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Little evidence for associations between the Big Five personality traits and variability in brain gray or white matter

Reut Avinun[a,b,*], **Salomon Israel**[b], **Annchen R. Knodt**[a], **Ahmad R. Hariri**[a]

[a]Laboratory of NeuroGenetics, Department of Psychology & Neuroscience, Duke University, Durham, NC, USA

[b]Department of Psychology, The Hebrew University of Jerusalem, Jerusalem, Israel

Abstract

Attempts to link the Big Five personality traits of Openness-to-Experience, Conscientiousness, Extraversion, Agreeableness, and Neuroticism with variability in trait-like features of brain structure have produced inconsistent results. Small sample sizes and heterogeneous methodology have been suspected in driving these inconsistencies. Here, using data collected from 1,107 university students (636 women, mean age 19.69 ± 1.24 years), representing the largest sample to date of unrelated individuals, we tested for associations between the Big Five personality traits and measures of cortical thickness and surface area, subcortical volume, and white matter microstructural integrity. In addition to replication analyses based on a prior study, we conducted exploratory whole-brain analyses. Four supplementary analyses were also conducted to examine 1) possible associations with lower-order facets of personality; 2) modulatory effects of sex; 3) effect of controlling for non-target personality traits; and 4) parcellation scheme effects. Our analyses failed to identify significant associations between the Big Five personality traits and brain morphometry, except for a weak association between greater surface area of the superior temporal gyrus and lower conscientiousness scores. As the latter association is not supported by previous studies, it should be treated with caution. Our supplementary analyses mirrored these predominantly null findings, suggesting they were not substantively biased by our analytic choices. Collectively, these results indicate that if there are associations between the Big Five personality traits and brain structure, they are likely of very small effect size and will require very large samples for reliable detection.

Keywords

Personality; MRI; Brain structure; DTI; Traits; Replication; Reproducibility

*Corresponding author. Laboratory of NeuroGenetics, Department of Psychology & Neuroscience, Duke University, Gray Building 2020 West Main St, Ste 0030 Durham, NC, 27705, USA., reut.avinun@mail.huji.ac.il (R. Avinun).

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Reut Avinun: Conceptualization, Formal analysis, Writing - original draft, Writing - review & editing. **Salomon Israel:** Conceptualization, Writing - review & editing. **Annchen R. Knodt:** Data curation, Formal analysis, Writing - review & editing. **Ahmad R. Hariri:** Resources, Funding acquisition, Writing - review & editing.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.neuroimage.2020.117092.

1. Introduction

Studies regarding the basic structure of individual differences in personality traits have yielded a relatively consistent five factor model, comprised of the higher-order dimensions of neuroticism, extraversion, agreeableness, conscientiousness, and openness-to-experience - each capturing a wide array of feelings, thoughts, and behaviors (Digman, 1990). Individuals high in neuroticism tend to perceive the world as distressing or threatening and frequently tend to experience negative emotions such as anger and anxiety. Extraversion reflects a tendency to be outgoing and assertive, to experience frequent positive moods, and to approach and explore one's environment. Agreeableness reflects a tendency to be trusting and compassionate, and to prefer cooperation over conflict. Individuals high in conscientiousness tend to be organized and planful, and to follow socially prescribed norms of behavior. Individuals high in openness-to-experience tend to be curious and reflective, show an appreciation for art and culture, and tend to be very imaginative.

The Big Five personality traits are considered to be broad and global factors that can be further partitioned to a set of hierarchically lower-order facets, reflecting narrower, yet intercorrelated, sub-components of each broad dimension. They have been found across cultures (McCrae and Costa, 1997), ages (Terracciano et al., 2010), and reporters (Goldberg, 1990), shown to be moderately genetically influenced (Vukasović and Bratko, 2015) and to predict various psychological outcomes from educational attainment to mental health (Ozer and Benet-Martinez, 2006). However, despite the statistical consistency of the Big Five personality traits, uncovering the biological mechanisms that underlie them has been challenging.

Numerous studies have attempted to find links between personality traits and brain morphometry (e.g., Bjørnebekk et al., 2013; Coutinho et al., 2013; DeYoung et al., 2010; Ferschmann et al., 2018; Hu et al., 2011; Kapogiannis et al., 2013; Liu et al., 2013; Lu et al., 2014; Owens et al., 2019; Privado et al., 2017; Schultz et al., 2017), but most have relied on relatively small samples ($N < 300$) and have not yielded consistent and replicable findings (reviewed in Allen and DeYoung, 2017; Yarkoni, 2015). Importantly, a recent study has suggested that even samples of 300 participants may be too small to reliably detect associations between psychological phenotypes and brain morphometry (Kharabian Masouleh et al., 2019). This lack of statistical power has been further compounded by varied methodological and analytic approaches across studies.

Here, we tested for associations between the Big Five personality traits and multiple features of brain structure in the largest sample to date of genetically unrelated individuals ($N = 1,107$). Notably, other than its size, our sample also had the advantage of being relatively homogeneous in age (18–22 years), which may affect associations between personality traits and brain structure (Ferschmann et al., 2018). Surface-based parcellation analyses were conducted, rather than traditional vertex- or voxel-based analyses, to maximize spatial resolution otherwise lost to smoothing across tissue types (i.e., CSF, gray matter, and white matter) and anatomical regions (Coalson et al., 2018; Glasser et al., 2016), restrict the number of tests conducted to anatomically defined regions, and enable a straightforward correction for multiple comparisons across the whole brain, personality traits, and

morphometric measures (i.e., cortical thickness, surface area, subcortical volume, and white matter integrity), which is rarely done in personality neuroscience and may affect replicability. Furthermore, we explicitly controlled for race/-ethnicity, because previous research has found it to be linked with brain structure (e.g., Brickman et al., 2008; Pfefferbaum et al., 2016; Xie et al., 2015) and personality (Foldes et al., 2008).

Using the above general strategy, we conducted three related sets of analyses. First, we attempted to replicate the personality associations with brain morphometry reported by Hyatt et al. (2019), which represents the largest previously published study of the structural brain correlates of personality based on data from 1,104 participants, mostly twins and siblings, from the Human Connectome Project (age range: 22–36). Second, we conducted whole-brain exploratory analyses to examine all possible associations between the Big Five personality traits and brain morphometry. Third, in the hope of further informing future research in personality neuroscience, and to address previous findings and the possibility of parcellation scheme effects, we also conducted four supplementary analyses: a) we examined whether lower-order facets of the Big Five personality traits better correspond with brain structure (Bjørnebekk et al., 2013); b) we tested if associations differ by sex (Nostro et al., 2016), by testing for an interaction between personality and sex; c) we examined if associations can be detected when controlling for non-target traits (e.g., DeYoung et al., 2010; Liu et al., 2013; Riccelli et al., 2017); and; d) we explored the possibility that a different cortical parcellation scheme may affect the findings.

2. Methods

2.1. Participants

1330 participants (762 women, mean age 19.70 ± 1.25 years) successfully completed the Duke Neurogenetics Study (DNS), which assessed a range of behavioral and biological traits among young adult, university students. The DNS was approved by the Duke University School of Medicine Institutional Review Board, and all participants provided written informed consent prior to participation. All participants were free of the following study exclusions: 1) medical diagnoses of cancer, stroke, diabetes requiring insulin treatment, chronic kidney or liver disease, or lifetime history of psychotic symptoms; 2) use of psychotropic, glucocorticoid, or hypolipidemic medication; and 3) conditions affecting cerebral blood flow and metabolism (e.g., hypertension). Current and lifetime DSM-IV (the Diagnostic and Statistical Manual of Mental Disorders) Axis I or select Axis II disorders (antisocial personality disorder and borderline personality disorder), were assessed with the electronic Mini International Neuropsychiatric Interview (Lecrubier et al., 1997) and Structured Clinical Interview for the DSM-IV Axis II subtests (First et al., 1997), respectively. Importantly, neither current nor lifetime diagnosis were an exclusion criterion, as the DNS seeks to establish broad variability in multiple behavioral phenotypes related to psychopathology. However, no individuals, regardless of diagnosis, were taking any psychoactive medication during or at least 14 days prior to their participation.

2.2. Brain morphometry analyses

Brain morphometry was assessed by measuring cortical thickness (CT), surface area (SA), subcortical volume, and white matter microstructural integrity. Based on the radial unit hypothesis (Rakic, 1988, 2009), SA is driven by the number of radial columns, while CT reflects the density of cells within a column. CT and SA exhibit different developmental trajectories (Wierenga et al., 2014) and are affected by distinct genetic factors (Panizzon et al., 2009). Consequently, we examined associations with CT and SA separately rather than the coarser measure of gray matter volume, which is the product of these two measures. To measure white matter microstructural integrity, we used fractional anisotropy (FA), which measures the directional diffusivity of water, and represents fiber diameter and density, degree of myelination, and fiber tract coherence (Basser, 1995; Basser and Pierpaoli, 1996; Beaulieu, 2002).

The current analyses of gray matter (i.e., CT, SA, and subcortical volume) were conducted on a subset of 1107 participants (636 women, mean age 19.69 ± 1.24 years) for whom there was T1-weighted structural imaging data available post quality control procedures (see below) as well as personality questionnaire and genetic race/ethnicity data. Amongst this subset, 224 participants had at least one DSM-IV diagnosis. Based on self-report, there were 499 non-Hispanic Caucasians, 125 African Americans, 294 Asians, 71 Latino/as, 2 Pacific Islanders, and 116 multiracial or other participants in this subset.

White matter microstructure analyses were conducted on a further subset of 778 participants (443 women, mean age 19.67 ± 1.25 years) for whom there was diffusion weighted imaging data available post quality control procedures (see below) as well as personality questionnaire and genetic race/ethnicity data. Amongst this subset, 156 participants had at least one DSM-IV diagnosis. Based on self-report, there were 351 non-Hispanic Caucasians, 92 African Americans, 213 Asians, 47 Latino/as, 2 Pacific Islanders, and 73 multiracial or other participants in this subset.

2.3. Race/ethnicity

Because self-reported race and ethnicity are not always an accurate reflection of genetic ancestry, an analysis of identity by state of whole-genome SNPs was performed in PLINK (Purcell et al., 2007). The first four multidimensional scaling components were used as covariates to reduce possible confounding effects of race/ethnicity. The decision to use only the first four components was based on an examination of a scree plot of eigenvalue, which showed that the eigenvalues became very similar after the fourth component (further information and relevant plots can be found at https://www.haririlab.com/methods/genetics.html).

2.4. Personality

The 240-item NEO personality inventory revised (NEO-PI-R; Costa and McCrae, 1995), was used to assess the Big Five personality dimensions and their underlying facets: 1) Neuroticism (based on the anxiety, angry hostility, depression, self-consciousness, impulsiveness, and vulnerability facets); 2) Agreeableness (based on the trust, straightforwardness, altruism, compliance, modesty, and tender-mindedness facets); 3)

Conscientiousness (based on the competence, order, dutifulness, achievement striving, self-discipline and deliberation facets); 4) Extraversion (based on the warmth, gregariousness, assertiveness, activity, excitement-Seeking, and positive emotions facets); and 5) Openness-to-Experience (based on the fantasy, aesthetics, feelings, actions, ideas, and values facets). Each facet was a sum of 8 items, and each personality trait was a sum of the facet scores (with certain items reverse coded as indicated). Participants rated the 240 items on a scale ranging from (0) *strongly disagree* to (4) *strongly agree.* The 6 lower order facets for each personality trait were modeled in our supplementary analyses. Internal consistency of the personality traits was assessed by Cronbach's alpha as fair to good, ranging between 0.70 and 0.85.

2.5. MRI data acquisition

Each participant was scanned using one of two identical research-dedicated GE MR750 3T scanners stationed at the same facility, the Duke-UNC Brain Imaging and Analysis Center (891 participants on scanner 1 and 216 participants on scanner 2. Additional details on the scanners can be found elsewhere: https://www.biac.duke.edu/facilities/scanners.asp). Each identical scanner was equipped with high-power high-duty cycle 50-mT/m gradients at 200 T/m/s slew rate and an eight-channel head coil for parallel imaging at high bandwidth up to 1 MHz. T1-weighted images were obtained using a 3D Ax FSPGR BRAVO sequence with the following parameters: TR = 8.148 ms; TE = 3.22 ms; 162 axial slices; flip angle, 12°; FOV, 240 mm; matrix = 256 × 256; slice thickness = 1 mm with no gap (voxel size 0.9375 × 0.9375 × 1 mm); and total scan time = 4 min and 13 s. Following an ASSET calibration scan, two 2-min 50-s diffusion imaging acquisitions were collected, providing full brain coverage with 2-mm isotropic resolution and 15 diffusion weighted directions (10-s repetition time, 84.9 ms echo time, b value 1,000 s/mm2, 240 mm field of view, 90° flip angle, 128 × 128 acquisition matrix, slice thickness = 2 mm). A variable indicating which scanner was used for each participant was included in all analyses as a covariate.

2.6. MRI data processing

To generate regional measures of brain morphometry, anatomical images for each subject were first skull-stripped using ANTs (Klein et al., 2009), then submitted to Freesurfer's (Version 5.3) recon-all with the "-noskullstrip" option (Dale et al., 1999; Fischl et al., 1999), using an x86_64 linux cluster running Scientific Linux. Of the 1321 participants who completed the high-resolution T1-weighted imaging protocol, 11 were excluded for the presence of motion-related or external artifacts, 4 were excluded for incidental findings, and 1 was unable to be processed with FreeSurfer. Additionally, the gray and white matter boundaries determined by recon-all were visually inspected using FreeSurfer QA Tools (https://surfer.nmr.mgh.harvard.edu/fswiki/QATools). This revealed small to moderate errors in gray matter boundary detection in 51 individuals who were consequently excluded.

CT and SA for 31 regions in each hemisphere, as defined by the Desikan-Killiany-Tourville atlas (Klein and Tourville, 2012), a modified version of the Desikan-Killiany atlas (Desikan et al., 2006), which was used in the Hyatt et al. (2019) study, were extracted using Freesurfer. The updated version of the atlas is meant to make region definitions as unambiguous as possible and define boundaries best suited to FreeSurfer's classifier

algorithm. To ensure that our exploratory analyses were not contingent on a specific parcellation scheme, CT and SA for 74 regions per hemisphere, as defined by the Destrieux atlas (Destrieux et al., 2010), were also extracted using Freesurfer. Additionally, gray matter volumes from eight subcortical regions (Cerebellum Cortex, Thalamus, Caudate, Putamen, Pallidum, Hippocampus, Amygdala, and Accumbens area) were extracted with Freesurfer's subcortical segmentation ("aseg") pipeline (Fischl et al., 2002). Estimated Total Intracranial Volume (ICV), total gray matter volume, cerebral white matter volume, and left and right hemisphere mean CT were also extracted from the "aseg" pipeline, and average whole-brain CT was calculated based on the estimates for the left and right hemispheres.

Diffusion weighted images were processed according to the Diffusion Tensor Imaging (DTI) protocol developed by the Enhancing Neuro Imaging Genetics Through Meta-Analysis (ENIGMA) consortium (Jahanshad et al., 2013; or http://enigma.ini.usc.edu/protocols/dti-protocols/). In brief, raw diffusion-weighted images underwent eddy current correction and linear registration to the non-diffusion weighted image in order to correct for head motion. These images were skull-stripped and diffusion tensor models were fit at each voxel using FMRIB's Diffusion Toolbox in FSL (FDT; http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FDT), and the resulting two FA maps were linearly registered to each other and then averaged. Average FA images from all subjects were non-linearly registered to the ENIGMA-DTI target FA map, a minimal deformation target calculated across a large number of individuals (Jahanshad et al., 2013). The images were then processed using the tract-based spatial statistics (TBSS) analytic method (Smith et al., 2006) modified to project individual FA values onto the ENIGMA-DTI skeleton. Following the extraction of the skeletonized white matter and projection of individual FA values, tract-wise regions of interest, derived from the Johns Hopkins University (JHU) white matter parcellation atlas (Mori et al., 2005), were transferred to extract the mean FA across the full skeleton and average whole-brain FA values for a total of 24 (partially overlapping) regions across the two scans. All FA measures from the right and left hemispheres were averaged. Additionally, volume-by-volume head motion was quantified by calculating the root mean square (RMS) displacement of the six motion parameters (three translation and three rotation components), determined during eddy current correction for each pair of consecutive diffusion-weighted brain volumes. The resulting volume-by-volume RMS deviation values were averaged across all images, yielding a summary statistic of head motion for each participant to add to the FA analyses as a covariate (M = 0.34, SD = 0.057), as previously recommended for DTI analyses (Yendiki et al., 2014).

2.7. Statistical analyses

We first attempted to replicate the significant associations between personality and brain morphometry reported by Hyatt et al. (2019; Table 1) at $p < .005$ (i.e., the significance threshold used in their paper). We next proceeded to conduct exploratory parcellation-based analyses across the whole-brain (31 SA regions, 31 CT regions, 8 subcortical regions, 24 FA measures, and total gray matter volume, cerebral white matter volume, whole-brain average FA, and whole-brain average CT) for each of the Big Five personality traits (a total of 5*98 = 490 tests). Lastly, to assess the robustness of our findings, we conducted four supplementary analyses: 1) whole-brain parcellation-based analyses of the Big Five

personality facets; 2) whole-brain parcellation-based analyses of the interaction between sex and the Big Five personality traits; 3) whole-brain parcellation-based analyses of each Big Five personality trait while controlling for the other four traits; and 4) whole-brain parcellation-based analyses of each Big Five personality trait, while using a different cortical parcellation scheme, specifically, the Destrieux atlas (Destrieux et al., 2010).

Analyses were conducted in R version 3.5.1 (R Core Team, 2018), with the packages "broom" (Robinson and Hayes, 2018), "tidyr" (Wickham and Henry, 2018), "dplyr" (Wickham et al., 2019), "lmtest" (Zeileis and Hothorn, 2002), "readr" (Wickham et al., 2018), and "sandwich" (Zeileis, 2004). Linear regression analyses with robust standard errors were performed with brain measures as outcomes (as previously done, e.g., Bjørnebekk et al., 2013; DeYoung et al., 2010; Liu et al., 2013; Nostro et al., 2016), personality measures as independent variables, and sex, age, scanner, and four ancestry-informative genetic MDS components as covariates of no interest. With the exception of the Hyatt et al. (2019) replication analyses which included lateralized associations, all brain morphometry measures were averaged across the two hemispheres, as there is no strong evidence to support a lateralization effect of personality on brain structure. ICV, average CT, and average FA, were used as additional covariates for analyses of subcortical volume and surface area, CT, and FA, respectively. For the FA analyses, which can be particularly sensitive to motion, head motion was also included as a covariate. The Big Five personality traits were standardized (M = 0, SD = 1) in SPSS version 25 before analyses and for the interaction analyses sex was mean centered (Schielzeth, 2010). Variance explained (i.e., R^2) by the independent variable of interest, when it is last in the regression, was calculated in R with the package "relaimpo" (Grömping, 2006). The "false discovery rate" (FDR) adjustment (Benjamini and Hochberg, 1995) was applied to correct for multiple comparisons with the p.adjust function in R.

3. Results

Descriptive statistics for the personality and brain morphometry variables are available in Supplementary Table 1.

3.1. Replication of Hyatt et al. (2019)

As reported in Table 2, none of the 15 associations that were significant at $p < .005$ in Hyatt et al. (2019) were significant in our analyses, even without correcting for multiple comparisons (i.e., using an uncorrected $p < .05$ threshold). As Hyatt et al. did not control for race/-ethnicity, we also ran analyses without the genetic MDS components to test whether these could account for the different results. Again, none of the associations remained significant after correcting for multiple comparisons, but three associations were significant at an uncorrected $p < .05$, although not necessarily in the same direction as found in Hyatt et al.: a positive association between the right supramarginal gyrus SA and neuroticism (b = 24.047, SD = 11.43, p = .036, R^2 = 0.23%; this association was negative in Hyatt et al.); a negative association between the left pars orbitalis CT and neuroticism (b = −0.013, SD = 0.005, p = .021, R^2 = 0.33%; this association was positive in Hyatt et al.), and a positive association between the left superior frontal gyrus CT and neuroticism (b = 0.0072, SD =

0.003, p = .02, R^2 = 0.21%; this association was also positive in Hyatt et al.). When comparing the analyses with and without controlling for race/ethnicity (Table 2), it is noticeable that race/ethnicity can affect the obtained results.

As the race/ethnic composition of our sample differed from the race/ethnic composition of the Human Connectome Project (HCP) sample on which the analyses of Hyatt et al. were based (i.e., 44.6% vs. 74.8% of non-Hispanic Caucasians, 11.4% vs. 15.1% of African-Americans, and 27% vs. 5.7% of Asian-Americans, which also included Native Hawaiian, or other Pacific Islander in the HCP), we also separately present the results from our three largest ethnic subsamples, as determined based on self-reports and genetic ancestry components, when available. Here, the sample sizes are larger because individuals with missing genetic data were also included based on self-reported race/ethnicity: non-Hispanic Caucasians (n = 559), Asians (n = 336), and African-Americans (n = 143). As shown in Table 2, there were differences between the groups, further supporting our decision to control for race/ethnicity (e.g., in Asians the association between the left superior frontal gyrus CT and neuroticism was positive and significant at an FDR corrected p value < .05, but it was somewhat negative in African Americans. This association was also significant at an uncorrected p < .05 in the mixed race/ethnicity sample, when race/ethnicity was not included as a covariate).

3.2. Exploratory whole-brain analyses

The top associations (i.e., uncorrected p < .005) are reported in Table 3 along with their R^2. Only one of the associations between the Big Five personality traits and brain morphometry (CT, SA, subcortical volume, or FA) remained significant after the FDR correction for multiple comparisons: the association between the SA of the superior temporal gyrus and conscientiousness (b = −33.91, SE = 8.66, p = 9.55e-05, FDR adjusted p = 0.047, R^2 = 0.44%). All associations and related variance explained (R^2) are presented in Supplementary Table 2.

3.3. Supplementary analyses testing for the robustness of our null findings

Our supplementary analyses (i.e., testing personality facets instead of the Big Five personality traits [Supplementary Table 3], examining interactions between the Big Five personality traits and sex [Supplementary Table 4], using non-target personality traits as covariates [Supplementary Table 5] or using a different cortical parcellation scheme [Supplementary Table 6]) revealed that these generally null findings were not biased by our analytic approach. Only the associations between the SA of the superior temporal gyrus and either the dutifulness facet of conscientiousness (b = −39.50, SE = 8.79, p = 7.76e-06, FDR adjusted p = 0.04; R^2 = 0.62%) or conscientiousness itself (b = −41.13, SE = 9.56, p = 1.85e-05,FDR adjusted p = 0.048; R^2 = 0.52%), remained significant after the FDR correction for multiple comparisons across all the tests conducted in the current study (5,150 tests in total). Higher dutifulness was associated with reduced superior temporal gyrus SA.

Although none of the interactions between the Big Five personality traits and sex remained significant after applying a multiple comparisons correction, the supplementary also includes whole-brain parcellation-based analyses of the Big Five personality traits for males

and females separately (Supplementary Tables 7–8). This was done to enable comparisons to previous studies and inform future meta-analyses.

4. Discussion

In the current study, with the largest sample of unrelated individuals to date, we failed to identify robust links between the Big Five personality traits and multiple, trait-like features of brain structure. Several supplementary analyses, in which we tested the facets of personality, explored a possible moderation by sex, included the non-target personality traits as covariates, and used a different parcellation scheme, confirmed these primary null findings. There was one exception: an association between greater SA of the superior temporal gyrus, an area involved in language perception and production, and lower scores on conscientiousness, and, more specifically, dutifulness. However, this association is novel and does not correspond with previous findings (Bjørnebekk et al., 2013; Hyatt et al., 2019; Lewis et al., 2018; Nostro et al., 2016). Consequently, it should be treated with caution. Generally, the supplementary analyses suggested that the primarily null results of the primary analyses did not depend on specific analytic or methodological choices. This is further supported by a recent large study which applied a voxel-wise approach and also did not find robust associations between personality traits and brain morphometry (Kharabian Masouleh et al., 2019).

There are several possible reasons for the lack of replicable associations between personality and brain structure, including the current failure to replicate associations identified by Hyatt et al. (2019). With regard to this specific failure, Hyatt et al., did not use statistical methods, such as multilevel modeling (e.g., Hanley et al., 2003; Huang, 2016; Liang and Zeger, 1993), that can account for the dependency and clustering within their data, which is derived primarily from twins and siblings (only 4% of the sample is not genetically related; https://wiki.humanconnectome.org). Because individuals within families share genes and environments, not accounting for family clustering may have biased their findings. Additionally, even though we used a similar atlas (original study: the Desikan-Killiany atlas; our study: the updated Desikan-Killiany-Tourville atlas), a similar personality measure (original study: the 60-item NEO-FFI; our study: the 240-item NEO-PI-R), and a similar scanner (original study: the 3T Siemens Skyra; our study: the 3T GE MR750), it is possible that these small differences in data collection affected our results. However, if such differences account for the lack of replicability, this raises questions regarding the robustness of the original findings. We also used multiple regression analyses, which are more similar to semi-partial correlations, while Hyatt et al. employed partial correlations. To ensure the robustness of our findings, we repeated our analyses using partial correlations; our results were robust across either estimation procedure. More generally, most of the correlations reported by Hyatt et al. were smaller than 0.10, and, similarly, in our study almost all the R^2 were smaller than 1%. This suggests that effect sizes for associations between personality traits and brain structure are likely to be very small and will require very large sample sizes to be reliably detected.

Furthermore, differences between and within samples may also limit replicability in personality neuroscience. Age is known to affect brain structure, and indeed has been shown

to moderate associations between brain structure and personality (Ferschmann et al., 2018). Sex differences may also be relevant (Nostro et al., 2016), although interactions with sex did not remain significant after applying a multiple comparisons correction. Our results also suggest that accounting for race/ethnicity may be advised when testing for personality-brain structure associations. Indeed, previous research has shown differences in brain structure as a function of race/ethnicity (e.g., Brickman et al., 2008; Pfefferbaum et al., 2016; Xie et al., 2015) and measures, such as stress (O'Doherty et al., 2015), that correlate with brain structure have also been shown to differ by race/ethnicity (Avinun et al., 2019). Furthermore, due to the identification of significant ethnic differences in brain structure between Caucasians and Chinese, a different brain atlas was constructed for Chinese (Tang et al., 2010). Thus, it may be insufficient to simply control for race/ethnicity in statistical models.

Although we used the largest sample of unrelated individuals to date, relied on 240 items to assess personality traits, and employed different methodologies to test for the associations between the Big Five personality traits and brain structure, our study does have several limitations. First, we did not exhaust all the possible ways to assess personality. For example, an alternative classification approach is represented by personality "types," which defines categories of individuals based on similar configurations of interacting traits. A large analysis of personality types indicated that there are 4 personality types that can be clustered based on scores on the Big Five personality traits (Gerlach et al., 2018). Thus, for example, someone low on neuroticism may also have an average or a high conscientiousness score, which may correspond differently with brain structure. Future studies could focus on such "types" in examining personality-brain structure associations. Second, our acquisition protocol precluded the application of more anatomically precise parcellation schemes (e.g., Glasser et al., 2016). Third, our sample of volunteer students at a top university may not be representative of the general population. Fourth, we examined each brain region and measure individually in the search for localized effects. Multivariate statistical methods (McIntosh and Mišić, 2013) that can jointly model several brain regions and personality traits and look for possible covariance patterns (Smith and Nichols, 2018), could help to decrease the number of analyses. Additionally, it is possible that these covariance patterns better reflect the complexity and interconnectedness between brain regions and personality traits, and may consequently lead to different findings and insights (Kharabian Masouleh et al., 2019). Lastly, we did not examine brain function or conduct network analyses. The brain correlates of personality may be more readily identified in functional measures and/or network analyses, such as functional connectivity. Importantly, as functional MRI studies often rely on small sample sizes, here as well caution will be needed in the interpretation of findings until replicable findings emerge.

Our largely null findings echo comments made by Yarkoni (2015): "There is no guarantee that any particular psychometric model of individual differences in personality will map onto underlying biological process models in any straightforward way. In fact … a clear-cut relationship between the two is likely to be the exception rather than the rule." As well as those by Kharabian Masouleh et al. (2019) that associations between psychological measures (including personality) and specific brain structures in a healthy sample are "highly unlikely" (Kharabian Masouleh et al., 2019). That said, small effect sizes and possible moderating effects of sex, age, and race/ethnicity suggest the possibility that with

ever larger and more homogeneous samples reliable links between personality and trait-like features of the brain may yet emerge. The field of personality neuroscience may benefit from following the lead of genome-wide association studies that have, after many failed attempts with candidate gene studies and small samples (e.g., Avinun et al., 2018; Bosker et al., 2011), begun to reveal the genetic architecture of complex traits through massive samples (Plomin and von Stumm, 2018). The growth of shared imaging data through research consortia (e.g., the "enhancing neuroimaging genetics through meta-analysis" project [ENIGMA]) may allow for such gains in personality neuroscience sooner than later.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Significant personality and brain structure (SA and CT) associations reported by Hyatt et al. (2019).

	CT	SA	Subcortical volume
Neuroticism	Left caudal middle frontal gyrus (+) Left pars orbitalis (+) Left pars triangularis (+) Left superior frontal gyrus (+)	Left cuneus (−) Left pars triangularis (−) Left superior parietal lobule (−) Right supramarginal gyrus (−) Superior frontal gyrus (−)	
Openness	Left rostral middle frontal gyrus (−) Left superior parietal lobule (−)	Left inferior temporal gyrus (+)	Left caudate (+)
Agreeableness	Left caudal middle frontal gyrus (−)		
Extraversion		Right superior frontal gyrus (+)	

Note. +/− indicate the direction of the associations (i.e., positive or negative respectively). SA = surface area; CT = cortical thickness.

Table 2

Regression coefficients from our attempt to replicate the associations reported by Hyatt et al. (2019) in all participants and within the three largest racial/ethnic subgroups from the Duke Neurogenetics Study.

	All participants (N = 1107)			Without controlling for ethnicity (N = 1107)			Caucasians (n = 559)			Asians (n = 336)			Africans Americans (n = 143)		
	b	SD	R^2	b	SD	R^2	b	SD	R^2	b	SD	R^2	b	SD	R^2
Left cuneus (SA) on Neuroticism	−4.263	7.610	0.02%	−0.787	6.977	0.00%	5.879	11.276	0.04%	−9.265	12.485	0.13%	−26.246	18.164	1.11%
Left pars triangularis (SA) on Neuroticism	6.955	6.536	0.07%	9.857	6.095	0.14%	15.075	10.201	0.29%	−6.948	11.284	0.08%	35.221^	17.922	2.06%
Left superior parietal lobule (SA) on Neuroticism	12.858	13.331	0.05%	14.002	12.589	0.06%	1.494	19.656	0.00%	3.814	24.208	0.01%	55.496	33.263	1.02%
Right supramarginal gyrus (SA) on Neuroticism	20.087	12.314	0.16%	24.047*	11.431	0.23%	12.800	18.403	0.05%	21.931	19.676	0.24%	13.398	40.240	0.08%
Superior frontal gyrus (SA) on Neuroticism	6.484	16.093	0.00%	5.956	14.653	0.00%	13.210	22.515	0.02%	9.396	25.668	0.01%	23.617	47.999	0.06%
Left inferior temporal gyrus (SA) on Openness	14.579	11.062	0.09%	16.364	10.347	0.11%	28.913^	15.301	0.38%	−9.463	20.097	0.04%	57.369^	29.662	1.48%
Right superior frontal gyrus (SA) on Extraversion	19.777	18.350	0.03%	19.780	17.327	0.03%	4.725	26.898	0.00%	−57.200	34.859	0.29%	79.808	55.550	0.44%
Left caudate on Openness	−17.406	12.350	0.11%	−17.243	11.604	0.11%	−39.654*	16.342	0.60%	−2.500	25.816	0.00%	27.527	44.681	0.21%
Left caudal middle frontal gyrus (CT) on Neuroticism	0.003	0.004	0.03%	0.004	0.004	0.07%	0.007	0.006	0.17%	0.006	0.008	0.13%	0.001	0.015	0.00%
Left pars orbitalis (CT) on Neuroticism	−0.008	0.006	0.14%	−0.013*	0.005	0.33%	−0.016^	0.008	0.54%	−0.006	0.010	0.08%	−0.018	0.019	0.55%
Left pars triangularis (CT) on Neuroticism	−0.003	0.004	0.02%	−0.004	0.004	0.07%	−0.005	0.006	0.08%	0.004	0.007	0.06%	−0.010	0.012	0.34%
Left superior frontal gyrus (CT) on Neuroticism	0.005	0.003	0.11%	0.007*	0.003	0.21%	0.001	0.004	0.01%	0.016**	0.005	1.22%	−0.004	0.009	0.06%
Left rostral middle frontal gyrus (CT) on Openness	−0.002	0.004	0.02%	−0.001	0.003	0.01%	0.000	0.005	0.00%	0.002	0.007	0.01%	−0.012	0.012	0.42%
Left superior parietal lobule (CT) on Openness	−0.001	0.003	0.01%	−0.002	0.003	0.02%	0.000	0.004	0.00%	−0.001	0.006	0.00%	−0.011	0.008	0.79%
Left caudal middle frontal gyrus (CT) on Agreeableness	−0.002	0.004	0.01%	−0.003	0.004	0.03%	−0.005	0.005	0.11%	−0.002	0.008	0.01%	0.011	0.014	0.31%

Note. CT = cortical thickness; SA = surface area; R^2 = variance explained; All participants = entire sample, controlling for 4 genetic MDS components. In all analyses, sex, age and either mean CT or intracranial volume were included as covariates.

^ uncorrected p < .06,

* uncorrected $p < .05$,

** uncorrected $p < .005$ and FDR corrected $p < .05$.

Table 3

Top results ($p < .005$) from whole-brain exploratory analyses between the Big Five personality traits and structural brain measures in the Duke Neurogenetics Study.

	b	SE	p value	FDR adjusted p value	R^2
Superior temporal gyrus (SA) on Conscientiousness	−33.912	8.659	9.55E-05	0.047	0.44%
Thalamus Proper on Conscientiousness	−54.921	15.690	0.000483	0.12	0.49%
Postcentral gyrus (CT) on Openness	0.007	0.002	0.001413	0.23	0.45%
Cerebral peduncle on Neuroticism	−0.002	0.0005	0.002643	0.32	0.82%
Transverse temporal gyrus (SA) on Conscientiousness	−3.858	1.327	0.003724	0.36	0.44%