Personality, Health and Brain Integrity: The Lothian Birth Cohort Study 1936

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Abstract

Objective: To explore associations between the five factor model (FFM; Neuroticism, Extraversion, Openness/Intellect, Agreeableness and Conscientiousness) personality traits and measures of whole brain integrity in a large sample of older people, and to test whether these associations are mediated by health-related behaviours.

Method: Participants from the Lothian Birth Cohort 1936 completed the International Personality Item Pool measure of the FFM and underwent a structural MR brain scan at mean age 73 years yielding three measures of whole-brain integrity: average white matter fractional anisotropy (FA), brain tissue loss, and white matter hyperintensities (N=529 to 565). Correlational and mediation analyses were used to test the potential mediating effects of health-related behaviours on the associations between personality and integrity.

Results: Lower conscientiousness was consistently associated with brain tissue loss (β=-0.11,p<0.01), lower FA (β=0.16,p<0.001) and white matter hyperintensities (β=-0.10,p<0.05). Smoking, alcohol consumption, diet, physical activity, body mass index and a composite health behaviour variable displayed significant associations with measures of brain integrity (range of r=0.10 to 0.25). The direct effects of conscientiousness on brain integrity were mediated to some degree by health behaviours, with the proportions of explained direct effects ranging from 0.1% to 13.7%.

Conclusions: The personality trait conscientiousness was associated with all three measures of brain integrity, which we tentatively interpret as the effects of personality on brain ageing. Small proportions of the direct effects were mediated by individual health behaviours. Results provide initial indications that life-time stable personality traits may influence brain health in later life through health promoting behaviours.

Keywords: Five factor model; personality; brain volume; white matter hyperintensities; fractional anisotropy; health behaviours.

Introduction

In recent years, the field of personality neuroscience has emerged as a formalisation of efforts to understand the biological basis of personality traits (DeYoung, 2010). Research has largely focussed on understanding the biological underpinnings of the traits featured in the major psychometric models of non-clinical personality, particularly the Five Factor Model (FFM: Costa & McCrae, 1992).As a result, many studies have reported associations between personality traits and brain imaging variables and provided functional explanations for such associations (e.g. DeYoung et al., 2010). In the present paper, we argue that the plausibility of such functional explanations is dependent on the particular measures of the brain utilised, and propose an alternative hypothesis for the association between gross measures of the whole brain and personality via health behaviours.

Personality and Neuroimaging Measures of the Brain. Brain imaging methods can be broadly split into two types, functional and structural. Functional imaging methods focus on regions and patterns of activation elicited by a given task, whereas structural magnetic resonance imaging (MRI) methods provide volumetric estimates of the whole brain, brain regions or tissue types (e.g grey and white matter) and other metrics such as regional thickness of cortical tissue. In addition, diffusion tensor imaging (DTI) can be used to measure the integrity of the white matter tracts connecting brain regions. We focus here on structural methods; though we note an expanding literature on functional imaging studies and personality (see DeYoung, 2010).

A number of recent studies have shown a large number of associations for all of the FFM domains with regional tissue volumes (DeYoung et al., 2010; Kapogiannis, Sutin, Davatzikos, Costa & Renick, 2012). However, it has been extraversion and neuroticism which have been shown to most regularly associate with imaging measures. For example, Bjornebekk, et al. (2013) investigated associations between the FFM, brain volume, cortical morphometry and white matter tract integrity in a sample of 265 individuals (mean age 49.8years, sd=17.4years). Neuroticism showed the strongest associations with all metrics, specifically reduced cortical thickness in the right caudal and rostral middle frontal regions, frontal pole, anterior cingulate and across the right superior temporal lobe; and with white matter tract integrity primarily in the long association fibres connecting frontal, occipital, parietal and temporal lobes (see also McIntosh et al., 2012; Xu & Potenza, 2011). Bjornebekk et al. (2013) also noted associations between extraversion and reduced cortical thickness in the left pars traingularis and inferior frontal gyrus, and conscientiousness with reduced cortical thickness in two areas in the left hemisphere (caudal parts of the superior temporal and supramarginal regions).

Two recent studies have considered personality associations with regional tissue volumes (Jackson, Balota & Head, 2011) and cortical thickness (Wright, Feczko, Dickerson & Williams, 2007) in ageing samples. Jackson et al. (2011) found neuroticism was significantly associated with grey matter volume in the ventro- and dorsolateral prefrontal and the orbitofrontal cortices. Wright et al. (2007) found significant associations for neuroticism with lower cortical thickness in the right superior and inferior frontal cortices, as well as associations between extraversion and increased cortical thickness in the right superior frontal and middle frontal cortices.

Personality-Brain Integrity Associations: An Alternative Hypothesis. An important distinction exists between global brain measures and regional or specific estimates of volumes or integrity in specific connective tracts, with respect to the specificity of information they yield. Though the majority of studies have considered personality associations with specific regional or localised integrity measures (see above), global measures of brain integrity, such as brain tissue loss (atrophy), brain-wide white matter tract integrity (e.g. Penke et al., 2012), and white matter hyperintensities (WMH), may also be associated with personality traits. For example, Bjornebekk, et al. (2013), found total brain volume was associated with neuroticism ($p<0.05$).

Here we maintain that the associations of global brain integrity variables with personality traits may still be of theoretical interest, but do not lend themselves to functional interpretations informing on the *neurological basis of traits*. Such functional explanations require the identification of specific causal pathways (DeYoung, 2010); with such information not discernible from global measures of the brain. Instead, we suggest that such global indices may be better viewed as markers of *brain health and integrity*. Therefore, any associations of personality traits with such measures may be equally or, we believe, even more parsimoniously and meaningfully explained through associations with health-related behaviours. That is, instead of interpreting any brain integrity parameter-personality trait association as the quality of brain connectivity somehow manifesting itself in broad behavioural, emotional and cognitive patterns captured in personality traits, we might think of these associations as personality traits' contributions to a range of (un)healthy behaviours, which in turn contribute to global brain integrity. Such mechanisms have been previously postulated to explain personality-brain associations (e.g. Jackson, et al., 2011).

Personality, Health and Health Behaviours. There is growing interest in the associations of personality traits—in particular, conscientiousness—with health and health-related behaviours (Goodwin & Friedman, 2006). Across multiple studies, conscientiousness has been the most consistent predictor of both health outcomes (e.g. longevity, Kern & Friedman, 2008; Hagger-Johnson et al., 2012) and behaviours. In a large scale meta-analysis of 194 studies, Bogg and Roberts (2004) found that conscientiousness was associated with lower alcohol (r=-0.28), drug and tobacco use (r=-0.21), less risky driving behaviours (r=-0.27), increased physical activity (r=0.21) and healthier eating (r=-0.18). Interestingly, all of these associations were significantly weaker (p<0.01) in over 30s when compared against under 30s. The meta-analysis of Rhodes and Smith (2006) found conscientiousness (r=0.20), as well as extraversion (r=0.23) and neuroticism (r=-0.11), to be significant correlates of physical activity.

Personality has also been associated with healthy diet. Mõttus, McNeill, Jia, Craig, Starr & Deary (2011) found higher conscientiousness (r=0.08) and agreeableness (r=0.11) to be associated with a *health aware* diet (higher fruit and lower meat consumption). In a similar study in a large Estonian sample, Mõttus et al., (2012) found using both self and informant ratings, that those lower in neuroticism (r=-0.12), and higher in extraversion (r=0.16), openness (r=0.17) and conscientiousness (r=0.11) had a healthier diet. Relatedly, conscientiousness is associated with higher body weight (Mõttus, McNeill et al., 2012; Sutin, Ferrucci, Zonderman & Terraciano, 2011).

Health Behaviours and Brain Integrity. As for the second link in the mediation chain from personality via health-related behaviours to brain integrity, multiple studies have demonstrated the impact of poor health-related behaviours and the integrity of brain tissue. Physical activity has been suggested to be a protective factor for white matter lesions (e.g. Podewilsw et al., 2007) and against structural declines in brain integrity in ageing (Benedict et al., 2012). Similar findings have been reported based on the same sample used in the current analysis with more physically active lifestyle, predicting less atrophy (β=-0.11,p<0.001), fewer white matter lesions (β=-0.09,p<0.05) and improved white matter tract integrity (β=0.10, p<0.05) (Gow et al., 2012). Other major health-related behaviours to be found to link to measures of brain integrity include smoking (Hudkins, O'Neill, Tobias, Bartzokis & London, 2012) and high alcohol consumption (Enzinger et al., 2005; Mukamal, Longstreth, Mittleman, Crum & Siscovick, 2001). Higher body-mass index (BMI), an outcome of health-related behaviours, has also been regularly associated with reduced overall brain integrity and lower tissue volumes (Gunstad, Paul, Cohen, Tate, Spitznagel & Grieve, 2008; Taki et al., 2008; Verstynen et al., 2012).

Taken together, there appears to be a strong case for proposing associations between FFM personality traits, particularly conscientiousness, and brain integrity that are mediated by common health-related behaviours. To the authors' knowledge, however, no studies have considered these associations in an ageing sample. Older age is especially meaningful for such enquiries as individual differences in brain integrity are then likely to be larger compared to younger ages and the effects of personality-related health behaviours may have accumulated over the life-course. Therefore, in the current study, we first test the associations between personality and whole brain integrity (global brain tissue loss, WMH and white matter integrity) in a large, age-homogenous cohort sample of older adults aged around 73 years. Next, we consider whether personality-brain integrity relationships are mediated by health-related behaviours.

Methodology

Participants

The Lothian Birth Cohort 1936 (LBC1936) is a longitudinal cohort study of healthy ageing. Participants were surviving members of the Scottish Mental Survey 1947 (SMS1947), who were all born in 1936 and who were living in Edinburgh and the surrounding area (the Lothians) when the study began. Full details of the recruitment procedures and tested protocols have been previously published (Deary et al. 2012; Wardlaw et al. 2011).

At Wave 1 of testing, 1091 participants with a mean age of 69.5 years (SD=0.8) completed an interview from which information on participant's social and medical history were gained. At entry into the study, all participants were free from major ageing related disorders including Alzheimer's and other dementias. Participants underwent a battery of cognitive ability tests, a physical examination, completed personality assessments and a number of further questionnaire measures assessing physical activity and dietary habits. At Wave 2, 866 participants returned and completed a near-identical battery of tests and questionnaires. Of these 866 participants, 700 underwent brain MRI (mean age years=72.7, SD=0.7).

The total samples for the analyses presented in the current paper range from 529 to 565, as a) not all participants had usable images from the MRI in order to assess brain integrity, and b) the mediation analyses in the current study (see Statistical Analysis) required complete case data. In order to maximize the total sample for each brain integrity outcome, a listwise deletion method was applied in three blocks—separately for all three brain integrity measures along with their predictors, mediators and covariates. Table 1 includes the total sample for each variable in the current study, whilst analysis-specific sample sizes are provided alongside the results for each analysis. All participants had Mini-Mental State test score of at least 22 at the time of the brain scans. Three people had a score below 24. Scores at this level and higher are commonly used as being indicative of being free from age related cognitive disorders. In order to assess the influence of these individuals on the results reported below, we ran the primary analyses removing these individuals. No substantive differences in parameters were noted. As such, we report on the full sample below.

Ethical Approval

Ethical permission for the LBC1936 study protocol was obtained from the Multi-Centre Research Ethics Committee for Scotland and the Lothian Research Ethics Committee. All research was carried out in compliance with the Helsinki Declaration.

Personality Measurement

The International Personality Item Pool (IPIP: Goldberg, 1992) 50 item measures the broad factors of the Five Factor Model (FFM), namely, Neuroticism (positively coded as Emotional Stability), Extraversion, Intellect, Agreeableness and Conscientiousness. Participants respond to a series of statements on a 5 point Likert-type scale of *Strongly Agree, Agree, Neither Agree nor Disagree, Disagree* and *Strongly Disagree.* Data were taken from Wave 1 testing of the LBC1936 (mean age 70 years). In the current study, we used simple mean scores of the 10 items within each broad factor as input variables to all subsequent analyses. Sum scores were standardized for use in mediation analyses. Cronbach's alphas were as follows: 0.87 (Neuroticism), 0.84 (Extraversion), 0.75 (Intellect), 0.80 (Agreeableness), and 0.79 (Conscientiousness). The correlations among the five factors are given in Table 1; the average of the absolute values of these correlations was 0.22 which is not substantially different from what typically reported in other studies (e.g. Van der Linden, te Nijenhuis & Bakker, 2010).

Health-Related Behaviours

We included measures of four common health-related behaviours which have been shown within the published literature to be associated with personality: smoking, alcohol consumption, diet, and physical activity (e.g. Bogg & Roberts, 2004; Mõttus et al. 2011; Mõttus et al., 2012; Rhodes & Smith, 2006). We also included BMI as a potential mediator as it represents one of the most direct outcomes of poor health behaviours. Data were again taken from Wave 1 of testing of the LBC1936.

Smoking history was measured in pack years, calculated as the average number of cigarettes per day multiplied by years as a smoker and divided by 20 (the typical number of cigarettes per pack). This variable has been used in previous studies on the LBC1936 sample (e.g. Corley, Gow, Starr & Deary, 2012).

Health-aware diet was measured using the component score derived in Mõttus et al., (2011) based on responses to the Food Frequency Questionnaire (FFQ; Jia, Craig, Aucott, Milne & McNeill, 2008). The FFQ contains a list of 168 foods and drinks, grouped under major food groups. Participants are presented with the foods and asked how frequently they typically consumed these items in predefined quantities based on a 9-point Likert-type scale ranging from *rarely or never* to *seven or more times per day.* As has been noted above, the health aware diet score is defined by increased consumption of fruit, and decreased consumption of meat products, eggs and spirits (Mõttus et al., 2011).

Physical activity was measured using a single item administered as part of a larger health questionnaire. Participants respond on the six-point scale ranging from basic movements for household chores, to heavy exercise or competitive sport. Again, this rating of physical activity has been used in previous studies on LBC1936 data (e.g. Gow et al., 2012).Participants reported average weekly alcohol intake as the type and quantity of alcohol consumed, which was then converted into alcohol unit (10 ml) equivalents, and also underwent a physical examination, at which height and weight were taken. This information was then used to calculate BMI.

Lastly, in order to assess the possibility that health behaviours may collectively and cumulatively mediate the association between personality and the three brain integrity measures, we computed a composite Health-Related Behaviours variable from physical activity, smoking, health-aware diet, and BMI (alcohol consumption was not included due to its very small correlations with other health behaviours). Full details of the calculation of the composite variable can be found in Supplementary Material E1. Briefly, we used minimum-residuals based factor analyses specifying only one factor. The loadings of the four health behaviours on the latent factor were r = |0.29| to |0.42| and the factor explained 13% of the variance in these four indicators. Regression based factor scores were used in subsequent analyses.

Image Acquisition

Participants underwent whole brain structural and high angular resolution 2mm isotropic voxel diffusion MRI (7 T2- and 64 diffusion-weighted (b = 1000 s/mm2) axial single-shot spin-echo echo-planar imaging volumes) using a 1.5T GE Sigma Horizon HDxt clinical scanner (General Electric, Milwaukee, WI, USA) operating in research mode using a shelf-shielding gradient set with maximum gradient of 33 mT/m, and an 8 channel phased-array head coil. The full imaging protocol for the LBC1936 has been published previously (Wardlaw, et al. 2011). Briefly, the protocol included a high resolution T1-weighted (T1W) volume scan, and whole brain T2- (T2W), T2*- (T2*W) and FLAIR-weighted sequences.

Structural MRI volumetric analysis: Measured Brain Tissue Loss

Intracranial volume (ICV) was semi-automatically extracted on T2*W images using the Object Extraction Tool in Analyze 9.0 (Mayo Clinic, Analyze 9.0. AnalyzeDirect, Inc. Mayo Clinic) followed by manual editing to remove erroneous structures as described in (Valdés Hernández et al, 2012). In order to estimate total brain tissue volume, cerebrospinal fluid (CSF), venous sinuses and meninges were subtracted from ICV. The CSF and these non-brain tissue structures were extracted using the combination of T2*W and FLAIR sequences and the MCMxxxVI method as described in (Valdés Hernández et al., 2010). Using the estimates of ICV and total brain tissue, we computed brain tissue loss as (1-(Brain Tissue/ICV))*100. This resulted in a single variable representing the percentage of brain tissue loss.

Quantitative WMH Assessment

Quantitative estimates of WMH were estimated using the same MCMxxxVI method (Valdés Hernández et al., 2010) fusing T2*W and FLAIR images. False positives and old infarcts were visually identified and removed manually. To control for overall size of the head, we use WMH as a percentage of ICV in subsequent analyses.

Tract Based Spatial Statistics: Average White Matter Fractional Anisotropy

All diffusion MRI data were preprocessed using "TractoR" (http://code.google.com/p/tractor/), which uses the FDT toolbox in FSL to extract the brain, remove image artefacts resulting from patient motion and eddy current, and to calculate fractional anisotropy (FA) maps for each participant. We conducted Tract Based Spatial Statistics (TBSS) in order to gain a measure of mean FA for each participant across the whole brain. We followed standard FSL (http://fsl.fmrib.ox.ac.uk/fsl/tbss) procedures for TBSS.

All FA maps were registered using nonlinear registration, to a 1x1x1mm standard space. As in an older sample, it was deemed inappropriate to use a standard skeleton derived from younger individuals, a study specific template was created from average of all FA images. This average was skeletonised and thresholded at the standard threshold of 0.20. Individual skeletons were created by projecting the centres of each subject's white matter (as defined by the maximum FA) onto the mean skeleton. Average FA across all voxels within the white matter skeleton was used as the variable of interest in the current study. This mean white matter FA was taken as a marker of overall white matter integrity and health.

Statistical Analysis

Pearson's correlations were computed, where appropriate, between each of the five personality dimensions, health variables and brain integrity variables. Next, multivariate regression was performed to assess the degree to which the five personality dimensions uniquely predicted later life brain integrity.

Causal Mediation Analysis (CMA; Imai, Keele, & Tingley, 2010) was used to estimate the degree to which the personality-brain integrity associations are accounted for by measured health-related behaviours and BMI. Specifically, we included only those personality traits which had been significant predictors of brain integrity measures in the multiple regression models, having therefore unique associations with brain integrity. We considered as potential mediators only those health variables which had significant associations with both the retained personality dimensions and the brain integrity measures.

The CMA is based on the counterfactual causal inference framework and attempts (e.g., via a bootstrapping strategy) to estimate the direct, mediated and total effects of a "treatment" variable (i.e., the independent variable such as, in the present case, a personality trait) via a mediator (here, for example, physical activity) to the outcome (e.g., WMH), given the list of "pretreatment" confounders (e.g., covariates such as age and sex). An important feature of the CMA is that it can accommodate various types of variables and their combinations as it is independent of any specific statistical model.

All mediation analyses were conducted in a dedicated software package called 'mediation' (Tingley, Yamamot, Keele, & Imai, 2011) that is based on R (R Development Core Team, 2012). All outcome and mediator variables were treated as continuous and modelled using standard linear regression except for the measure of smoking (pack-years), alcohol-units and WMH (see below for details). Personality traits were standardized before analyses, meaning that the "0" was modelled as the "non-treatment" level and "1" as the "treatment" level (e.g, the unit for treatment-effect was one standard deviation). A non-parametric bootstrapping strategy was used with 1,000 simulations. Age in days at the MRI scan and sex were used as pre-treatment confounders.

Results

Descriptive statistics are shown in Table 1. Most variables display low levels of skew and kurtosis, with the exception of WMH (Shapiro-Wilk $W = 076$, $p < 0.001$), alcohol units ($W = 0.38$, $p < 0.001$) and pack-years ($W = 0.70$, $p < 0.001$), all of these being non-normally distributed with long right-hand tails. Given the distributions of these variables, for correlation analyses the variables were log-transformed, resulting in more normal-like distributions (skew=-1.77, -0.13, and 0.45, respectively). In the mediation analysis, however, alcohol units and pack-years were modelled via quasi-Poisson regression (which is more robust to overdispersion than traditional Poisson regression) and WMH via tobit (censored) regression. For that, pack-years and alcohol-units were rounded to integers to yield proper count distribution. Since the WMH values cannot be conceptualized as counts and we could assume that very low levels of WMH had been undetectable and were therefore masked as non-existent, we modelled WMH using tobit (censored) regression (via vglm function as implemented in the 'VGAM' R-package, Yee, 2010) with the lower censoring threshold of 0.

(Insert Tables 1 & 2 about here)

Correlations between the five personality domains, health-related behaviours, brain integrity measures and covariates are shown in Table 2. Table 2 reports 55 correlations between brain imaging measures, health variables and covariates with the five personality traits. The Bonferroni adjusted p-value at an alpha level of 0.05, accounting for a small correlation between the health variables (mean r=0.14), was 0.00159. For information, the correlations which survive Bonferroni correction are shown in boldface in Table 2. The focus of the discussion which follows is primarily on the effect size of associations and the proportion of these effects which are mediated by health behaviours. As such, we report on the unadjusted significance levels.

Conscientiousness showed the highest mean absolute association with the brain integrity measures (absolute mean r=0.13), with the associations reaching significance for all three measures of whole brain integrity (p<0.01; although the correlation was not nominally significant for log-transformed WMH; r=-0.08,p=0.06). The direction of the correlations suggest that those with higher conscientiousness scores had less brain tissue loss, fewer WMH, and better white matter integrity. Agreeableness displayed the next highest mean association (absolute r=0.09) and had significant associations with tract FA (r=0.14,p<0.01) and brain tissue loss (r =-0.13,p<0.01), with those scoring higher on agreeableness having better integrity and less tissue loss. Neuroticism was correlated with poorer white matter FA (r=-0.11, p<0.05) but not tissue loss or WMH. Extraversion and Intellect were not significantly associated with any measures of brain integrity.

Importantly for the mediation hypotheses in the current study, both agreeableness (absolute mean *r*=0.13) and conscientiousness (absolute mean *r*=0.09) were also significantly associated with a number of health-related behaviours. Further, where associations failed to reach the nominal 0.05 level of significance, a trend in the appropriate direction was observed (e.g. conscientiousness and log-transformed WMH, r = -0.08, p=0.06; conscientiousness and health aware diet, r =0.08, p=0.052).

Lastly, there were consistent and significant associations between health behaviours and measures of brain integrity, particularly tissue loss and globally reduced FA. These associations were strongest for brain tissue loss (absolute mean *r*=0.18), followed by FA (absolute mean *r*=0.14), and log-transformed WMH (absolute mean *r*=0.05). A number of associations failed to reach significance at $p<0.05$ for WMH. However, as the general pattern of associations were in the expected directions, the associations with both FA and brain tissue loss were mostly significant, and given the non-normal distribution of WMH, the bivariate correlations appeared to provide tentative support for each aspect of the proposed mediation associations.

In order to investigate the multivariate associations between personality and brain integrity whilst controlling for major covariates (sex and age, see correlations in Table 2), three multiple regressions were conducted. Brain tissue loss, WMH and FA were dependent variables, with the five broad personality traits, sex and age as predictors (Table 3). For WMH, tobit regression was used.

(Insert Table 3 about here)

In each model, conscientiousness was the only personality trait to predict whole brain integrity significantly. Age, even in this age-homogeneous sample, was a significant predictor of all brain integrity measures: older participants had poorer global FA, more tissue loss and more WMH. Sex was also a significant predictor of brain tissue loss. The direction of the association indicated men had greater tissue loss. Based on the results of the multiple regression and correlational analyses, we built a series of CMA models in which the effect of conscientiousness on brain tissue loss, FA and WMH was tested for mediation by physical activity, pack-years, alcohol units, health aware diet, BMI, and the composite health-related behaviours variable.

Full results for the mediation analyses are presented in Supplementary Material E2. Here the main effects of interest are summarized. The direct effects from conscientiousness to FA (β=0.19,p<0.01), brain tissue loss (β=-0.10, p<0.05), and WMH (tobit regression estimate=-0.08,p<0.05) were all significant. Mediated effects through all of the individual health behaviours were generally small (proportions of mediated variance ranged between 0 and 0.14, Table 4). Physical activity showed the most consistent and largest mediation effects. Although the confidence intervals did not include zero for the mediating effects of physical activity on all three brain integrity variables (proportions of mediated effect ranging from 0.06 to 0.14), the spread of the confidence intervals was large and therefore the mediating effects failed to reach nominal statistical significance according to the CMA procedure (p=0.07 to 0.14). The composite Health-related behaviour variable resulted in one nominally-significant mediation effect: it mediated 18% of the effect of conscientiousness on brain tissue loss. The confidence intervals of its mediating effect on FA also did not cover zero, although the p-value was p=0.14. Taken together, therefore, there was some tentative evidence for physical activity and the latent health behaviours factor mediating the effect from low conscientiousness to relatively worse brain white matter integrity.

(Insert Table 4 about here)

Discussion

This study tested the hypothesis that individual differences in personality traits, especially conscientiousness, might be associated with three aspects of brain integrity in older age: average white matter integrity (FA), brain tissue loss, and WMH. We hypothesized that personality trait-brain integrity associations might be interpreted as personality traits contributing to brain integrity rather than the other way around. The reason for such interpretation was two-fold. First, traits are known to be linked with numerous aspects of physical health, which is typically interpreted as personality traits, in a fairly general manner, contributing to health via common health behaviours. Second, while it is possible that changes to the brain at a macro level may be a contributing factor for changes in outwardly manifested behaviours (personality traits), we suggest that this direction of association is more likely in the presence of ***major*** brain injury or disease. Thus, in the current, relatively healthy ageing sample, the more parsimonious explanation may be one of personality traits driving lifestyle factors which in turn impact upon brain health. It is important to note that we are not suggesting that functional explanations of personality-brain associations are invalid, only that the neurological foundations of personality traits are typically sought or assessed using different measures of functionality in more specific regions of the brain rather than global measures of integrity.

The findings of the current study generally supported our hypotheses. The personality trait conscientiousness, which was indeed expected to be the most relevant trait in the context of health behaviours (Bogg & Roberts, 2004), had small but significant associations with all three brain integrity variables. Although the strength of the associations (in the correlations metric between 0.10 and 0.20) is not large, the associations were consistent across the three integrity aspects. Furthermore, these effect sizes were in a very typical range for personality-health associations (see introduction). Arguably, the observed effect sizes might accurately correspond to a realistic expectation for this kind of associations. In other words, it may be sensible to expect a broad behavioural trait to explain no more than one or two percent of variance in a physical health outcome (here whole brain integrity), which may have a myriad of life-course determinants with complex interactions among them (Mõttus et al., 2012).

We also hypothesized that the associations between personality traits and brain integrity might be mediated by common health behaviours such as smoking, alcohol consumption, physical activity, and dietary habits. All these health behaviours have been associated with personality traits in previous research and they also tend to be linked with brain integrity, so there was a clear rationale for expecting this mediation. We also considered BMI as a possible mediator, given that it is presumably closely linked to health behaviours. However, although these health behaviours and BMI had a tendency to be linked to conscientiousness in the present data, the associations were weak and sometimes marginally fell short of statistical significance. As a result, we found only modest support for the mediation hypothesis, with some tentative evidence for the roles of physical activity and a latent health behaviours factor in mediating the effect from low conscientiousness to relatively worse brain white matter integrity.

The generally larger effects for the latent health behaviour variable would be generally indicative with a cumulative effect of health behaviours on brain integrity. Health outcomes may be influenced by a large array of health-related behaviours of which the current study only included a subsample of what were considered to be important and well-researched behaviours. This may in part explain why only relatively small percentages of the direct effects of conscientiousness on whole brain integrity were mediated in the current study, in that additional contributing variables were not measured. In addition, a number of the health behaviours included in the current study may have complex associations with measured outcomes. For example, Hudkins et al. (2012) suggest that the effects of smoking on health outcomes are non-linear. As a result, the mediation effects that we did observe may be substantial enough to merit further consideration.

In the current study, we report a number of effects which have been previously published based on the same cohort of people. Mõttus et al. (2011) reported a significant association between conscientiousness, BMI and dietary habits. McIntosh and colleagues (2012) reported an association between neuroticism and the integrity of specific white matter tracts. Although there are key differences between McIntosh et al. and the current study, specifically the use of individual white matter tract integrity rather than global integrity, our finding of a significant univariate association between neuroticism and white matter FA is, to some extent, a confirmation of their findings. Further, Gow et al. (2012) reported significant associations between increased physical activity and lower WML load and atrophy. Taken collectively, the previously reported results from the same cohort and the results from the extant literature (discussed above) provided the empirical impetus for the testing of a specific explanatory hypothesis as to the associations between personality and whole brain integrity, tested herein.

It has been suggested that both personality and neurological changes may precede onset of conditions such as Alzheimer's and dementia. Results however have been equivocal as to a common neurological basis to personality traits and conditions such as Alzheimer's (e.g. Wilson, Arnold, Schneider, Li & Bennett, 2007). Conscientiousness has been suggested to have a potential protective effect against Alzheimer's and dementia (e.g. Duberstein et al., 2011; Terracciano et al., 2013). At time of testing, the current sample was free from clinical diagnosis of either Alzheimer's or dementia, and the current findings do not, in and of themselves, support any conclusions with respect to such conditions. However, the Lothian Birth Cohort 1936 is a longitudinal study of ageing, and as such, future studies may explore further the general observation of conscientiousness as the main associate of improved brain integrity.

There are several strengths to the present study. First, the sample size was larger than in most studies utilizing brain-imaging measures. This is important because the associations of single behavioural variables such as personality traits or health behaviours with biological variables are expected to be fairly weak and therefore small studies are likely to be underpowered for reliably detecting these associations. Therefore, at a simple level, the current study provides somewhat unique and robust estimates of the correlations between measures of overall brain integrity in later life, the major domains of personality and health-related behaviours.

Second, the present study addressed brain integrity in a comprehensive and multifaceted way, including gross measures of overall tissue loss, integrity of the communicative pathways of the brain (white matter tracts), and measures of general tissue damage (WMH). Collectively, all have been shown to be important aspects of healthy brain ageing. In a study on the same sample as in the current study, Penke et al. (2012) demonstrated that brain-wide white matter integrity was significantly associated with cognitive ability, and processing speed in old age. Similar effects between the integrity of the brain and cognitive functioning have been shown in a large number of studies (e.g. Mailard, et al., 2012), with some arguing that volume of brain tissue may be protective against cognitive decline and risk of dementia and Alzheimer's (e.g., the passive reserve hypothesis by Stern, 2012). To the extent that the current findings are generalizable, personality, and in particular conscientiousness, may be an influential factor in maintaining the integrity of the brain through health-promoting behaviours and, as a result, may also help protect against declines in ageing associated brain integrity.

Third, the fact the current sample was both drawn from an older population, and is age-homogenous, is advantageous. Specifically, an older sample is most likely to yield greater variability in brain health or integrity. Further, given that the life-course effects of personality traits via heath-related behaviours on objective markers of brain health are likely to be cumulative across the life-course, ageing samples are most appropriate for consideration of these effects. However, chronological age is strongly associated with general decline in brain integrity, and therefore is a major confound in studies of health and ageing (Hofer, Flaherty & Hoffman, 2006). The narrow age range in the current study provides a natural control for this effect. It is notable that even within the current sample, age was still significantly associated with measures of brain integrity and so was still required to be retained as a covariate.

A limitation of the study is the lack of life-course information on personality traits and relevant health behaviours. The current study utilises data from two time points in later life spaced three years apart. However, given that the processes discuss are life-long, we consider the data to be, to all intents and purposes, cross-sectional. Cross-sectional associations are more open to incorrect causal interpretations than the findings based on longitudinal multi-timepoint assessments. As a result, extended longitudinal data would be required to confirm the interpretations of our findings suggested here. In addition, more detailed information on personality traits would have been highly desirable (e.g., the facets of the broad personality domains), as this may have provided more informative associations.

Further, a fuller test of the health behaviour mediation hypothesis would require more thoroughly measured health behaviours. In the current study, a number of the health behaviour measures utilised were suboptimal, for example, the use of a single self-report item for physical activity. An extended list of health-related behaviour measures may have allowed a more stringent test of the cumulative mediation effects of health behaviours on the associations between personality and brain integrity. However, we note that obtaining comprehensive measurements of various health behaviours in studies that link personality traits to objective brain measurements might be an ideal that is difficult to reach, as the amount of information that can be obtained from individual participants has obvious constraints.

In sum, the current paper extends research on the associations between personality, specifically trait conscientiousness, health-related behaviours and health outcomes. To the authors' knowledge, the current study is the first to explore whether the association between major personality domains and brain integrity can be explained by health-related behaviours. Such a mechanism has been previously discussed in the literature (e.g. Jackson, Balota & Head, 2011), but not explicitly tested. In addition to the direct association between Conscientiousness and the brain integrity variables, our findings provide some limited supporting evidence for this mediation effect. However, we acknowledge that the proportions of mediated effects by health behaviours are small. It has been noted that, despite a growing body of research, there remains little consistency in the associations between personality traits and neuroimaging measures (Kapogiannis et al., 2012). Thus, we also emphasize the robust estimates of the associations between the personality traits of the FFM, brain tissue loss, white matter tract integrity and white matter lesion volume.

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Table 1

Correlations, Means, standard deviations and total sample

	1	**2**	**3**	**4**	**5**
1. Neuroticism	-				
2. Extraversion	-0.22	-			
3. Intellect	-0.07	0.35	-		
4. Agreeableness	-0.14	0.28	0.28	-	
5. Conscientiousness	-0.25	0.13	0.20	0.30	-
	N	**Mean**	**SD**	**Skew**	**Kurtosis**
Personality Wave 1 – Age 70					
Neuroticism	628	1.48	0.75	0.29	-0.05
Extraversion	628	2.10	0.70	-0.10	0.02
Intellect	628	2.38	0.58	-0.15	0.44
Agreeableness	628	3.11	0.55	-0.58	0.17
Conscientiousness	628	2.79	0.61	-0.36	-0.17
Health-Related Behaviours Wave 1 - Age 70					
Packs Years	624	14.46	22.52	1.83	3.00
Physical activity	624	3.06	1.10	0.54	0.62
Health-aware diet	579	0.00	1.00	0.43	3.13
Alcohol Consumption	628	10.61	13.81	2.87	12.90
BMI	627	27.60	4.22	0.79	1.91
Health-Related Behaviours	573	0.00	1.00	0.59	1.41
Brain Integrity Wave 2 – Age 73					
Tract FA	581	0.40	0.02	-0.53	0.71
Brain Tissue Loss	617	22.39	3.84	0.16	0.08
WML	617	0.81	0.88	2.61	11.42
Covariates – Wave 2 – Age 73					
Age	628	72.66	0.72	-0.01	-0.95

Note: FA = Fractional Anisotropy; WML = White Matter Lesion Volume; BMI = Body-Mass Index.

Table 2

Bivariate Correlations Between the Study-Variables

	N	E	I	A	C	Tract FA	Brain Tissue Loss	WML (raw)	WML (log)
Tract FA	-0.11^{*}	0.07	0.06	0.14^{**}	$\mathbf{0.20^{***}}$	-	-	-	-
Brain Tissue Loss	-0.04	0.04	-0.03	$\mathbf{-0.18^{***}}$	-0.13^{**}	-0.31^{***}	-	-	-
WML (raw)	0.03	0.01	-0.04	0.03	-0.11^{**}	-0.43^{***}	0.07	-	-
WML (log)	0.03	0.00	-0.05	-0.02	-0.08	-0.34^{***}	0.07	0.70^{***}	-
Pack-years (raw)	0.13^{**}	-0.06	-0.05	-0.13^{**}	-0.10^{*}	-0.22^{***}	0.18^{***}	0.10^{*}	0.05
Pack-years (log)	0.09^{*}	0.02	-0.03	-0.12^{**}	-0.07	-0.17^{***}	0.17^{***}	-0.08	0.04
Physical Activity	-0.12^{**}	0.04	0.14^{**}	-0.03	0.13^{**}	0.16^{***}	-0.09^{*}	-0.10^{*}	-0.02
Health-Aware Diet	-0.02	-0.05	0.12^{**}	$\mathbf{0.20^{***}}$	0.08	0.10^{*}	-0.24^{***}	0.05	0.01
Alcohol Consumption (log)	-0.09^{*}	$\mathbf{0.12^{***}}$	0.02	$\mathbf{-0.19^{***}}$	-0.02	0.01	0.22^{***}	-0.01	0.08
Alcohol Consumption (raw)	-0.05	0.11^{**}	-0.02	$\mathbf{-0.20^{***}}$	-0.07	-0.06	0.23^{***}	-0.02	0.05
BMI	0.03	0.04	-0.08	0.00	-0.10^{*}	-0.18^{***}	0.05	0.06	0.08
Health-Related Behaviours	0.10^{*}	0.01	-0.13^{**}	$\mathbf{-0.15^{***}}$	-0.14^{**}	-0.25^{***}	0.24^{***}	0.06	0.03
Age	0.05	0.01	-0.03	0.00	-0.09^{*}	-0.12^{***}	0.17^{***}	0.14^{***}	0.16^{***}
Sex	0.01^{*}	0.00	0.00	$\mathbf{0.15^{***}}$	0.001	0.00	0.11^{***}	0.005	0.001

Note: N = Neuroticism; E = Extraversion; I = Intellect; A = Agreeableness; C = Conscientiousness; FA = Fractional Anisotropy; WML = White Matter Lesion Volume; BMI = Body-Mass Index; $^{*}p<0.05$; $^{**}p<0.01$; $^{***}p<0.001$. Associations between personality traits and all other variables which are shown in boldface are those which survive Bonferroni correction.

Table 3

Multiple Regression Analysis Predicting Tract FA (n=529), Atrophy (n=565) and WML (n=565).

	Estimate	Std. Error	t-value	*p*
		Tract FA		
Neuroticism	-0.049	0.043	-1.151	0.250
Extraversion	0.018	0.045	0.403	0.687
Intellect	-0.004	0.045	0.095	0.925
Agreeableness	0.072	0.048	1.477	0.140
Conscientiousness	0.155	0.044	3.524	<0.001
Sex	0.065	0.089	0.734	0.463
Age	-0.148	0.057	-2.598	0.010
		Brain Tissue Loss		
Neuroticism	-0.041	0.042	-1.032	0.302
Extraversion	0.070	0.041	1.704	0.089
Intellect	-0.008	0.041	-0.185	0.854
Agreeableness	-0.055	0.045	-1.218	0.224
Conscientiousness	-0.111	0.040	-2.753	0.006
Sex	-0.623	0.082	-7.581	<0.001
Age	0.248	0.052	4.783	<0.001
		WML (Tobit Regression)		
	Estimate	Std. Error	z-value	*p*
Neuroticism	0.002	0.039	0.050	0.960
Extraversion	0.017	0.041	0.409	0.682
Intellect	-0.032	0.040	-0.800	0.424
Agreeableness	0.058	0.044	1.309	0.191
Conscientiousness	-0.102	0.040	-2.568	0.010
Sex	0.064	0.081	0.794	0.427
Age	0.166	0.051	3.254	<0.001

Note: FA = Fractional Anisotropy; WML = White Matter Lesion Volume

Table 4

Proportion of Mediation Effects of Health Behaviours on the Direct Effects of Conscientiousness on Measures of Brain Integrity.

	FA			Brain Tissue Loss			WML		
	Est.	2.5% CI	97.5% CI	Est.	2.5% CI	97.5% CI	Est.	2.5% CI	97.5% CI
Physical Activity	**0.061**	**0.005**	**0.168**	**0.137**	**0.028**	**0.622**	**0.119**	**0.014**	**0.475**
Pack-years	0.064	-0.025	0.181	0.063	-0.024	0.222	0.055	-0.025	0.271
Health-Aware Diet	0.019	-0.010	0.095	0.094	-0.034	0.413	-0.032	-0.150	0.037
Alcohol Intake	0.009	-0.016	0.049	0.114	-0.013	0.458	0.002	-0.076	0.084
BMI	0.056	-0.004	0.182	-0.007	-0.135	0.078	0.033	-0.055	0.183
Health Behaviours Composite	**0.107**	**0.022**	**0.259**	**0.177**	**0.049**	**0.798**	0.072	-0.022	0.365

Note: FA = Fractional Anisotropy; WML = White Matter Lesion Volume; BMI = Body-Mass Index. Bold values are significant at $p<0.05$. Here our primary focus was on the proportion of the mediated effect, not the level of significance derived from the non-parametric bootstrap. Full results from the mediation analysis (mediated and direct effect, proportion of mediated effects and p-values are reported in Supplementary Material E2).