 0.0036 |
| *'7Networks_LH_Vis_4'* | 0.4836 | 0.0439 | 0.0000 |
| *'7Networks_LH_Vis_5'* | 0.4083 | 0.0522 | 0.0000 |
| *'7Networks_LH_Vis_6'* | 0.4480 | 0.0501 | 0.0000 |
| *'7Networks_LH_Vis_7'* | 0.4963 | 0.0470 | 0.0000 |
| *'7Networks_LH_Vis_8'* | 0.2402 | 0.0513 | 0.0000 |
| *'7Networks_LH_Vis_9'* | 0.4775 | 0.0471 | 0.0000 |
| *'7Networks_LH_Vis_10'* | 0.5194 | 0.0463 | 0.0000 |
| *'7Networks_LH_Vis_11'* | 0.3290 | 0.0522 | 0.0000 |
| *'7Networks_LH_Vis_12'* | 0.4718 | 0.0516 | 0.0000 |
| *'7Networks_LH_Vis_13'* | 0.5551 | 0.0466 | 0.0000 |
| *'7Networks_LH_Vis_14'* | 0.4452 | 0.0519 | 0.0000 |
| *'7Networks_LH_SomMot_1'* | 0.4736 | 0.0497 | 0.0000 |
| *'7Networks_LH_SomMot_2'* | 0.2755 | 0.0555 | 0.0000 |
| *'7Networks_LH_SomMot_3'* | 0.5145 | 0.0480 | 0.0000 |
| *'7Networks_LH_SomMot_4'* | 0.3997 | 0.0531 | 0.0000 |
| *'7Networks_LH_SomMot_5'* | 0.2452 | 0.0547 | 0.0000 |
| *'7Networks_LH_SomMot_6'* | 0.5276 | 0.0462 | 0.0000 |
| *'7Networks_LH_SomMot_7'* | 0.2888 | 0.0575 | 0.0000 |
| *'7Networks_LH_SomMot_8'* | 0.2808 | 0.0589 | 0.0000 |
| *'7Networks_LH_SomMot_9'* | 0.3392 | 0.0544 | 0.0000 |
| *'7Networks_LH_SomMot_10'* | 0.5155 | 0.0479 | 0.0000 |
| *'7Networks_LH_SomMot_11'* | 0.2151 | 0.0550 | 0.0000 |
| *'7Networks_LH_SomMot_12'* | 0.3585 | 0.0543 | 0.0000 |
| *'7Networks_LH_SomMot_13'* | 0.3296 | 0.0584 | 0.0000 |
| *'7Networks_LH_SomMot_14'* | 0.3638 | 0.0514 | 0.0000 |
| *'7Networks_LH_SomMot_15'* | 0.4356 | 0.0492 | 0.0000 |
| *'7Networks_LH_SomMot_16'* | 0.4002 | 0.0578 | 0.0000 |
| *'7Networks_LH_DorsAttn_Post_1'* | 0.3267 | 0.0586 | 0.0000 |
| *'7Networks_LH_DorsAttn_Post_2'* | 0.2151 | 0.0535 | 0.0000 |
| *'7Networks_LH_DorsAttn_Post_3'* | 0.3442 | 0.0544 | 0.0000 |
| *'7Networks_LH_DorsAttn_Post_4'* | 0.3499 | 0.0561 | 0.0000 |
| *'7Networks_LH_DorsAttn_Post_5'* | 0.2148 | 0.0550 | 0.0000 |
| *'7Networks_LH_DorsAttn_Post_6'* | 0.2283 | 0.0590 | 0.0000 |
| *'7Networks_LH_DorsAttn_Post_7'* | 0.4602 | 0.0527 | 0.0000 |

| | | | |
|---|---|---|---|
| *'7Networks_LH_DorsAttn_Post_8'* | 0.3059 | 0.0551 | 0.0000 |
| *'7Networks_LH_DorsAttn_Post_9'* | 0.4502 | 0.0506 | 0.0000 |
| *'7Networks_LH_DorsAttn_Post_10'* | 0.4682 | 0.0529 | 0.0000 |
| *'7Networks_LH_DorsAttn_FEF_1'* | 0.2673 | 0.0550 | 0.0000 |
| *'7Networks_LH_DorsAttn_FEF_2'* | 0.3613 | 0.0562 | 0.0000 |
| *'7Networks_LH_DorsAttn_PrCv_1'* | 0.1866 | 0.0585 | 0.0005 |
| *'7Networks_LH_SalVentAttn_ParOper_1'* | 0.1303 | 0.0574 | 0.0096 |
| *'7Networks_LH_SalVentAttn_ParOper_2'* | 0.2800 | 0.0527 | 0.0000 |
| *'7Networks_LH_SalVentAttn_ParOper_3'* | 0.2185 | 0.0581 | 0.0000 |
| *'7Networks_LH_SalVentAttn_FrOper_1'* | 0.3500 | 0.0537 | 0.0000 |
| *'7Networks_LH_SalVentAttn_FrOper_2'* | 0.4083 | 0.0535 | 0.0000 |
| *'7Networks_LH_SalVentAttn_FrOper_3'* | 0.4316 | 0.0528 | 0.0000 |
| *'7Networks_LH_SalVentAttn_FrOper_4'* | 0.2426 | 0.0610 | 0.0000 |
| *'7Networks_LH_SalVentAttn_PFCl_1'* | 0.4391 | 0.0476 | 0.0000 |
| *'7Networks_LH_SalVentAttn_Med_1'* | 0.3362 | 0.0589 | 0.0000 |
| *'7Networks_LH_SalVentAttn_Med_2'* | 0.3337 | 0.0577 | 0.0000 |
| *'7Networks_LH_SalVentAttn_Med_3'* | 0.2462 | 0.0571 | 0.0000 |
| *'7Networks_LH_Limbic_OFC_1'* | 0.2963 | 0.0532 | 0.0000 |
| *'7Networks_LH_Limbic_OFC_2'* | 0.3585 | 0.0556 | 0.0000 |
| *'7Networks_LH_Limbic_TempPole_1'* | 0.3385 | 0.0583 | 0.0000 |
| *'7Networks_LH_Limbic_TempPole_2'* | 0.3692 | 0.0498 | 0.0000 |
| *'7Networks_LH_Limbic_TempPole_3'* | 0.2432 | 0.0529 | 0.0000 |
| *'7Networks_LH_Limbic_TempPole_4'* | 0.4492 | 0.0520 | 0.0000 |
| *'7Networks_LH_Cont_Par_1'* | 0.2170 | 0.0570 | 0.0000 |
| *'7Networks_LH_Cont_Par_2'* | 0.2715 | 0.0536 | 0.0000 |
| *'7Networks_LH_Cont_Par_3'* | 0.0448 | 0.0556 | 0.2068 |
| *'7Networks_LH_Cont_Temp_1'* | 0.1930 | 0.0574 | 0.0003 |
| *'7Networks_LH_Cont_PFCl_1'* | 0.2604 | 0.0512 | 0.0000 |
| *'7Networks_LH_Cont_PFCl_2'* | 0.2964 | 0.0557 | 0.0000 |
| *'7Networks_LH_Cont_PFCl_3'* | 0.3926 | 0.0532 | 0.0000 |
| *'7Networks_LH_Cont_PFCl_4'* | 0.2659 | 0.0547 | 0.0000 |
| *'7Networks_LH_Cont_PFCl_5'* | 0.4091 | 0.0501 | 0.0000 |
| *'7Networks_LH_Cont_PFCl_6'* | 0.2063 | 0.0572 | 0.0001 |
| *'7Networks_LH_Cont_pCun_1'* | 0.3744 | 0.0516 | 0.0000 |
| *'7Networks_LH_Cont_Cing_1'* | 0.5313 | 0.0487 | 0.0000 |
| *'7Networks_LH_Cont_Cing_2'* | 0.3678 | 0.0568 | 0.0000 |
| *'7Networks_LH_Default_Temp_1'* | 0.2854 | 0.0595 | 0.0000 |
| *'7Networks_LH_Default_Temp_2'* | 0.2831 | 0.0547 | 0.0000 |
| *'7Networks_LH_Default_Temp_3'* | 0.3428 | 0.0543 | 0.0000 |

| | | | |
|---|---|---|---|
| *'7Networks_LH_Default_Temp_4'* | 0.1930 | 0.0585 | 0.0004 |
| *'7Networks_LH_Default_Temp_5'* | 0.2131 | 0.0585 | 0.0001 |
| *'7Networks_LH_Default_Temp_6'* | 0.2821 | 0.0539 | 0.0000 |
| *'7Networks_LH_Default_Temp_7'* | 0.3019 | 0.0572 | 0.0000 |
| *'7Networks_LH_Default_Temp_8'* | 0.2422 | 0.0561 | 0.0000 |
| *'7Networks_LH_Default_Temp_9'* | 0.2643 | 0.0520 | 0.0000 |
| *'7Networks_LH_Default_PFC_1'* | 0.3635 | 0.0525 | 0.0000 |
| *'7Networks_LH_Default_PFC_2'* | 0.2708 | 0.0581 | 0.0000 |
| *'7Networks_LH_Default_PFC_3'* | 0.1493 | 0.0560 | 0.0032 |
| *'7Networks_LH_Default_PFC_4'* | 0.5135 | 0.0459 | 0.0000 |
| *'7Networks_LH_Default_PFC_5'* | 0.3168 | 0.0578 | 0.0000 |
| *'7Networks_LH_Default_PFC_6'* | 0.3310 | 0.0538 | 0.0000 |
| *'7Networks_LH_Default_PFC_7'* | 0.5053 | 0.0483 | 0.0000 |
| *'7Networks_LH_Default_PFC_8'* | 0.3889 | 0.0572 | 0.0000 |
| *'7Networks_LH_Default_PFC_9'* | 0.4656 | 0.0478 | 0.0000 |
| *'7Networks_LH_Default_PFC_10'* | 0.3767 | 0.0515 | 0.0000 |
| *'7Networks_LH_Default_PFC_11'* | 0.4263 | 0.0481 | 0.0000 |
| *'7Networks_LH_Default_PFC_12'* | 0.4694 | 0.0486 | 0.0000 |
| *'7Networks_LH_Default_PFC_13'* | 0.4649 | 0.0493 | 0.0000 |
| *'7Networks_LH_Default_PCC_1'* | 0.3913 | 0.0550 | 0.0000 |
| *'7Networks_LH_Default_PCC_2'* | 0.2794 | 0.0537 | 0.0000 |
| *'7Networks_LH_Default_PCC_3'* | 0.3900 | 0.0539 | 0.0000 |
| *'7Networks_LH_Default_PCC_4'* | 0.3922 | 0.0556 | 0.0000 |
| *'7Networks_LH_Default_PHC_1'* | 0.4640 | 0.0536 | 0.0000 |
| *'7Networks_RH_Vis_1'* | 0.3649 | 0.0531 | 0.0000 |
| *'7Networks_RH_Vis_2'* | 0.3496 | 0.0569 | 0.0000 |
| *'7Networks_RH_Vis_3'* | 0.3773 | 0.0566 | 0.0000 |
| *'7Networks_RH_Vis_4'* | 0.5840 | 0.0417 | 0.0000 |
| *'7Networks_RH_Vis_5'* | 0.2794 | 0.0551 | 0.0000 |
| *'7Networks_RH_Vis_6'* | 0.4662 | 0.0502 | 0.0000 |
| *'7Networks_RH_Vis_7'* | 0.5079 | 0.0463 | 0.0000 |
| *'7Networks_RH_Vis_8'* | 0.4341 | 0.0539 | 0.0000 |
| *'7Networks_RH_Vis_9'* | 0.5773 | 0.0433 | 0.0000 |
| *'7Networks_RH_Vis_10'* | 0.4768 | 0.0535 | 0.0000 |
| *'7Networks_RH_Vis_11'* | 0.2379 | 0.0536 | 0.0000 |
| *'7Networks_RH_Vis_12'* | 0.5188 | 0.0479 | 0.0000 |
| *'7Networks_RH_Vis_13'* | 0.4779 | 0.0490 | 0.0000 |
| *'7Networks_RH_Vis_14'* | 0.4356 | 0.0522 | 0.0000 |
| *'7Networks_RH_Vis_15'* | 0.2731 | 0.0558 | 0.0000 |

| | | | |
|---|---|---|---|
| *'7Networks_RH_SomMot_1'* | 0.4370 | 0.0532 | 0.0000 |
| *'7Networks_RH_SomMot_2'* | 0.3421 | 0.0590 | 0.0000 |
| *'7Networks_RH_SomMot_3'* | 0.3498 | 0.0573 | 0.0000 |
| *'7Networks_RH_SomMot_4'* | 0.3403 | 0.0554 | 0.0000 |
| *'7Networks_RH_SomMot_5'* | 0.1911 | 0.0576 | 0.0003 |
| *'7Networks_RH_SomMot_6'* | 0.2971 | 0.0572 | 0.0000 |
| *'7Networks_RH_SomMot_7'* | 0.4346 | 0.0501 | 0.0000 |
| *'7Networks_RH_SomMot_8'* | 0.1921 | 0.0546 | 0.0001 |
| *'7Networks_RH_SomMot_9'* | 0.3351 | 0.0603 | 0.0000 |
| *'7Networks_RH_SomMot_10'* | 0.1718 | 0.0602 | 0.0016 |
| *'7Networks_RH_SomMot_11'* | 0.3010 | 0.0532 | 0.0000 |
| *'7Networks_RH_SomMot_12'* | 0.4576 | 0.0501 | 0.0000 |
| *'7Networks_RH_SomMot_13'* | 0.3075 | 0.0531 | 0.0000 |
| *'7Networks_RH_SomMot_14'* | 0.3848 | 0.0524 | 0.0000 |
| *'7Networks_RH_SomMot_15'* | 0.3496 | 0.0590 | 0.0000 |
| *'7Networks_RH_SomMot_16'* | 0.2815 | 0.0593 | 0.0000 |
| *'7Networks_RH_SomMot_17'* | 0.4880 | 0.0494 | 0.0000 |
| *'7Networks_RH_SomMot_18'* | 0.3781 | 0.0504 | 0.0000 |
| *'7Networks_RH_SomMot_19'* | 0.4382 | 0.0534 | 0.0000 |
| *'7Networks_RH_DorsAttn_Post_1'* | 0.2420 | 0.0563 | 0.0000 |
| *'7Networks_RH_DorsAttn_Post_2'* | 0.2431 | 0.0565 | 0.0000 |
| *'7Networks_RH_DorsAttn_Post_3'* | 0.3086 | 0.0533 | 0.0000 |
| *'7Networks_RH_DorsAttn_Post_4'* | 0.2197 | 0.0572 | 0.0000 |
| *'7Networks_RH_DorsAttn_Post_5'* | 0.1940 | 0.0576 | 0.0002 |
| *'7Networks_RH_DorsAttn_Post_6'* | 0.3929 | 0.0523 | 0.0000 |
| *'7Networks_RH_DorsAttn_Post_7'* | 0.1424 | 0.0564 | 0.0047 |
| *'7Networks_RH_DorsAttn_Post_8'* | 0.3550 | 0.0542 | 0.0000 |
| *'7Networks_RH_DorsAttn_Post_9'* | 0.3334 | 0.0539 | 0.0000 |
| *'7Networks_RH_DorsAttn_Post_10'* | 0.4139 | 0.0513 | 0.0000 |
| *'7Networks_RH_DorsAttn_FEF_1'* | 0.3090 | 0.0586 | 0.0000 |
| *'7Networks_RH_DorsAttn_FEF_2'* | 0.2329 | 0.0569 | 0.0000 |
| *'7Networks_RH_DorsAttn_PrCv_1'* | 0.3154 | 0.0553 | 0.0000 |
| *'7Networks_RH_SalVentAttn_TempOccPar_1'* | 0.2310 | 0.0572 | 0.0000 |
| *'7Networks_RH_SalVentAttn_TempOccPar_2'* | 0.1702 | 0.0549 | 0.0008 |
| *'7Networks_RH_SalVentAttn_TempOccPar_3'* | 0.2479 | 0.0547 | 0.0000 |
| *'7Networks_RH_SalVentAttn_PrC_1'* | 0.1571 | 0.0568 | 0.0022 |
| *'7Networks_RH_SalVentAttn_FrOper_1'* | 0.2728 | 0.0570 | 0.0000 |
| *'7Networks_RH_SalVentAttn_FrOper_2'* | 0.5003 | 0.0520 | 0.0000 |

| | | | |
|---|---|---|---|
| *'7Networks_RH_SalVentAttn_FrOper_3'* | 0.3183 | 0.0530 | 0.0000 |
| *'7Networks_RH_SalVentAttn_FrOper_4'* | 0.2536 | 0.0567 | 0.0000 |
| *'7Networks_RH_SalVentAttn_Med_1'* | 0.2638 | 0.0558 | 0.0000 |
| *'7Networks_RH_SalVentAttn_Med_2'* | 0.4131 | 0.0515 | 0.0000 |
| *'7Networks_RH_SalVentAttn_Med_3'* | 0.3440 | 0.0594 | 0.0000 |
| *'7Networks_RH_Limbic_OFC_1'* | 0.4121 | 0.0566 | 0.0000 |
| *'7Networks_RH_Limbic_OFC_2'* | 0.3526 | 0.0496 | 0.0000 |
| *'7Networks_RH_Limbic_OFC_3'* | 0.3785 | 0.0545 | 0.0000 |
| *'7Networks_RH_Limbic_TempPole_1'* | 0.1799 | 0.0560 | 0.0005 |
| *'7Networks_RH_Limbic_TempPole_2'* | 0.3495 | 0.0556 | 0.0000 |
| *'7Networks_RH_Limbic_TempPole_3'* | 0.5059 | 0.0498 | 0.0000 |
| *'7Networks_RH_Cont_Par_1'* | 0.1538 | 0.0562 | 0.0021 |
| *'7Networks_RH_Cont_Par_2'* | 0.1959 | 0.0554 | 0.0001 |
| *'7Networks_RH_Cont_Par_3'* | 0.1328 | 0.0566 | 0.0081 |
| *'7Networks_RH_Cont_Temp_1'* | 0.2258 | 0.0600 | 0.0000 |
| *'7Networks_RH_Cont_PFCv_1'* | 0.2109 | 0.0579 | 0.0001 |
| *'7Networks_RH_Cont_PFCl_1'* | 0.2699 | 0.0546 | 0.0000 |
| *'7Networks_RH_Cont_PFCl_2'* | 0.3055 | 0.0549 | 0.0000 |
| *'7Networks_RH_Cont_PFCl_3'* | 0.3266 | 0.0515 | 0.0000 |
| *'7Networks_RH_Cont_PFCl_4'* | 0.4177 | 0.0506 | 0.0000 |
| *'7Networks_RH_Cont_PFCl_5'* | 0.3271 | 0.0519 | 0.0000 |
| *'7Networks_RH_Cont_PFCl_6'* | 0.3110 | 0.0512 | 0.0000 |
| *'7Networks_RH_Cont_PFCl_7'* | 0.3489 | 0.0573 | 0.0000 |
| *'7Networks_RH_Cont_pCun_1'* | 0.2582 | 0.0545 | 0.0000 |
| *'7Networks_RH_Cont_PFCmp_1'* | 0.4633 | 0.0479 | 0.0000 |
| *'7Networks_RH_Cont_PFCmp_2'* | 0.4163 | 0.0537 | 0.0000 |
| *'7Networks_RH_Cont_PFCmp_3'* | 0.2755 | 0.0573 | 0.0000 |
| *'7Networks_RH_Cont_PFCmp_4'* | 0.4503 | 0.0546 | 0.0000 |
| *'7Networks_RH_Default_Par_1'* | 0.2263 | 0.0589 | 0.0000 |
| *'7Networks_RH_Default_Par_2'* | 0.2045 | 0.0563 | 0.0001 |
| *'7Networks_RH_Default_Par_3'* | 0.1980 | 0.0561 | 0.0001 |
| *'7Networks_RH_Default_Temp_1'* | 0.3255 | 0.0543 | 0.0000 |
| *'7Networks_RH_Default_Temp_2'* | 0.3169 | 0.0556 | 0.0000 |
| *'7Networks_RH_Default_Temp_3'* | 0.4308 | 0.0562 | 0.0000 |
| *'7Networks_RH_Default_Temp_4'* | 0.2967 | 0.0533 | 0.0000 |
| *'7Networks_RH_Default_Temp_5'* | 0.2504 | 0.0595 | 0.0000 |
| *'7Networks_RH_Default_PFCv_1'* | 0.3596 | 0.0550 | 0.0000 |
| *'7Networks_RH_Default_PFCm_1'* | 0.2831 | 0.0532 | 0.0000 |
| *'7Networks_RH_Default_PFCm_2'* | 0.2488 | 0.0552 | 0.0000 |

| | | | |
|---|---|---|---|
| *'7Networks_RH_Default_PFCm_3'* | 0.3565 | 0.0609 | 0.0000 |
| *'7Networks_RH_Default_PFCm_4'* | 0.5538 | 0.0463 | 0.0000 |
| *'7Networks_RH_Default_PFCm_5'* | 0.4769 | 0.0474 | 0.0000 |
| *'7Networks_RH_Default_PFCm_6'* | 0.3159 | 0.0539 | 0.0000 |
| *'7Networks_RH_Default_PFCm_7'* | 0.1779 | 0.0539 | 0.0003 |
| *'7Networks_RH_Default_PCC_1'* | 0.3857 | 0.0577 | 0.0000 |
| *'7Networks_RH_Default_PCC_2'* | 0.4159 | 0.0549 | 0.0000 |
| *'7Networks_RH_Default_PCC_3'* | 0.2319 | 0.0547 | 0.0000 |

**Supplementary Table 6. Heritability of cortical thickness.** Heritability of cortical thickness calculated using solar 8.4.0. regions are named according to the Schaefer 200 atlas, based on 7-networks. Here we report heritability values, standard errors (SE), and p-values. Nomenclature of the regions is based on the official parcel names of the Schaefer 200 – 7 networks parcel solution.

| **Agreeableness** | **HCP un** | **HCP all** | **GSP** | **Conscientiousness** | **HCP un** | **HCP all** | **GSP** |
|---|---|---|---|---|---|---|---|
| *HCP all* | 0.66 ** | 1 | | | 0.44 ** | 1 | |
| *GSP* | 0.23 ** | 0.06 | 1 | | 0.05 | 0.09 | 1 |
| *eNKI* | -0.13 | -0.28 ** | -0.05 | | 0.03 | 0.16 * | -0.07 |
| **Extraversion** | **HCP un** | **HCP all** | **GSP** | **Neuroticism** | **HCP un** | **HCP all** | **GSP** |
| *HCP all* | 0.70 ** | 1 | | | 0.67 ** | 1 | |
| *GSP* | 0.09 | 0.04 | 1 | | -0.05 | -0.08 | 1 |
| *eNKI* | 0.03 | 0.22 ** | 0.1 | | 0.04 | -0.04 | 0.03 |
| **Openness** | **HCP un** | **HCP all** | **GSP** | | | | |
| *HCP all* | 0.61 ** | | | | | | |
| *GSP* | 0.05 | 0.21 ** | 1 | | | | |
| *eNKI* | 0.25 ** | 0.43 ** | 0.09 | | | | |

**Supplementary Table 7. Correlation between spatial patterns of phenotypical correlation between personality and cortical thickness across samples.** To assess whether sub-threshold patterns of phenotypic correlations were similar across samples we correlated the spatial distributions of Spearman rho-values for each personality trait and cortical thickness across samples. ** indicates Bonferroni corrected $p<0.05$ (corrected for number of tests per personality trait), whereas * indicates $p<0.05$.

| | $\rho_e$ | p | $\rho_g$ | p |
|---|---|---|---|---|
| ***Agreeableness*** | | | | |
| *7Networks_LH_Cont_PFCl_4* | -0.12 | 0.04 | -0.08 | 0.61 |
| *7Networks_LH_Default_PFC_7* | -0.01 | 0.84 | -0.22 | 0.06 |
| *7Networks_LH_Default_PFC_9* | -0.05 | 0.44 | -0.21 | 0.08 |
| *7Networks_LH_Default_PFC_11* | 0.01 | 0.90 | -0.36 | 0.004 |
| *7Networks_LH_Default_PFC_12* | -0.04 | 0.53 | -0.17 | 0.17 |
| *7Networks_LH_Default_PFC_13* | -0.02 | 0.72 | -0.26 | 0.03 |
| *7Networks_RH_Default_PFCm_5* | 0.03 | 0.64 | -0.33 | 0.005 |
| ***Neuroticism*** | | | | |
| *7Networks_LH_Vis_14* | -0.08 | 0.22 | -0.18 | 0.12 |
| *7Networks_LH_DorsAttn_FEF_2* | -0.03 | 0.69 | 0.27 | 0.03 |
| *7Networks_LH_SalVentAttn_ParOper_2* | 0.10 | 0.10 | 0.06 | 0.65 |
| *7Networks_LH_Default_Temp_6* | -0.09 | 0.12 | -0.10 | 0.49 |
| *7Networks_LH_Default_PFC_9* | 0.08 | 0.23 | 0.17 | 0.13 |
| *7Networks_LH_Default_PFC_11* | 0.01 | 0.84 | 0.19 | 0.09 |
| *7Networks_RH_Cont_PFCl_6* | 0.03 | 0.63 | 0.26 | 0.04 |
| *7Networks_RH_Default_PFCm_5* | 0.04 | 0.54 | 0.21 | 0.05 |
| ***Openness*** | | | | |
| *7Networks_LH_Vis_1* | -0.05 | 0.46 | 0.25 | 0.005 |
| *7Networks_LH_SalVentAttn_PFCl_1* | -0.01 | 0.83 | -0.20 | 0.02 |
| *7Networks_LH_Cont_PFCl_3* | -0.03 | 0.69 | -0.18 | 0.05 |
| *7Networks_LH_Cont_PFCl_4* | -0.13 | 0.05 | -0.15 | 0.17 |
| *7Networks_RH_Limbic_TempPole_1* | -0.01 | 0.94 | 0.37 | 0.005 |
| *7Networks_RH_Cont_PFCl_5* | -0.05 | 0.40 | -0.16 | 0.10 |
| *7Networks_RH_Default_PCC_1* | 0.00 | 0.99 | 0.19 | 0.05 |

**Supplementary Table 8. Phenotypic correlations in the complete HCP sample are partly driven by genetic effects.** Using the regions that showed significant phenotypic correlation in the complete HCP sample, we explored whether these regions also had a genetic relationship with the respective personality trait. Nomenclature of the regions is based on the parcel names of the Schaefer 200 – 7 networks parcel solution.

| | **HCP all** | **HCP unrelated** | **GSP** | **eNKI** |
|---|---|---|---|---|
| *Agreeableness:* | | | | |
| *7Networks_LH_Default_Temp_5* | 0.03 | -0.06 | -0.04 | -0.03 |
| *7Networks_RH_SalVentAttn_Med_3* | -0.04 | -0.04 | -0.01 | -0.01 |
| *7Networks_RH_Default_PFCm_6* | -0.02 | 0.04 | 0.02 | -0.03 |
| *Extraversion:* | | | | |
| *7Networks_LH_Default_Temp_9* | 0.10 * | 0.06 | 0.02 | 0.02 |

**Supplementary Table 9. No robust phenotypic association between personality and cortical thickness in regions that showed significant genetic correlation between personality trait and cortical thickness.** Using the regions that showed significant genetic correlation, we explored whether these regions also had a phenotypic relationship with the respective personality trait in all samples. ** indicates a Bonferroni corrected at $p<0.05$, whereas * indicates $p<0.05$.

| Personality trait | A | C | E | N | O |
|---|---|---|---|---|---|
| *Agreeableness* | 1 | | | | |
| *Conscientiousness* | 0.17 ** | | | | |
| *Extraversion* | 0.36 ** | 0.29 ** | | | |
| *Neuroticism* | -0.25 ** | -0.34 ** | -0.41 ** | | |
| *Openness* | 0.10 * | -0.03 | 0.05 | 0.01 | |

**Supplementary Table 10. Phenotypic correlation of personality traits in GSP.** Phenotypic correlation across personality traits ** indicates a Bonferroni corrected at p<0.05, controlled for number of analysis (10), whereas * indicates p<0.05.

| Personality trait | A | C | E | N | O |
|---|---|---|---|---|---|
| *Agreeableness* | 1 | | | | |
| *Conscientiousness* | 0.18 ** | | | | |
| *Extraversion* | 0.17 ** | 0.35 ** | | | |
| *Neuroticism* | -0.23 ** | -0.41 ** | -0.41 ** | | |
| *Openness* | 0.13 ** | 0.02 | 0.12 ** | 0.07 | |

**Supplementary Table 11. Phenotypic correlation of personality traits in eNKI.** Phenotypic correlation across personality traits ** indicates a Bonferroni corrected at p<0.05, controlled for number of analysis (10), whereas * indicates p<0.05.

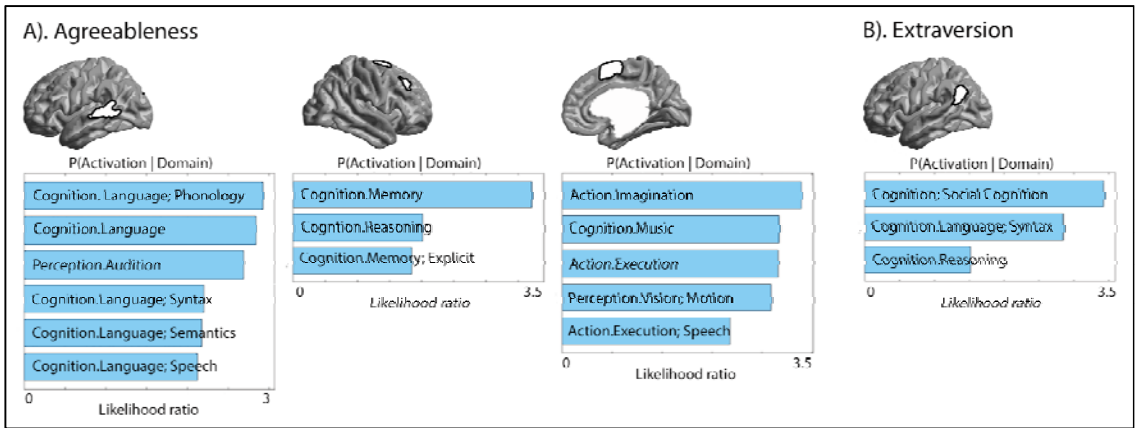
| Personality trait | A | C | E | N | O |
|---|---|---|---|---|---|
| *Agreeableness* | 1 | | | | |
| *Conscientiousness* | 0.04 (0.13) | | | | |
| *Extraversion* | 0.38 (0.12) ** | 0.33(0.09) ** | | | |
| *Neuroticism* | -0.14 (0.14) | -0.27(0.10) * | -0.31(0.10) * | | |
| *Openness* | 0.17 (0.11) | -0.24 (0.09) * | 0.05(0.09) | -0.01(0.10) | |

**Supplementary Table 12. Genetic correlation of personality traits.** Genetic correlation across personality traits using solar 8.4.0. ** indicates a Bonferroni corrected at p<0.05, controlled for number of analysis (10), whereas * indicates p<0.05.

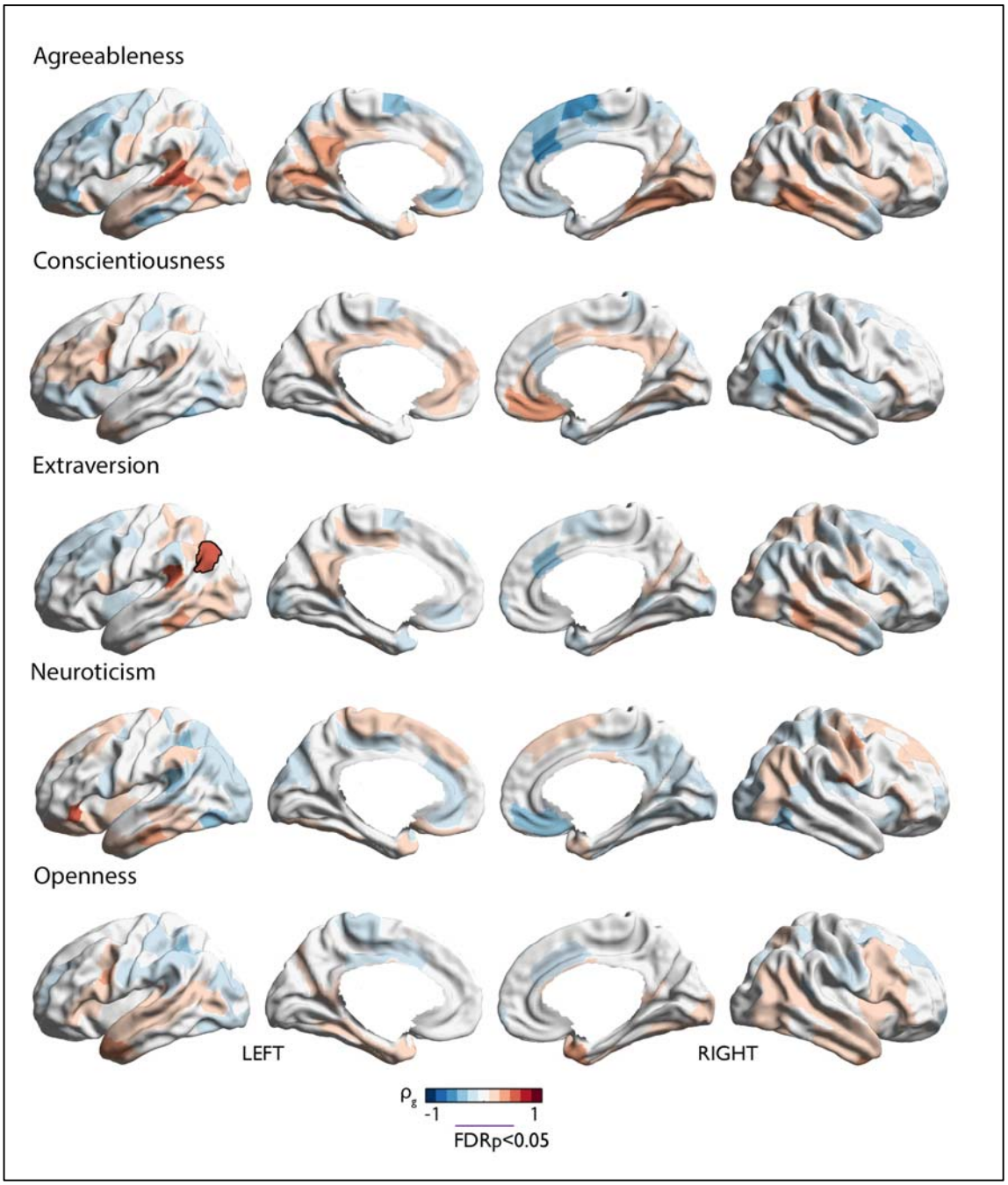
| Personality trait | A | C | E | N | O |
|---|---|---|---|---|---|
| *Agreeableness* | 1 | | | | |
| *Conscientiousness* | 0.32 (0.06) ** | | | | |
| *Extraversion* | 0.26 (0.06) ** | 0.24(0.06) ** | | | |
| *Neuroticism* | -0.41(0.06) ** | -0.51(0.05) ** | -0.39(0.06) ** | | |
| *Openness* | 0.06 (0.06) | 0.01 (0.07) | 0.14(0.07) * | 0.02(0.07) | |

**Supplementary Table 13. Environmental correlation of personality traits.** Environmental correlation across personality traits using solar 8.4.0. ** indicates a Bonferroni corrected at p<0.05, controlled for number of analysis (10), whereas * indicates p<0.05.

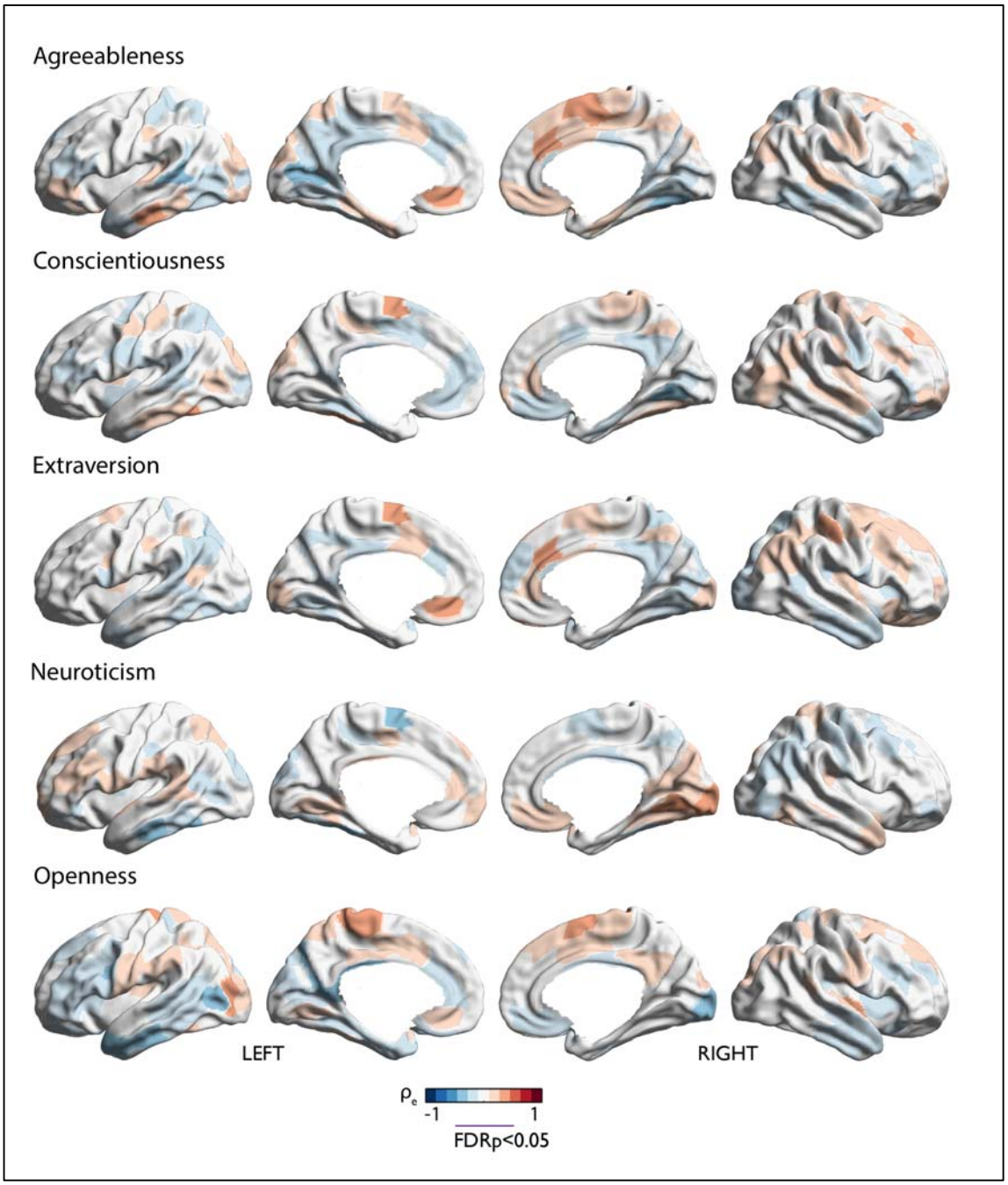
## SUPPLEMENTARY FIGURES



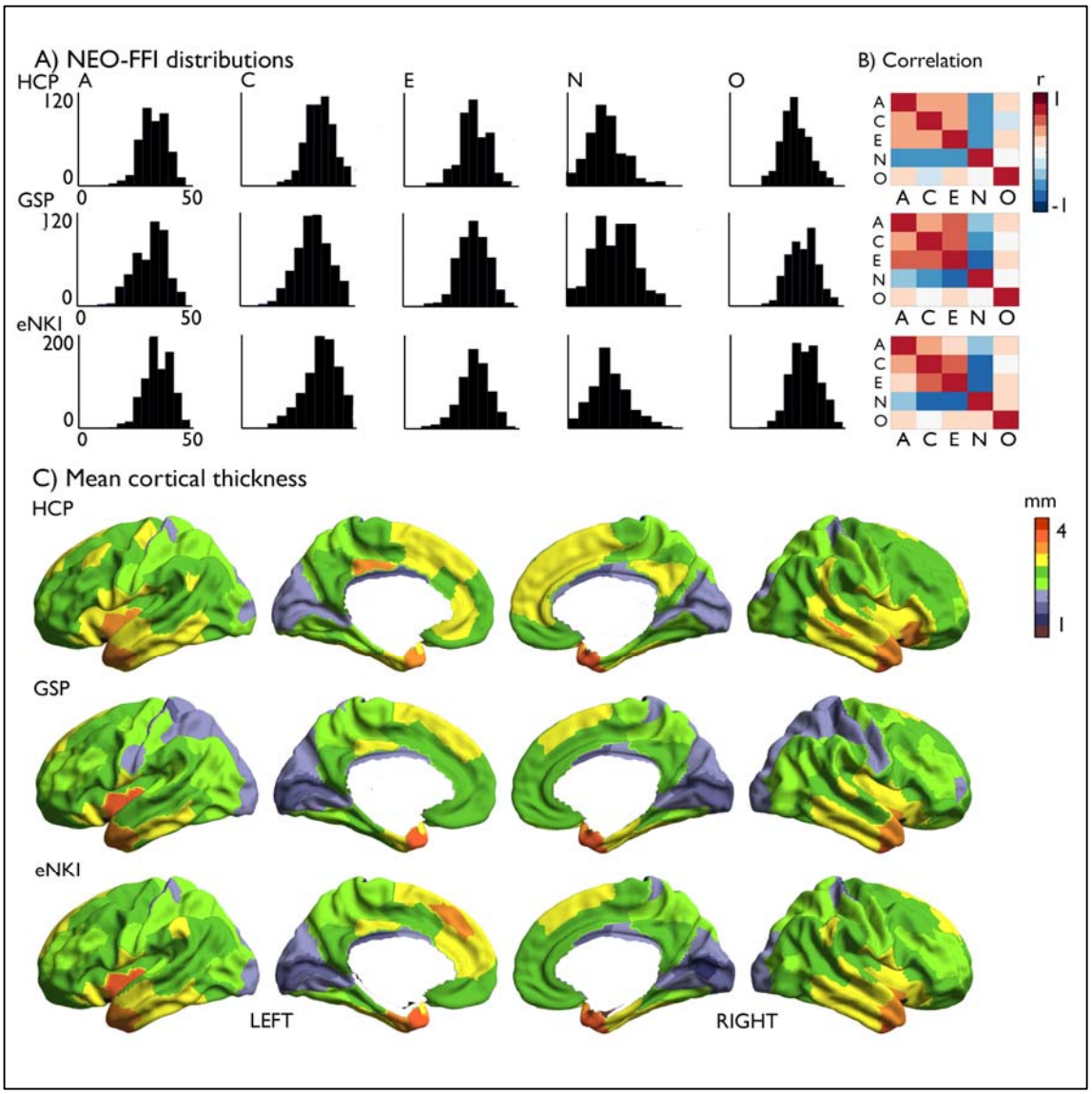

**Supplementary Figure 1. Genetic correlates between cortical thickness and personality traits functionally relate to (socio-) cognitive and language processing.** Quantitative functional decomposition of neurogenetic markers of personality based on the FDR-corrected clusters of phenotypical relationships of Figure 2.



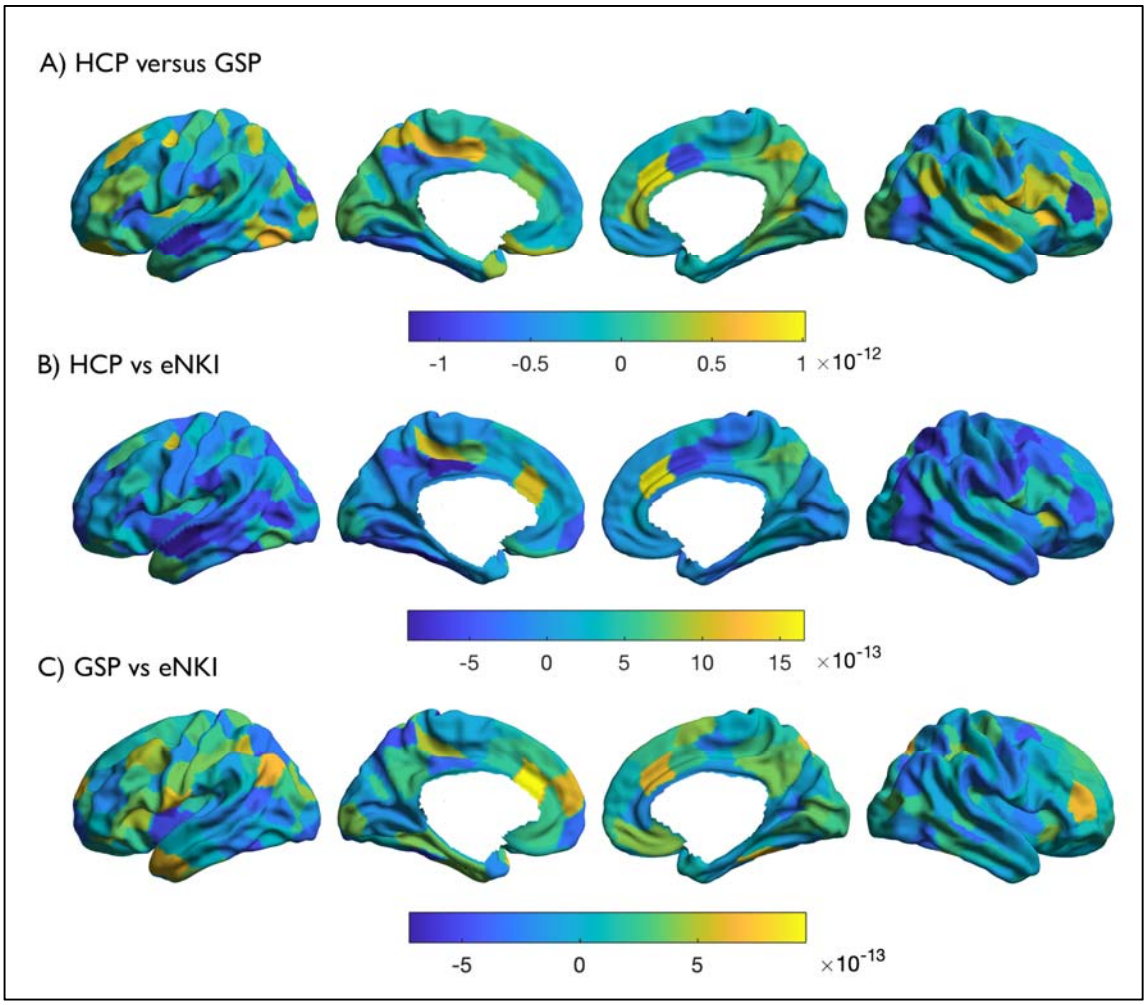

**Supplementary Figure 2. Genetic correlations between personality traits and cortical thickness controlled for total cognitive score.** Red values indicate positive genetic correlation whereas blue values indicate negative genetic correlation between parcel-wise thickness and personality traits. Findings at FDRp<0.05 are outlined in black.



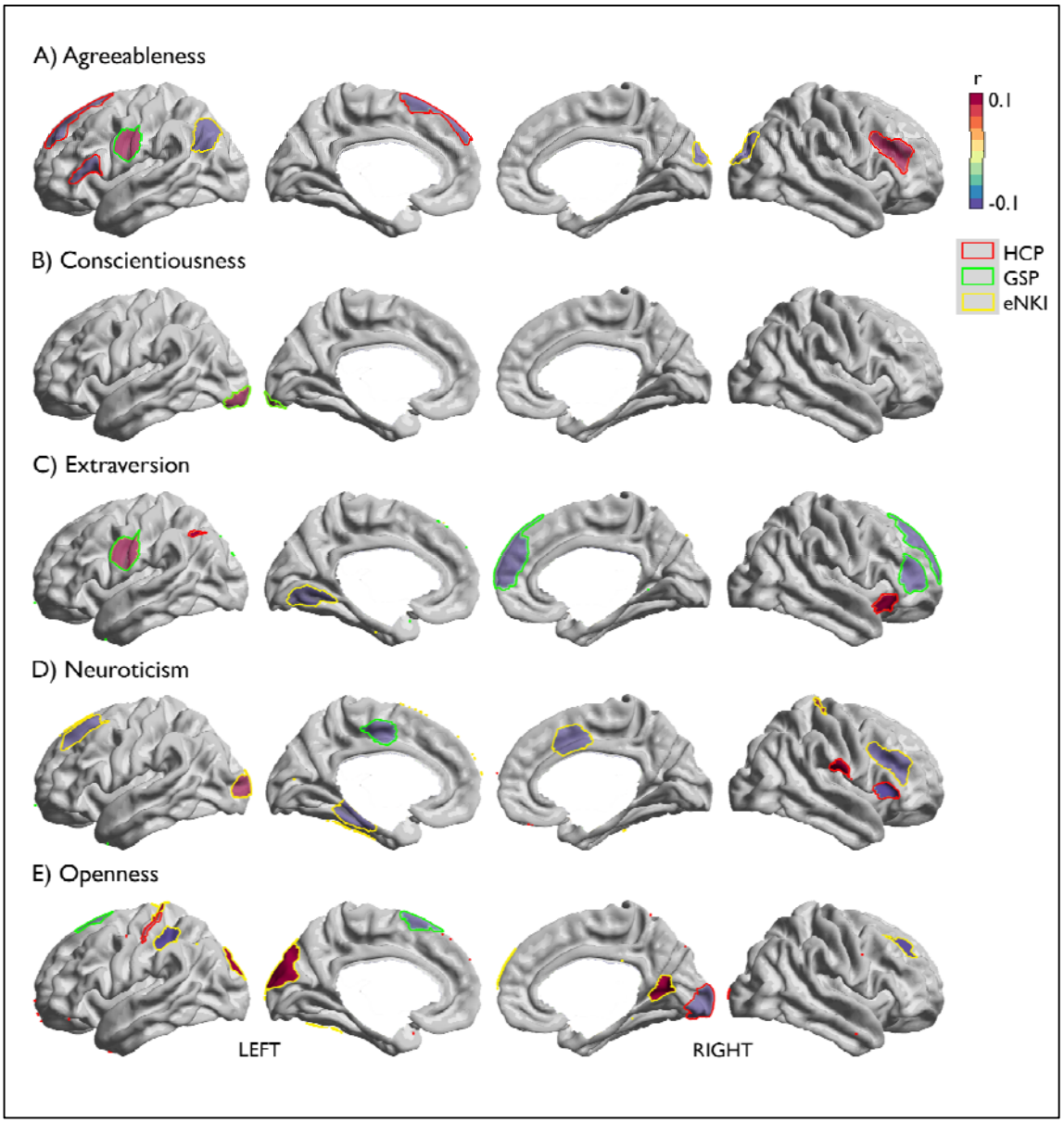

**Supplementary Figure 3. Environmental correlations between personality traits and cortical thickness.** Red values indicate positive environmental correlation whereas blue values indicate negative environmental correlation between parcel-wise thickness and personality traits. Findings at FDRp<0.05 are outlined in black.



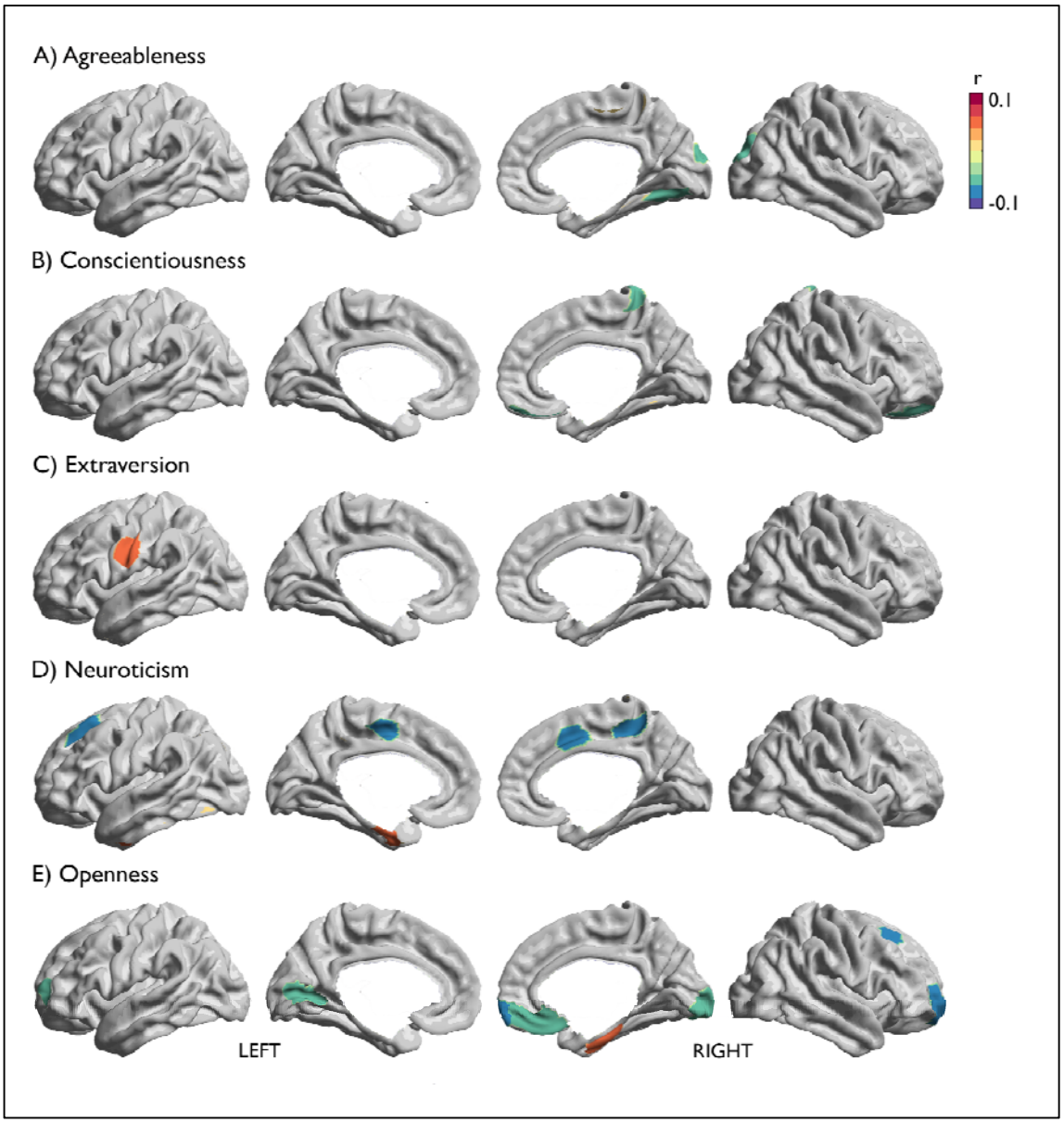

**Supplementary Figure 4. Distribution of NEO-FFI scores, their intercorrelation, and parcel-wise cortical thickness in three independent samples.** A). Distributions of NEO-FFI scores in three unrelated samples (HCP; GSP; eNKI). B). Intercorrelation of personality trait scores in each sample. C). Distribution of mean parcel-wise thickness in mm in the three unrelated samples.



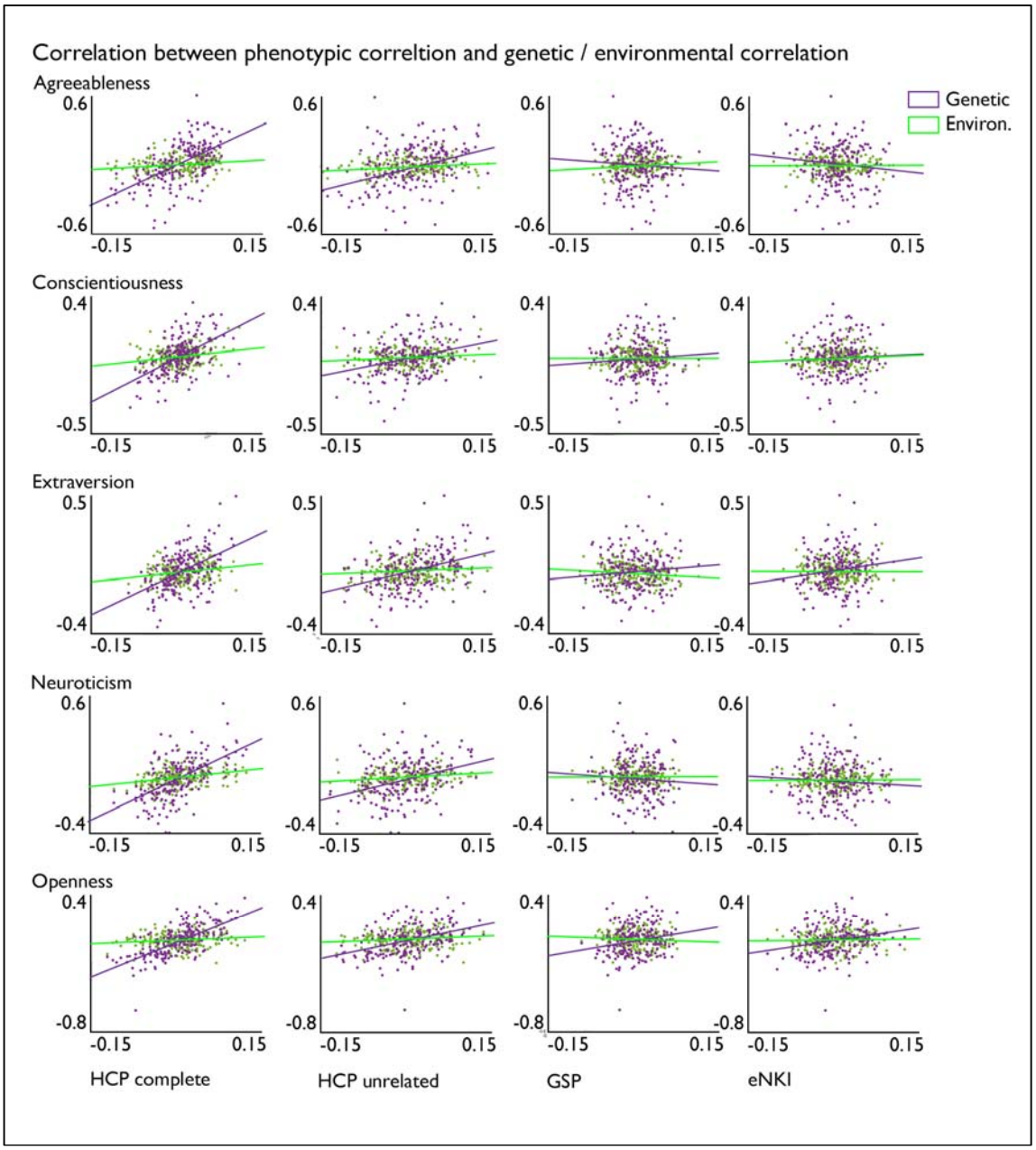

**Supplementary Figure 5. Comparability of parcel-wise cortical thickness values across samples.** To test whether the distribution of cortical thickness is comparable across samples, we performed an unpaired Students t-test for each parcel between the three unrelated samples (HCP, GSP and eNKI). Distributions of t-statistics are visualized above.




**Supplementary Figure 6. No consistent phenotypic relationship between cortical thickness and personality.** Findings in each sample are displayed at p<0.01, positive Spearman's ρ is displayed in red, whereas negative spearman's ρ is displayed in blue. Findings are outlined with specific color per sample (red=HCP unrelated subsample; green=GSP, yellow= eNKI). Multiple comparisons were accounted for by using FDRp<0.05 correcting for the number of parcels (200), as well as number of samples (3).




**Supplementary Figure 7. No significant phenotypic correlation in sample of 2137 unrelated individuals from three different datasets.** Phenotypic correlation between personality traits and cortical thickness in largest sample to data by combining HCP unrelated sub-sample, GSP and eNKI. Trends are displayed at $p<0.01$, observations at FDR $p<0.05$ correcting for number of parcels have a black outline (none present).




**Supplementary Figure 8. Correlation between cortex-wide spatial distributions of phenotypic and genetic/environmental correlation.** Scatterplots of the correlation between spatial patterns of phenotypic correlation between personality traits and cortical thickness (X-axis) and genetic correlation between personality and cortical thickness (Y-axis).

## SUPPLEMENTARY RESULTS

*Phenotypical correlation between NEO-FFI and cortical thickness in three samples.*

Additionally, we sought to assess whether there is a phenotypical correlation between personality and cortical thickness which is replicable across samples. First, we selected unrelated individuals from the HCP sample (n=419), as well as GSP sample (n=926) and eNKI sample (n=792). Then we correlated each personality trait with cortical thickness at each parcel, which we corrected for multiple comparisons using FDR (controlling for the number of parcels as well as number of datasets). Though distributions of cortical thickness and personality traits were comparable across samples (Supplementary Figure 4 and 5), we did not find significant relationships between NEO-FFI traits and parcel-wise cortical thickness in any of the samples (Supplementary Figure 6). Also, trend-level ($p<0.01$) relationships between NEO-FFI traits and cortical thickness did not overlap between samples (Supplementary Figure 6). Combining samples while controlling for site also did not generate significant results (Supplementary Figure 7). This suggests that in the largest sample of unrelated individuals to date, no robust local associations between personality traits and cortical thickness exist.