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Neuronal correlates of the five factor model (FFM) of human personality: Multimodal imaging in a large healthy sample

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Advances in neuroimaging techniques have recently provided glimpse into the neurobiology of complex traits of human personality. Whereas some intriguing findings have connected aspects of personality to variations in brain morphology, the relations are complex and our current understanding is incomplete. Therefore, we aimed to provide a comprehensive investigation of brain–personality relations using a multimodal neuroimaging approach in a large sample comprising 265 healthy individuals. The NEO Personality Inventory was used to provide measures of core aspects of human personality, and imaging phenotypes included measures of total and regional brain volumes, regional cortical thickness and arealization, and diffusion tensor imaging indices of white matter (WM) microstructure. Neuroticism was the trait most clearly linked to brain structure. Higher neuroticism including facets reflecting anxiety, depression and vulnerability to stress was associated with smaller total brain volume, widespread decrease in WM microstructure, and smaller frontotemporal surface area. Higher scores on extraversion were associated with thinner inferior frontal gyrus, and conscientiousness was negatively associated with arealization of the temporoparietal junction. No reliable associations between brain structure and agreeableness and openness, respectively, were found. The results provide novel evidence of the associations between brain structure and variations in human personality, and corroborate previous findings of a consistent neuroanatomical basis of negative emotionality.

Introduction

The search for the neuronal foundation of human personality has guided research within the cognitive neurosciences for decades. Recent advances in structural neuroimaging have produced intriguing findings connecting aspects of personality to variations in regional or total brain volumes (Cherbuin et al., 2008; DeYoung et al., 2010; Gardini et al., 2009; Iidaka et al., 2006; Jackson et al., 2011; Knutson et al., 2001; Lebreton et al., 2009; Matsuo et al., 2009; Omura et al., 2005; Pujol et al., 2002; Yamasue et al., 2008), the volume and thickness of the cerebral cortex (Blankstein et al., 2009; Fecteau et al., 2007; Knoch et al., 2006; Rauch et al., 2005; Schilling et al., 2012), and white matter connectivity and microstructure (Bjørnebekk et al., 2011; Cohen et al., 2009; Jung et al., 2010a, 2010b; Kim and Whalen, 2009; Taddei et al., 2012; Takeuchi et al., 2010; Volpe et al., 2008; Westlye et al., 2011; Xu and Potenza, 2012). However, such relations are complex and our current understanding of the brain networks modulating factors of human personality is incomplete.

The Five Factor Model (FFM) is one of the most widely accepted taxonomies of personality, including factors characterizing various aspects of social behavior and emotional responsiveness: openness, conscientiousness, extraversion, agreeableness, and neuroticism. Each factor captures a wide array of behaviors. Openness reflects a preference for novelty and variety, which may be manifested as intellectual curiosity and interests. People high on conscientiousness are typically described as organized, disciplined, and oriented towards achievement. Extraverted people show a high degree of sociability, talkativeness, warmth, and assertiveness. People high on agreeableness tend to be helpful, sympathetic, and cooperative towards others. Lastly, neuroticism captures dimensions of emotional negativity, stability, anxiety, vulnerability, and impulse control.

Diffusion tensor imaging (DTI) allows in vivo examination of properties of water diffusion in biological tissues (Beaulieu, 2002; Le Bihan, 2003). DTI takes advantage of the anisotropic diffusivity pattern in the brain to provide details of the local tissue microstructure and the fiber tract arrangement in the brain WM (Pierpaoli and Basser, 1996). Morphometric measures of the cortical GM include cortical thickness and surface area, which together constitute the

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common index of GM volume. Cortical thickness and surface area carry distinct biological information (Chenn and Walsh, 2002; Panizzon et al., 2009; Rakic, 1995; Raznahan et al., 2010, 2011; Winkler et al., 2010), are genetically unrelated (Panizzon et al., 2009; Winkler et al., 2010), show distinct developmental trajectories (Hogstrom et al., in press; Østby et al., 2009; Raznahan et al., 2011), and are differentially altered by environmental manipulation (Park et al., 2009) and allelic variations within established risk genes for developmental disorders (Joyner et al., 2009), emphasizing the importance of dissociating the two sources of GM volume when aiming to link personality to brain structure. Associations between GM structure and personality have only been investigated using GM volume or cortical thickness, and knowledge of how surface arealization relates to personality is lacking. Thus, investigating both metrics provide unique contributions to the understanding of the biological underpinnings of personality. Moreover, combining multiple structural imaging parameters would provide a more comprehensive picture of brain–personality relations.

Attempts have been made to map the neuroanatomical correlates of one or several of the FFM traits (Blankstein et al., 2009; DeYoung et al., 2010; Jackson et al., 2011; Knutson et al., 2001; Omura et al., 2005; Rauch et al., 2005; Wright et al., 2006, 2007; Xu and Potenza, 2012). Whereas predominantly negative correlations between neuroticism and thickness of specific prefrontal regions (Wright et al., 2007), ratio of whole brain-volume to intracranial volume (Knutson et al., 2001) and regional volumes (DeYoung et al., 2010; Jackson et al., 2011; Omura et al., 2005), have been reported, a complex pattern of positive and negative correlations has been reported between extraversion and cortical thickness in ventral, medial and lateral prefrontal regions (Blankstein et al., 2009; DeYoung et al., 2010; Rauch et al., 2005; Wright et al., 2006, 2007). One study has reported relationships between FFM and DTI, demonstrating widespread negative relations between neuroticism and WM integrity and positive relations between WM integrity and openness and agreeableness, respectively, in cortico-subcortical pathways (Xu and Potenza, 2012).

In the current study a multimodal imaging approach is implemented to investigate associations between the FFM and brain structure in a large sample comprising 265 healthy adults. Parameters of investigation include measures of total and regional brain volumes, regional cortical thickness and arealization, and DTI indices of WM microstructure. Full-brain surface-based analysis and tract-based spatial statistics (TBSS) provide unbiased regional analysis of cortical morphometry and DTI, respectively. Moreover, a detailed account of the associations between brain structure and personality are provided by follow-up analysis on the facet level. Based on previous studies, we in general hypothesized negative correlations between brain structure and neuroticism, including decreasing thickness, surface arealization, brain volume and WM microstructural integrity with increasing neuroticism. Furthermore, there is some support linking extraversion to dopaminergic functioning (Andersson et al., 2007a, 2007b; Depue and Collins, 1999; Netter, 2006; Reuter and Hennig, 2005; Smillie et al., 2010; Wacker and Gatt, 2010; Wacker et al., 2006), and previous MRI studies of cortical thickness find prefrontal correlates to extraversion (Blankstein et al., 2009; DeYoung et al., 2010; Rauch et al., 2005; Wright et al., 2006, 2007). Thus, for extraversion strongest relationships were expected in fronto-striatal regions. Inconclusive findings related to the remaining three traits suggest that strong hypothesis regarding brain correlates of agreeableness, openness and conscientiousness would be premature and speculative.

Material and methods

Sample

The sample was drawn from a large longitudinal research project *Cognition and Plasticity through the Life-Span* (Fjell et al., 2008; Westlye et al., 2009). Volunteers were recruited by newspaper advertisements, and underwent a health-screening interview before enrollment to ensure that the study sample represented a healthy population. Participants were required to be right-handed native Norwegian speakers older than 20 years, have vision and hearing that were normal or corrected to normal, and be free of neurological injuries or diseases known to affect nervous system functioning. Individuals were excluded if they (1) reported any previous or current psychiatric diagnosis or (2) had received any psychological or pharmacological treatment for psychiatric disease within the last 2 years. The health-screening interview was administered by phone at enrollment, and repeated at the time of the first assessment. In addition, all eligible participants were assessed for symptoms of depression using the Beck Depression Inventory (BDI) (Beck et al., 1987), and exclusion criterion was set to scores higher than 16 (aggregate consistent with a mild depression). None of the participants were excluded based on this criterion. Self-reported weekly alcohol consumption in standard units was recorded and used to control for mediating effects of alcohol use on the relationships between FFM and brain structure.

MRI scans were examined by a neuroradiologist and deemed free of significant anomalies. One participant was excluded based on the radiological evaluation. Complete datasets including DTI and NEO-PI-R were available from 265 participants (150 females) ranging 20–85 years of age (mean: 49.8 years, SD = 17.4 years). All participants scored > 26 on Mini Mental State Examination (MMSE) (Folstein et al., 1975) and < 17 on BDI (Beck et al., 1987). Mean full-scale IQ (FIQ) as measured by Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999) was 114.4 (range: 92–145 SD = 8.9). The study was approved by the Regional Ethical Committee of Southern Norway (REK-Sør) and conducted in accordance with the Helsinki Declaration. Written informed consent was obtained from all participants prior to the examinations.

NEO Personality Inventory

A validated Norwegian translation (Nordvik et al., 1998) of the self-report version of the 240-items revised NEO Personality Inventory (NEO-PI-R) was administered, yielding dimension scores for Neuroticism, Extraversion, Openness, Agreeableness and Conscientiousness (Costa and McCrae, 1992).

Items are rated on a five-point Likert scale ranging from 1 (totally disagree) to 5 (totally agree). Each trait consists of six sub-components or facet scales (Costa and McCrae, 1992). The *neuroticism* facets include: *anxiety* measuring the level of free floating anxiety, *angry hostility* describing the tendency to experience anger, frustration and bitterness, *depression* indicative of the tendency to experience feelings of guilt, sadness and loneliness, *self-consciousness* a measure of the individuals' level of shyness or social anxiety, *impulsiveness* describing the tendency to act on cravings and urges rather than reining them in and delaying gratification, and *vulnerability* describing the individuals' general susceptibility to stress. The *extraversion* facets include: *warmth* describing the tendency to show interest in and friendliness toward others, *gregariousness*: describing the tendency to seek and enjoy the company of others, *assertiveness*: featuring dominance, forcefulness and expression, *activity*: measuring the individual's pace of living, *excitement seeking*: measuring the individuals need for environmental stimulation, and *positive emotion*: describing the tendency to experience positive emotions. The *openness* dimension includes the following facets: *fantasy*: describing the individual's receptivity to the inner world of imagination, *esthetics*: capturing appreciation of art and beauty, poetry and music, *feelings*: openness to inner feelings and emotions, *actions*: describes the tendency to be open to new experiences on a practical level, *ideas*: featuring intellectual curiosity, *values*: measuring a person's readiness to re-examine social, political, and religious values. The *agreeableness* facets include *trust*: describing the tendency to believe that others are honest and well intentioned, *straightforwardness*: describing the tendency to be frank, sincere, and genuine, *altruism*: describes the tendency to be helpful, considerate and concerned for the welfare of others, *compliance*: describing the tendency to submit to others in interpersonal conflicts and seek to inhibit aggression, *modesty*: describes the tendency to play down own achievements and be humble, *tender mindedness*: measuring sympathy and concern for others. The *conscientiousness* trait captures an individual's degree of organization, persistence, control and motivation in goal directed behavior and comprises the facets *competence*: measuring one's belief in own self efficacy, *order*: a measure of personal organization, *dutifulness*: describing the tendency to be governed by conscience, being strictly adhere to ethical principles and scrupulously fulfilling moral obligations, *achievement striving*: capturing the need for personal achievement and ability to work hard to achieve goals, *self-discipline*: measuring the capacity to begin tasks and follow through to completion despite boredom or distractions, and finally *deliberation*: which is the tendency to think things through before acting or speaking.

MRI acquisition

MRI data was collected using a 12-channel head coil on a 1.5 T Siemens Avanto scanner (Siemens Medical Solutions, Erlangen, Germany). The pulse sequence used for morphometric analysis was a 3D T1-weighted Magnetization Prepared Rapid Gradient Echo (MP-RAGE) with the following parameters: repetition time/echo time/time to inversion/flip angle = 2400 ms/3.61 ms/1000 ms/8°, matrix 192 × 192, field of view = 240. Each volume consisted of 160 sagittal slices with voxel size 1.25 × 1.25 × 1.20 mm. Scan time was 7 min 42 s. Two repeated acquisitions were averaged during processing to increase signal-to-noise-ratio (SNR).

For diffusion weighted imaging a single-shot twice-refocused spin-echo planar imaging pulse sequence with 30 diffusion sensitized gradient directions and the following parameters was used: repetition time/echo time = 8200 ms/82 ms, b-value = 700 s/mm^2, voxel size = 2.0 × 2.0 × 2.0 mm, and 64 axial slices. The sequence was repeated in two runs with 10 b = 0 and 30 diffusion weighted images collected per run. Acquisition time was 11 min 21 s.

Imaging analysis

Cortical thickness, surface area and subcortical volumes were estimated using FreeSurfer (http://surfer.nmr.mgh.harvard.edu). Cortical thickness and surface area were estimated vertex-wise across the brain surface using an automated approach described in details elsewhere (Dale and Sereno, 1993; Dale et al., 1999; Fischl and Dale, 2000; Fischl et al., 1999a, 1999b, 2001; Segonne et al., 2004, 2005). Briefly, a representation of the gray/white matter boundary was reconstructed, using intensity and continuity information from the entire 3D MR volume in segmentation and deformation procedures. Thickness measurements were obtained by reconstructing representation of GM/WM boundary and the pial surface (Dale and Sereno, 1993; Dale et al., 1999) and then calculating the distance between the surfaces at each vertex across the cortical mantle. Surface area maps of the GM-WM intersection were computed for each subject by calculating the area of every triangle in a cortical surface tessellation. The triangular area at each point in native space is compared to the area of the analogous points in registered space to give an estimate of regional surface area expansion or contraction along the surface (Fischl et al., 1999a). Surfaces were created using spatial intensity gradients across tissue classes, and were therefore not simply reliant on absolute signal intensity. The surface reconstructions and segmentations are run automatically but require supervision of the accuracy of the spatial registration and tissue segmentations. All reconstructed data sets were visually inspected. The individual surface area and thickness maps were resampled, mapped to a common surface, smoothed using a Gaussian kernel of 15 mm and submitted to statistical analyses.

The volume segmentation procedure automatically assigns a neuroanatomical label to each voxel in an MRI volume based on probabilistic information automatically estimated from a manually labeled training set (Fischl et al., 2002, 2004). Subcortical regions of interest (ROIs) include the amygdala, accumbens area, caudate and putamen and were chosen on the basis of their implication in avoidance as well as exploration and approach behavior (Alcaro and Panksepp, 2011; Schultz et al., 2000; Vytal and Hamann, 2010), which are all core fundaments of human personality. In addition, estimated intra cranial volume (ICV) (Buckner et al., 2004) and total brain volume were computed and included in the analyses.

DTI processing and analyses were performed using FSL (http://www.fmrib.ox.ac.uk/fsl/) (Smith et al., 2004; Woolrich et al., 2009). First, each volume was affine registered to the T2-weighted b = 0 volume using FLIRT (Jenkinson and Smith, 2001) correcting for motion between scans and residual eddy-current distortions present in the diffusion weighted images. In order to preserve the orientational information after motion correction, we reoriented each volume's B matrix by applying the corresponding transformation matrix from the motion-correction procedure. After removal of nonbrain tissue (Smith, 2002), FA, eigenvector and eigenvalue maps were computed. MD was defined as the mean of the three eigenvalues ($(\lambda_1+\lambda_2+\lambda_3)/3$) and radial diffusivity (RD) as the mean of the second and third eigenvalue ($(\lambda_2+\lambda_3)/2$). AD was defined as the largest eigenvalues (λ_1). Next, all individuals' FA volumes were skeletonized and transformed into a common space as employed in TBSS (Smith et al., 2006, 2007). Briefly, all volumes were nonlinearly warped to the FMRIB58_FA template by the use of local deformation procedures performed by FNIRT (Andersson et al., 2007a, 2007b), a nonlinear registration toolkit using a b-spline representation of the registration warp field (Rueckert et al., 1999). Next, a mean FA volume of all subjects was generated and thinned to create a mean FA skeleton representing the centers of all common tracts. We thresholded and binarized the mean skeleton at FA > 0.2 to reduce partial voluming at the boundaries between tissue classes, yielding a mask of 127650 WM voxels.

Individual FA values were warped onto this mean skeleton by searching perpendicular from the skeleton for maximum FA, which further minimizes partial voluming (Smith et al., 2006). The resulting tract invariant skeletons for each participant were fed into voxelwise permutation-based cross-subject statistics. Similar warping and analyses were employed on AD, MD and RD data, yielding AD, MD and RD skeletons.

Statistical analysis

FFM questionnaire data

The internal consistency of the FFM scales was investigated by calculating Cronbach's alpha for each of the five factors. Pearson correlations were used to investigate associations between personality traits, FIQ, BDI, alcohol consumption and age. Gender differences in personality were inspected using ANOVAs.

FFM and total and regional brain volumetry

Global and regional subcortical volumetry–personality relations were evaluated using general linear models (GLMs) with ROI volume as dependent variable, sex as a fixed factor, and age, total brain volume and the five traits (all included into the same model) as continuous covariates. First correlations between personality and global brain volume were investigated and only when this approach yielded significant (surviving a Bonferroni adjustment to $\alpha = .01$, divided by five ROIs) further regional analysis were conducted. Uncorrected volumetry–personality correlations are presented in Supplementary Table 1.

FFM and regional cortical thickness and arealization

We used GLMs controlling for the effect of age, sex and the five traits to investigate the relations between FFM and cortical thickness and area continuously across the brain surface, respectively. To reduce the possibility of Type I errors, thickness and surface area analyses were corrected for multiple comparisons using cluster size inference by means of Z Monte Carlo simulations as implemented by FreeSurfer (Hagler et al., 2006; Hayasaka and Nichols, 2003).

FFM and DTI indices of WM microstructure

Voxelwise DTI analyses were carried out using non-parametric permutation-based inference (Nichols and Holmes, 2002) as implemented in the randomize tool in FSL. Linear effects of neuroticism, extraversion, openness, agreeableness and conscientiousness on FA, AD, MD and RD were tested voxelwise with GLMs allowing age and sex to co-vary. Threshold-free cluster enhancement (TFCE) (Smith and Nichols, 2009) was used for statistical inference. 5000 permutations were performed for each contrast. Statistical p value maps were thresholded at $p<0.05$, corrected for multiple comparisons across space. To estimate effect sizes of the various covariates, we performed linear regressions with individual DTI values averaged across significant voxels from the voxelwise analyses as dependent variable, and the five temperament traits, age and sex as covariates. In addition, since we recently published associations between a measure of trait anxiety from Cloninger's Temperament and Character Inventory (Cloninger et al., 1993), which share variance with neuroticism, and DTI parameters in a largely overlapping sample (Westlye et al., 2011), we repeated the linear regressions including harm avoidance as an additional covariate.

Covarying for possible modulating factors and investigating influence of sex

Since brain–personality associations may be confounded by various health and life-style factors, we included subclinical depression, alcohol consumption and full scale IQ in follow-up analysis of the significant effects. Age and sex were included as covariates in all analyses.

Possible influence of sex on the associations between brain structure and personality are investigated by post-hoc GLM analyses on selected findings (total brain volume and FA values from the voxelwise analyses as dependent variables), including the sex∗personality interaction term as a covariate.

Further, to provide a more detailed account of the associations between brain structure and personality post-hoc GLM analyses testing for linear effects of the facets on total brain volume, surface area, and on FA were performed while including age and sex as covariates.

Split half analyses

In order to assess the robustness of the results, split-half confirmatory analyses were run, on a random selection of approximately 50% (filtered by SPSS) of the sample cases followed by analyses of the remaining half, and then we tested whether the effect sizes differed between the two subsamples. The split half analyses were performed on the tests for associations between personality and total brain volume, regional arealization, and a representative DTI index, respectively.

Results

Scale scores, reliability, age, sex, IQ and Beck Depression Inventory

Table 1 summarizes the sample characteristics of openness, conscientiousness, extraversion, agreeableness and neuroticism scores from NEO-PI-R, age, FIQ, alcohol consumption and BDI per decade and in total. Females (162.6 ± 19.9) scored significantly higher than males (156 ± 23.4) on openness ($F=4.6$, $p<.05$), conscientiousness (175.4 ± 15.8, versus 169.5 ± 20.2, $F=5.8$, $p<.05$), extraversion (164.6 ± 18.4, versus 158.9 ± 20.8, $F=5.5$, $p<.05$), and agreeableness (180.0 ± 15.8, versus 167.7 ± 17.7, $F=35.0$, $p<.001$), but not on neuroticism (120.0 ± 24.1, versus 116.7 ± 19.1, $F=1.5$, $p=.23$). Alcohol consumption was larger in males (5.3 ± 4.9, standard units/week versus 4.2 ± 3.5 for women, $F=4.6$, $p<.05$), whereas there were no differences between genders regarding age, years of education, subclinical depression or FIQ.

Table 2 presents the Cronbach's alpha coefficients for each NEO-PI factor and the inter-correlations between FFM scores, alcohol consumption, general intellectual abilities and subclinical depression ratings. The Cronbach's alpha coefficient ranged from .87 to .91 suggesting good internal factor consistencies. Openness was positively correlated with extraversion ($r=.43$, $p<.01$), FSIQ and years of education ($r=.13$, $p<.05$, and $r=16$, $p<.05$), and negatively with age ($r=-.26$, $p<.01$). Conscientiousness correlated positively with extraversion ($r=.20$, $p<.01$), agreeableness ($r=.16$, $p<.05$), and negatively with neuroticism ($r=-.42$, $p<.01$) and BDI ($r=-.21$, $p<.01$). Extraversion was negatively correlated with neuroticism ($r=-.18$, $p<.05$), BDI ($r=-.27$, $p=.01$), and age ($r=-.32$, $p<.01$). Extraversion correlated positively with the traits of openness and conscientiousness, as reported above. Agreeableness showed weak negative correlation with neuroticism ($r=-.17$, $p<.05$) and years of education ($r=-.13$, $p<.05$). As reported above, neuroticism correlated negatively with the traits of conscientiousness, extraversion and agreeableness, and shows a weak negative correlation with FSIQ ($r=-.12$, $p<.05$). Neuroticism correlated with BDI ($r=.50$, $p<.01$). Moderate positive correlations were found between alcohol consumption and age ($r=.13$, $p<.05$) and FSIQ ($r=.13$, $p<.05$), respectively. Years of education correlated positively with FSIQ ($r=.32$, $p<.01$), and negatively with BDI ($r=-.13$, $p<.05$).

Associations between FFM and brain volumes

Neuroticism was the only personality trait negatively related to total brain volume ($t=-2.63$, corrected $p<.05$). Accordingly, post-hoc facet analyses were only performed for the neuroticism–total brain volume relation. These analyses found that neuroticism also was negatively related to ICV ($t=-2.42$, $p<.05$). For total brain volume, all facets except hostility showed negative associations with brain volume, including anxiety ($t=-2.13$, $p<.05$), depression ($t=-2.61$, $p<.01$), self-consciousness ($t=-2.12$, $p<.05$), impulsiveness ($t=-2.19$, $p<.05$) and vulnerability to stress ($t=-3.22$, $p<.001$). Post-hoc analysis of sex by personality interactions was not significant ($t=1.52$), indicating that the association between total brain volume and neuroticism was not significantly different between the sexes. Volumetry relations for all FFM traits are summarized in Supplementary Table 1 (uncorrected).

A split half rerun of a random selection of approximately 50% of the cases ($n=142$, 78 females and 64 males) confirmed the results from the main findings showing a negative correlation between neuroticism and total brain volume ($t=-2.03$). Rerunning the remaining half ($n=123$, 73 females and 50 males) resulted in a trend in the same direction ($t=-1.63$). Further, a test comparing the neuroticism–total brain volume relations from these two subsamples showed that there the effect sizes did not differ between subsamples ($t=-.52$, $p=.61$).

Associations between FFM and cortical morphometry

Fig. 1 shows the result from the vertex-wise full-cortex analysis testing for associations between cortical thickness and the FFM, and the extraversion facets. Extraversion was associated with thinner cortex in the left pars triangularis (cluster size: 1496 mm^2, MNI coordinates of the maximum vertex [−47.0, 33.3, 5.0], $z=-2.87$, $p<.05$) in the inferior frontal gyrus, roughly corresponding to Brodmann area 45. None of the other NEO-PI traits was related to cortical thickness. Facet analyses suggested that excitement seeking was the major contributor to the extraversion-thickness associations.

Fig. 2 shows significant vertex wise relations between neuroticism and cortical surface area. Increasing neuroticism was associated with reduced regional arealization of frontal regions including right caudal and rostral middle frontal areas (cluster size: 3500 mm^2, MNI coordinates of the maximum vertex [22.4, 34.3, 32.5], $z=-4.44$, $p<.001$) also illustrated by scatterplots (Fig. 3B), the frontal pole, anterior cingulate and parts of the medial orbitofrontal area (cluster size: 2043 mm^2, MNI coordinates of the maximum vertex [8.4, 25.9, 18.2], $z=-3.21$,

Table 1
Sample descriptive for age groups and the total sample.

Age group (years)	*N*	Age mean years ± SD	Females *n* ± %	O mean ± SD	C mean ± SD	E mean ± SD	A mean ± SD	N mean ± SD	Edu Mean ± SD	FIQ mean ± SD	BDI mean ± SD	Alco mean ± SD
20–29	50	23.9 ± 2.6	25 ± 50	169.5 ± 19.4	167.8 ± 23.3	171.0 ± 14.8	169.3 ± 16.2	124.2 ± 21.9	15.1 ± 1.9[a]	112.8 ± 7.0	3.5 ± 3.2	4.3 ± 4.1
30–39	32	34.7 ± 2.8	20 ± 63	161.3 ± 21.3	171.2 ± 18.8	166.7 ± 21.1	171.1 ± 16.9	124.8 ± 22.5	17.2 ± 2.4	115.8 ± 8.3	3.9 ± 3.7	3.4 ± 3.7
40–49	31	44.9 ± 3.1	20 ± 65	161.0 ± 20.6	172.9 ± 22.4	163.9 ± 22.0	174.0 ± 14.8	114.9 ± 24.9	15.5 ± 2.1	115.2 ± 7.3	3.7 ± 4.3	3.6 ± 2.7
50–59	68	54.2 ± 2.7	39 ± 57	159.6 ± 22.4	175.3 ± 18.9	159.9 ± 19.2	175.9 ± 17.1	114.6 ± 18.7	15.3 ± 2.2	113.5 ± 7.3	4.2 ± 3.2	5.3 ± 3.8
60–69	46	64.1 ± 2.8	28 ± 61	160.6 ± 19.5	176.0 ± 16.7	161.3 ± 18.9	177.2 ± 20.6	114.9 ± 24.3	16.4 ± 3.4	113.7 ± 10.8	4.7 ± 3.9	4.7 ± 4.8
70–79	27	72.7 ± 2.4	14 ± 52	147.1 ± 21.0	171.8 ± 19.1	154.1 ± 15.4	182.1 ± 17.0	119.7 ± 19.2	15.3 ± 3.8	117.7 ± 11.0	5.9 ± 4.3	6.1 ± 5.9
80–89	11	81.9 ± 1.7	4 ± 36	145.1 ± 21.4	175.6 ± 21.6	140.3 ± 19.5	175.8 ± 20.6	123.7 ± 24.7	15.0 ± 2.6	121.6 ± 11.7	6.9 ± 4.4	5.2 ± 3.7
Total	265	49.8 ± 17.4	150 ± 57	160.1 ± 21.6	172.9 ± 20.1	162.1 ± 19.6	174.7 ± 17.7	118.6 ± 22.1	15.7 ± 2.7	114.4 ± 8.9	4.4 ± 3.8[b]	4.7 ± 4.2[c]

O: openness to experience; C: Conscientiousness; E: Extraversion; A: Agreeableness; N: Neuroticism; FIQ: full-scale IQ; BDI: Beck Depression Inventory; Alco: alcohol.
[a] Many subjects in the 20–30 years group were still attending college or university at the time of assessment. Completed years of education at the time of assessment are used in the present study.
[b] Beck Depression inventory scores were available for 258 participants.
[c] Weekly alcohol consumption (in standard units) was available for 253 participants.

$p<.05$), and in temporal areas including the left superior temporal lobe together with the supramarginal area of the parietal lobe (cluster size: 3893 mm^2, MNI coordinates of the maximum vertex [62.2, −14.9, 2.8], $z=-4.21$, $p<.001$), and widespread areas of right inferior and superior temporal lobe (cluster size: 3964 mm^2, MNI coordinates of the maximum vertex [−62.7, −44.6, 13.1], $z=-5.20$, $p<.001$). Split-half analyses performed on the surface area findings in the right caudal and rostral middle frontal areas confirmed the results. Surface area explained 6.2% of the variance in neuroticism ($t=-2.96$, $p<.01$) in the first subsample ($n=142$), and 11.9% of the variance in neuroticism ($t=-3.95$, $p<.001$) in the second subsample ($n=123$).

As illustrated in Fig. 2 the surface-based facet analyses indicated strongest contributions for anxiety, depression and vulnerability to stress. These facets showed effects comparable to the main analysis, including the anterior cingulate, dorsolateral prefrontal and lateral temporal cortices. Minor or no associations were found between surface area, and hostility, self-consciousness, and impulsiveness, respectively.

Fig. 4 shows the significant associations between conscientiousness and cortical area. We observed negative associations in caudal parts of superior temporal and supramarginal regions in the left hemisphere (cluster size: 1872 mm^2, MNI coordinates of the maximum vertex [−61.9, −45.5, 12.9], $z=-3.35$, $p<.05$). Facet analysis revealed that achievement striving and self-discipline facets were associated with reduced surface area in caudal parts of the superior temporal and supramarginal areas of the left hemisphere, thus accounting for the observed effect. No significant relations were found between surface area and the other three traits.

Associations between FFM and DTI indices of WM microstructure

Fig. 5 shows the distribution of voxels showing significant effects of neuroticism on FA. Fig. 3C shows a plot of the mean FA averaged across the significant voxels as a function of neuroticism. Widespread negative associations between neuroticism and FA were found which among others include long association fibers connecting frontal, occipital, parietal and temporal lobes, tracts connecting orbitofrontal regions with limbic regions, fiber tracts connecting thalamic nuclei with the frontal lobes, and cross-hemispheric pathways including the corpus callosum.

Relations between neuroticism and MD and RD are illustrated in Fig. 6. Significant positive associations were found, including corpus callosum interconnecting the hemispheres, in tracts interconnecting medial and lateral surfaces of the frontal lobes, tracts interconnecting occipital lobes, as well as in long association fibers interconnecting frontal, occipital, parietal and temporal lobes. 20.7% of all skeleton voxels showed a negative relation between neuroticism and FA, and 10.2% and 21.4% showed a positive relation with MD and RD respectively. In these voxels, FA accounted for 8.1% ($t=-4.74$), MD for 5.6% ($t=3.90$), and RD for 6.1% of the variance in neuroticism ($t=4.09$). Post-hoc analysis investigating possible gender effects on the association between FA and neuroticism were not significant ($t=-.27$). Additional analyses including harm avoidance, from the TCI, which correlated with neuroticism ($r=.64$), as a covariate reduced the amount of explained variance by neuroticism to 2.3% ($t=-2.46$), whereas harm avoidance accounted for 1.7% of the explained variance in these voxels ($t=-2.06$). The relations between neuroticism and FA were driven by the facets anxiety,

Table 2
Internal consistency coefficients, and correlations of NEO factor scores, alcohol consumption, general intellectual abilities and subclinical depression ratings.

	α	O	C	E	A	N	Age	Alcohol	FIQ	Edu	BDI
O	.89	1									
C	.89	−0.04	1								
E	.87	.43**	.20**	1							
A	.87	0.10	.16*	0.11	1						
N	.91	−0.02	−.42**	−.18**	−.17**	1					
Age		−.26**	0.10	−.32**	.20**	−0.11	1				
Alcohol		0.06	−0.06	−0.03	−0.11	−0.03	.13*	1			
FIQ		.13*	0.10	−0.11	0.01	−.12*	0.12	.14*	1		
Edu		.16**	0.12	0.06	−.13*	−0.03	−0.01	0.03	.32**	1	
BDI		−0.11	−.21**	−.27**	−0.06	.50**	.20**	0.07	0.03	−.13*	1

Abbreviations: α: Cronbach's alpha coefficient; O: openness to experience; C: Conscientiousness; E: Extraversion; A: Agreeableness; N: Neuroticism; FIQ: Full-scale IQ; Edu: education; BDI: Beck Depression Inventory.
* $p<.05$.
** $p<.01$.

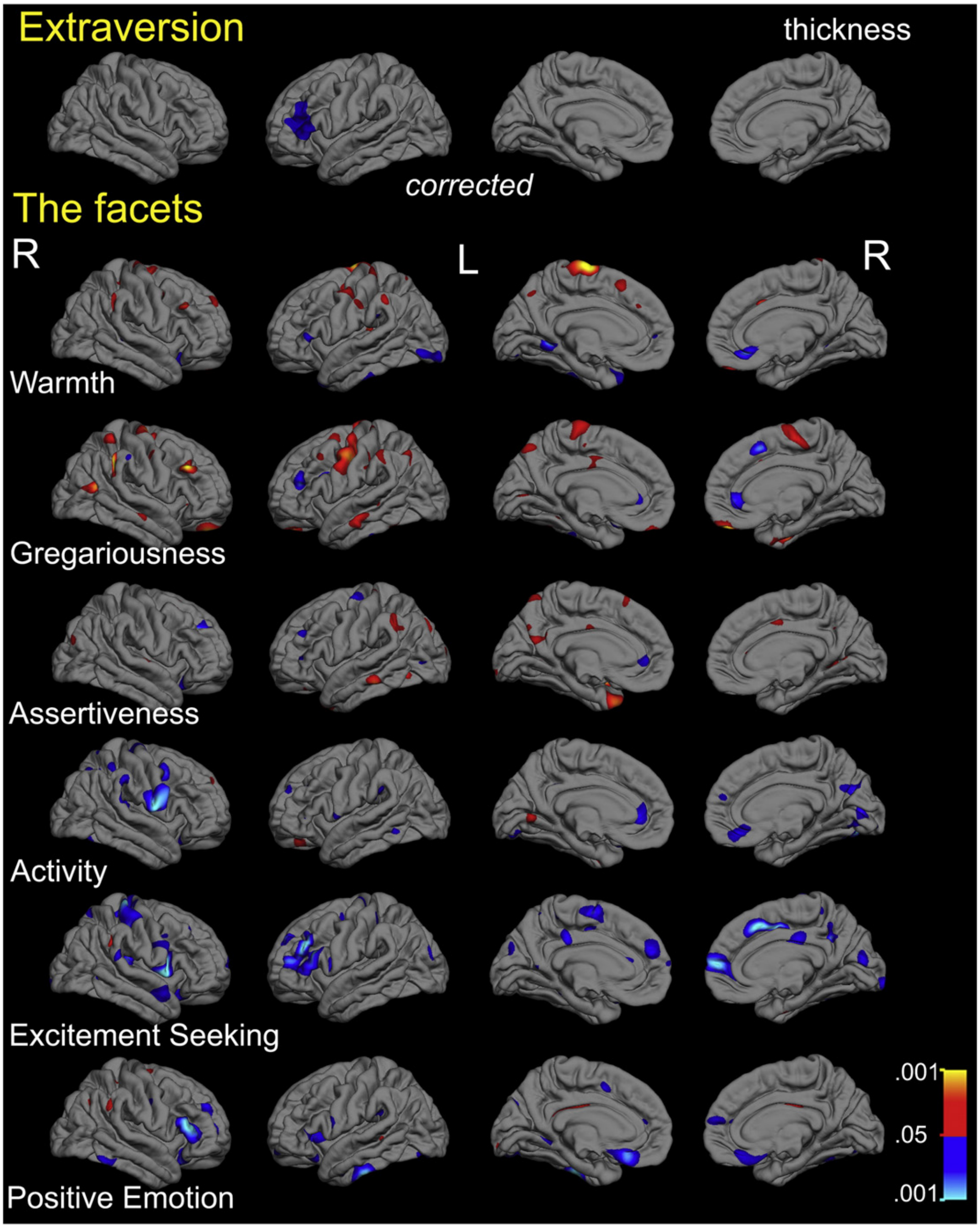


Fig. 1. Extraversion and cortical thickness. Extraversion was negatively correlated to cortical thickness in the left inferior frontal gyrus. The relations between cortical thickness and extraversion were tested vertex wise using general linear models while controlling for age, sex, and the remaining four traits. Thickness analyses were corrected for multiple comparisons using cluster size inference by means of Z Monte Carlo simulations. The displayed maps are thresholded at $p<0.05$. P-values range between 0.05 and 0.001, where positive relations are visualized with red-yellow and negative relations with blue color-scale.

self-consciousness and vulnerability to stressors where negative relations between the facet and FA were found in 35.2%, 25.4% and 33.4% of all skeleton voxels respectively (Fig. 2).

Exploratory split-half analyses confirmed the results from the above analyses. In a first split-half (n = 142, 78 females and 64 males) FA accounted for 10.8% of the explained variance in neuroticism (t = −4.02) which is a slight increase from the analyses of the whole sample. Rerunning the remaining half (n = 123, 73 females and 50 males) also confirmed initial analyses however effect sizes were decreased to 6.5% in this half of the sample (t = −2.83).

No associations between any of the DTI measures and openness, conscientiousness, extraversion or agreeableness were found.

Relationship between neuroticism and brain measures after covarying for possible modulating factors

BDI, alcohol consumption and FIQ were included as additional confounding variables in posthoc analysis in order to investigate possible modulating effects on the associations between brain structure and neuroticism. The results revealed that neither BDI, alcohol nor FIQ

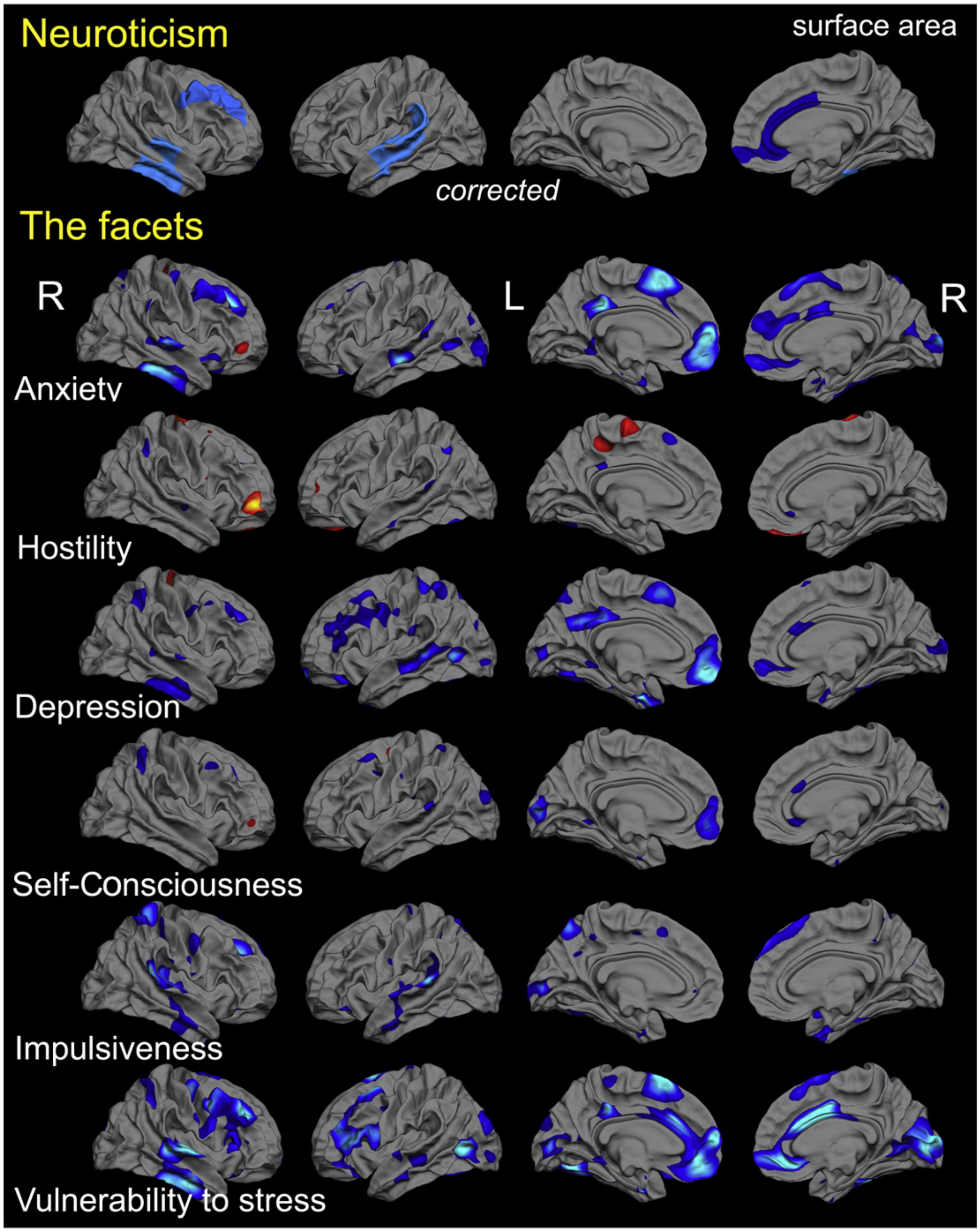


Fig. 2. Neuroticism and cortical surface area. Higher scores on neuroticism were associated with reduced cortical surface area in frontal and temporal cortical regions including anterior cingulate. The relations between surface area and neuroticism were tested vertex wise using general linear models while controlling for age, sex, and the remaining four traits. Analyses were corrected for multiple comparisons using cluster size inference by means of Z Monte Carlo simulations. Facet analysis revealed associations between surface arealization and anxiety, depression and vulnerability to stressors.

showed significant associations with any of the imaging measures. Further, including these variables as covariates in the statistical models had minimal influence on the explained variance of the structural measures by neuroticism. Including the additional covariates slightly increased the amount of variance of total brain volume explained by neuroticism from 2.6% to 2.9%, and for ICV from 2.2% to 2.3%.

Discussion

We have demonstrated associations between the FFM and multimodal imaging measures. Whereas we observed cortical correlates of extraversion and conscientiousness, neuroticism showed the strongest and most reliable links to brain structure, including negative correlations with total brain volume, frontotemporal surface area and WM microstructure. This indicates that personality dimensions reflecting vulnerability to life stressors, negative affect and emotional instability, all of which have been shown informative in predicting person at-risk for developing psychiatric symptoms, are consistently related to brain structural variables even in absence of psychiatric symptomatology.

Structural brain correlates of neuroticism

There is ample evidence that subjects scoring high on neuroticism are at increased risk for various forms of psychopathology (Distel et al., 2009; Goodwin et al., 2003; Lynam et al., 2005), particularly disorders of depression and anxiety (Bienvenu et al., 2007; Cox et al., 2004;

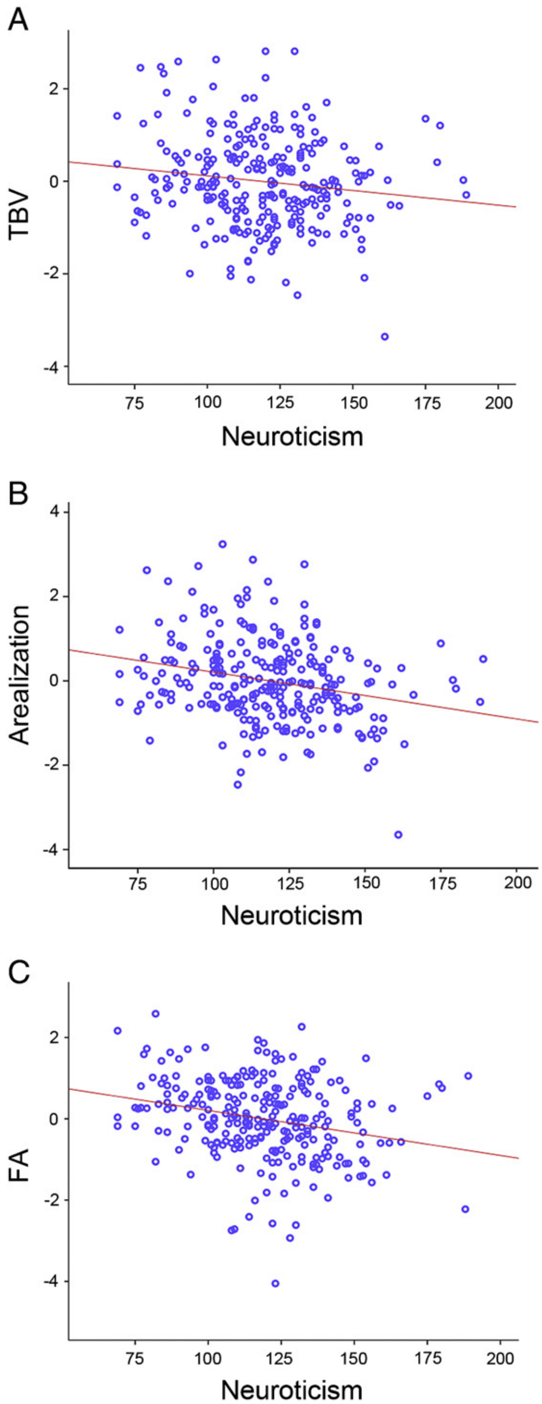


Fig. 3. Neuroticism and brain structure. The plots show individual neuroticism scores plotted as a function of total brain volume (TBV) (A), surface arealization in a selected cluster comprising the right caudal and middle frontal area (cluster size: 3500 mm^2) (B), and FA values in skeleton voxels showing a negative relation between neuroticism and FA (C). Variability associated with age, sex and the remaining four personality traits are removed and values are plotted as z-transformed residuals.

Hettema et al., 2006; Jylha et al., 2009; Weinstock and Whisman, 2006). In the elderly, increased neuroticism is associated with lower cognitive function (Boyle et al., 2010), higher rate of aging-related cognitive decline (Wilson et al., 2005a), mild cognitive impairment (Wilson et al., 2007), dementia (Wilson et al., 2003b, 2011) and even early death (Wilson et al., 2003a, 2005b). In the present study, we have demonstrated that neuroticism is the FFM dimension most consistently related to brain structure in a large healthy sample spanning the adult lifespan. Specifically, higher neuroticism was associated with reduced ICV and total brain volumes, reduced cortical surface area in frontotemporal regions, and decreased WM microstructure in widespread anatomical regions. The observed effects were generally independent of age, sex, subclinical depression and alcohol consumption. Moreover, the follow-up analysis on the facet level suggested that the associations between neuroticism and brain structure were particularly strong for the subcomponents anxiety and vulnerability to stress.

Whereas several factors are likely to contribute to variation in brain size, it is notable that brain volumes are associated with individual differences in a personality trait reflecting among other things stress reactivity in healthy adults. It is widely held that stress could be deleterious for brain morphology. Previous imaging studies have shown that post-traumatic stress disorder (PTSD) is associated with altered brain development (De Bellis et al., 1999) and reductions in GM and WM volumes (Bremner et al., 1995; Carrion et al., 2001; De Bellis et al., 2002; Wignall et al., 2004; Woodward et al., 2009; Yamasue et al., 2003). In animal models chronic and acute stress causes dendritic retraction of hippocampal (McEwen, 1999; McKittrick et al., 2000) and prefrontal cortices (Brown et al., 2005; Izquierdo et al., 2006; Radley et al., 2004, 2006), reduces neurogenesis (Gould et al., 1997, 1998), and alters neurochemistry (Anisman and Zacharko, 1986) and neuron excitability (Jedema and Grace, 2003).

In the present study, we have no reasons to believe that subjects scoring high on neuroticism have been exposed to objectively more stressful events than subjects scoring low on neuroticism. Rather, high scoring subjects perceive situations as more stressful than others, and also respond more inadequately to stressors. Importantly, whether smaller brain volumes is a consequence of increased subjective experiences of stressful events or a preexisting condition constituting a vulnerability factor for perceiving events as stressful, is difficult to determine on the basis of this study. The negative neuroticism and ICV association is likely established relatively early in life, as it is presumed that ICV is a relatively constant measure during the adult lifespan and an indicator of maximum mature brain volume (Courchesne et al., 2000; Pfefferbaum et al., 1994). Previously, it has been reported that increasing neuroticism is associated with a greater degree of brain shrinkage after the brain has reached its maximal volume (Knutson et al., 2001), whereas another study reported age-independent negative association between gray matter volume and neuroticism (Jackson et al., 2011). Longitudinal studies starting in early childhood, including genetics and detailed life history of traumatic or stressful events would shed light on this issue.

Reduced surface area in frontal and temporal regions with increasing neuroticism

Compared to other species the human brain has a disproportionally large cortical surface area relative to whole brain volume, which is thought to explain some of the idiosyncratic aspects of human behavior and intellect (Rakic, 1995). To our knowledge this is the first study to link personality with differences in cortical arealization, indicating reduced frontotemporal surface area in high neuroticism subjects. Furthermore, neuroticism was related to brain volume and surface area, but not cortical thickness. This is consistent with studies showing that brain volume is more closely related to surface area than to cortical thickness (Im et al., 2008; Pakkenberg and Gundersen, 1997).

In addition to the previous studies on neuroticism and total brain volume reviewed above, several studies have demonstrated associations between neuroticism and reduced GM volume in medial temporal and dorsomedial prefrontal (DeYoung et al., 2010), orbitofrontal (Gardini et al., 2009; Jackson et al., 2011; Kapogiannis et al., in press; Mahoney et al., 2011; Wright et al., 2006), ventral and dorsal lateral prefrontal cortex (Jackson et al., 2011; Kapogiannis et al., in press), anterior cingulate (Mahoney et al., 2011), occipital and

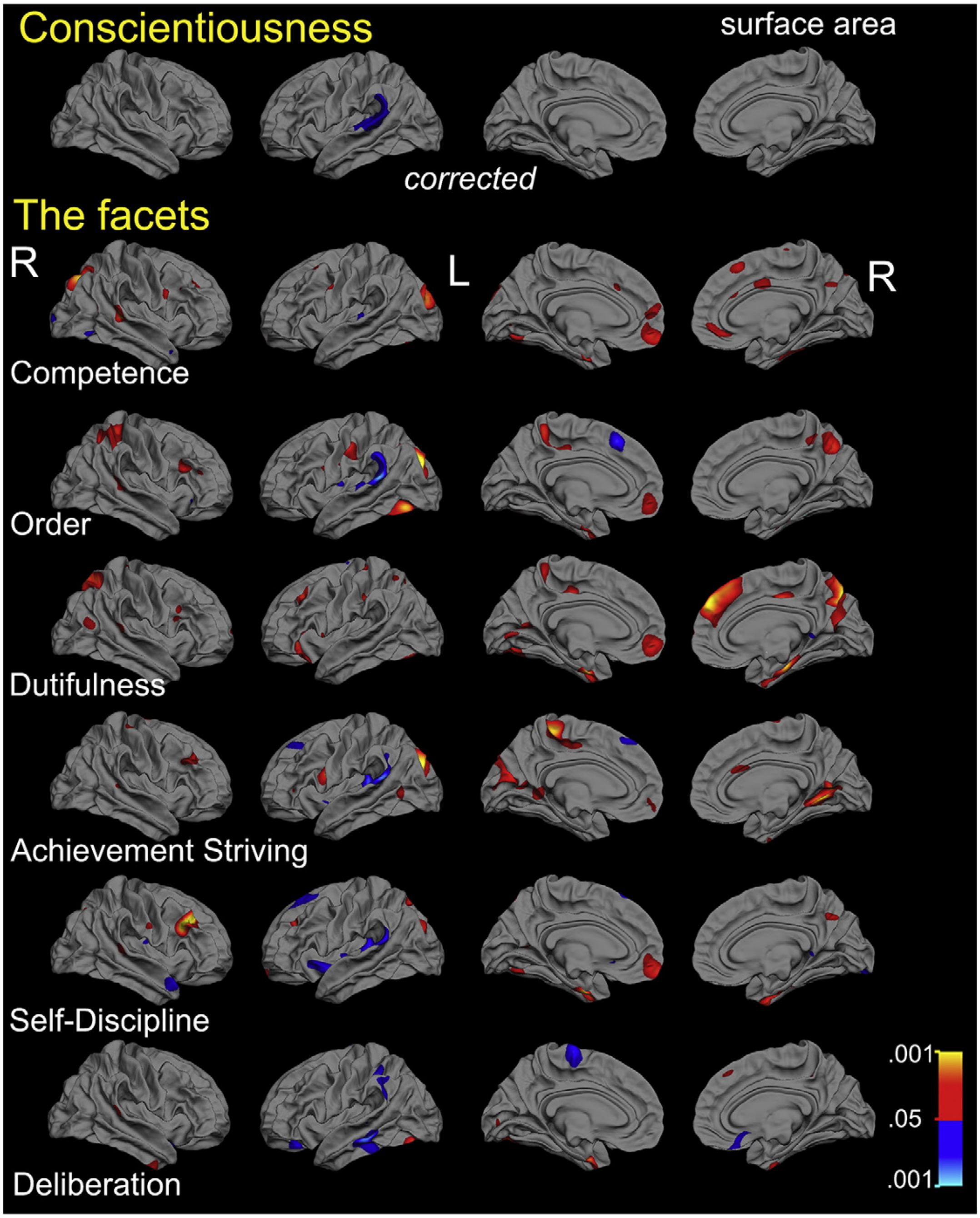
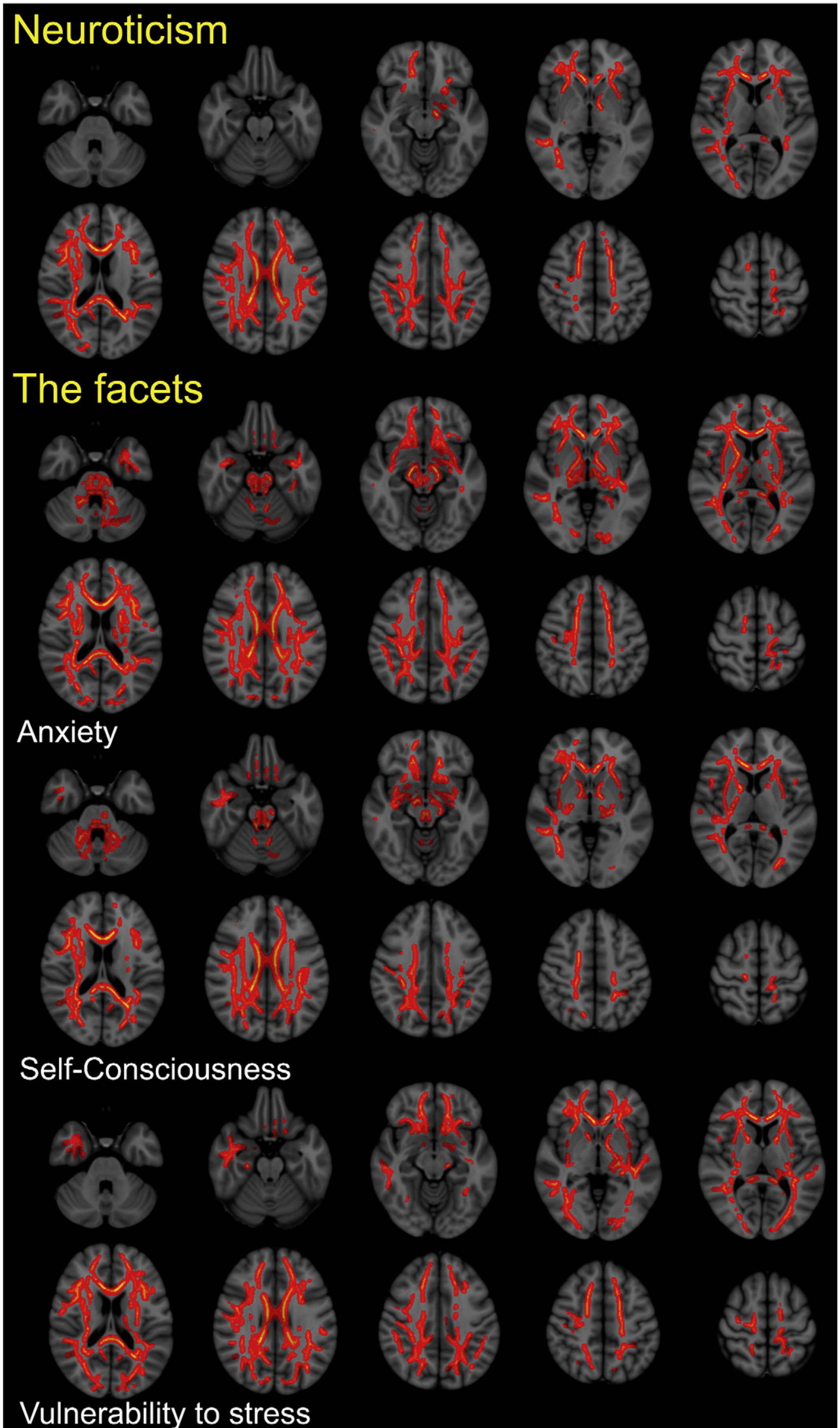


Fig. 4. Conscientiousness and cortical surface area. Relations between surface area and conscientiousness were tested vertex wise using GLM analyses controlling for age, sex, and the remaining four traits. Analysis revealed a negative relation between conscientiousness and caudal parts of the superior temporal and supramarginal areas in the left hemisphere. Surface analyses were corrected for multiple comparisons across space using cluster size inference by means of Z Monte Carlo simulations. Facet analyses showed associations mainly between surface area and the order, achievement striving and self-discipline facets, respectively.

parietal regions (Gardini et al., 2009), and one study found increased volume of the mid cingulate gyrus (DeYoung et al., 2010). Whereas these studies show a mixed picture of associations, possibly due to different methodological approaches and power, a converging finding is reduced volume of prefrontal regions with increasing neuroticism. Our observations of reduced prefrontal surface area are in line with the previous associations between frontal volume and neuroticism, but extend previous research by showing that the volume association is likely explained by cortical surface arealization, not thickness. In our study higher neuroticism was associated with reduced area in parts of the medial orbitofrontal cortex extending to the frontal pole, the anterior cingulate and middle frontal areas. In addition to frontal findings, negative associations were found in the lateral temporal lobe including supramarginal gyrus in the parietal lobe. The facet analysis revealed strongest associations with anxiety, depression and vulnerability to stressors, with the latter being the most influential.

Fig. 5. Neuroticism and white matter microstructure. The spatial distribution of voxels showing linear effects of neuroticism on FA covarying for age, sex and the remaining four personality traits. Yellow-red color illustrates negative relations with neuroticism superimposed on transversal sections (*z*-MNI coordinates spanning from 40 to 140) of a template brain. Facet analyses showed negative associations between FA and anxiety, self-consciousness and vulnerability to stress. Effects were found in anatomically widespread WM tracts throughout the brain.


Neuroticism
The facets
Anxiety
Self-Consciousness
Vulnerability to stress

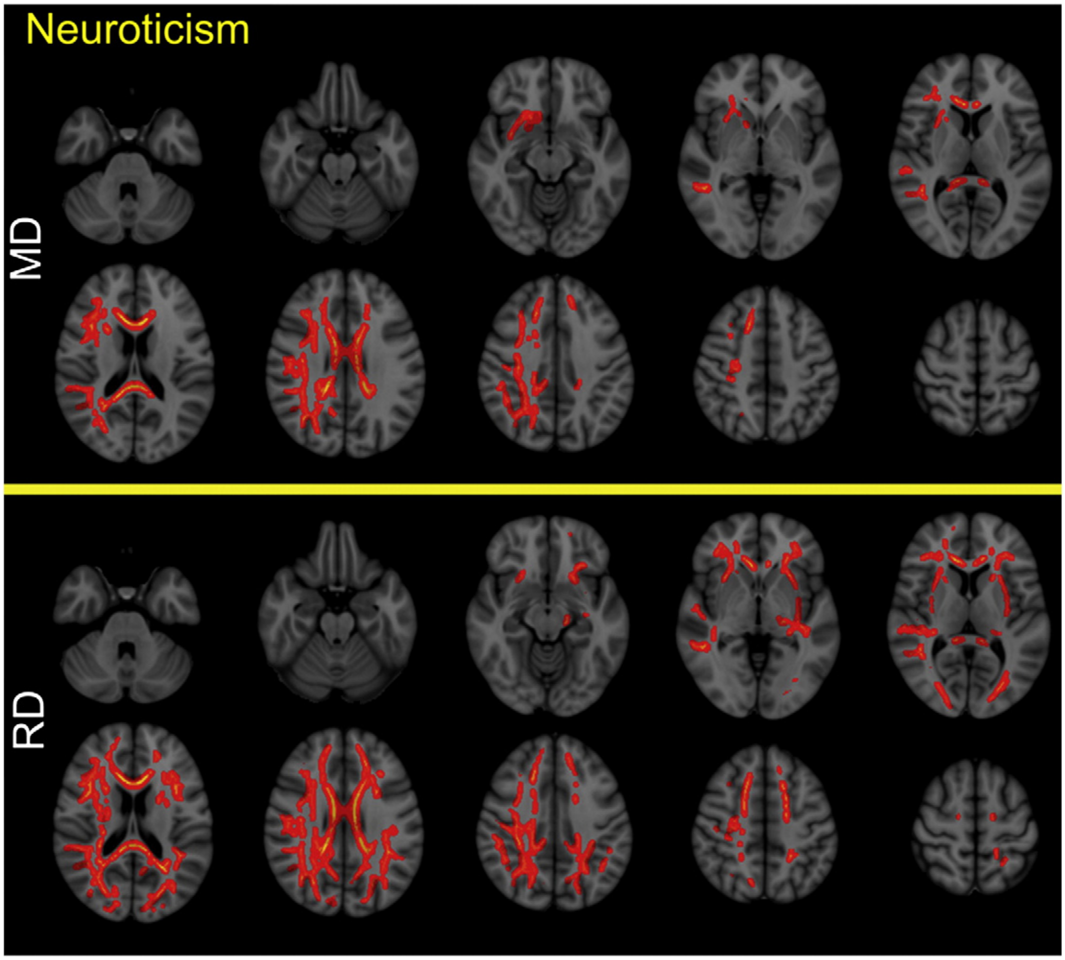


Fig. 6. Neuroticism, mean and radial diffusivity. The spatial distribution of voxels showing linear effects of neuroticism on MD and RD covarying for age, sex and the remaining four personality traits. Yellow-red color illustrates positive relations with neuroticism superimposed on transversal sections from inferior to superior of a template brain (*z*-coordinate, 40–140) referring to the MNI coordinate (millimeter) system. Effects were found in anatomically widespread WM tracts throughout the brain.

Reductions in surface area (Woodward et al., 2009), and thickness (Geuze et al., 2008; Hunter et al., 2011) of the superior temporal cortex, volume reductions of anterior cingulate cortex (Corbo et al., 2005; Karl et al., 2006; Kasai et al., 2008; Yamasue et al., 2003), and prefrontal reductions in volume (De Bellis et al., 2002; Woodward et al., 2009) and thickness (Geuze et al., 2008), have been reported in PTSD. It is known that only a minority of trauma victims develop PTSD, and that neuroticism is related to risk of developing PTSD (Cox et al., 2004). Interestingly, the regional distributions of the effects of PTSD are comparable to the current associations between surface area and neuroticism. Moreover, we found specific associations between anterior cingulate arealization and the vulnerability facet. Thus, a speculative but intriguing possibility is that previous findings in PTSD patients could be partly caused by neurodetrimental processes related to the trauma, but also modulated by a preexisting vulnerability to stress with similar neuronal correlates. A recent MRI twin study of combat-related PTSD reported lower GM density in pregenual anterior cingulate cortex to be characteristic of combat-exposed twins with PSTD, supporting that gray matter reduction in this region represents an acquired sign of PTSD that is consistent with stress-induced loss (Kasai et al., 2008). Follow-up studies are needed to delineate the temporal dynamics of structural brain alterations in response to exposure to trauma and its interactions with dimensions of personality.

It has been proposed that determinants of cortical surface area occur in early fetal life when neurons formed via mitosis at the ventricular zone migrate along radial glial cells to the outer layers of the brain. The number of radial units formed by symmetrical division along the ventricular zone is closely associated to surface area (Rakic, 1995). In the mature brain regional cortical surface area is likely a result of early determinants of neuronal number in addition to subsequent later developmental effects of synaptic pruning, dendritic aborizations, myelination and connectivity (Mota and Herculano-Houzel, 2012; Van Essen, 1997; White et al., 2010). Accordingly, the frontotemporal surface area associations with neuroticism might reflect a lower number of neurons, synapses and possibly decreased subjacent integrity. This is also consistent with the negative association between neuroticism and total brain volume, and demonstrations of a linear relationship between brain size and neuronal number in primates (Herculano-Houzel, 2011; Herculano-Houzel et al., 2007).

Associations between neuroticism and DTI indices of WM microstructure

Previously we have reported reduced WM integrity with increased social reward dependence (Bjørnebekk et al., 2011) and harm avoidance (Westlye et al., 2011) in a largely overlapping sample. Here, we also demonstrate that increased neuroticism is associated with decreased FA, as well as increased mean and radial diffusivity in widespread anatomical regions. Noteworthy, whereas the two anxiety related personality traits (neuroticism and harm avoidance) share phenotypic variance ($r = .64$), negative relations to FA were still found when adding harm avoidance as a covariate, suggesting unique contribution of the two traits.

A lower number of projecting cortical neurons along the surface could affect DTI values in subjacent areas, suggesting that the current

DTI findings could be related to the associations between surface area and neuroticism. The positive association between neuroticism and RD suggests that biological properties that provide hindrance of water diffusion perpendicular to the primary axis of the diffusion tensor are driving the effect. Thus, in addition to reductions in axonal density possibly related to decreased number of cortical neurons, alterations in membrane integrity and myelination are candidate mechanisms underlying individual differences in neuroticism (Beaulieu, 2002; Song et al., 2002, 2003). Importantly, the biological factors influencing diffusion in the brain are multiple and complex and interpretations likely represent simplifications of the underlying mechanisms.

Associations between neuroticism and WM microstructure were observed in long association fibers connecting frontal, occipital, parietal and temporal lobes, in tracts connecting orbitofrontal regions with limbic regions such as amygdala and the anterior temporal cortex, in tracts connecting thalamic nuclei with the frontal lobes, cross-hemispheric pathways including the corpus callosum, as well as in pathways connecting the lateral and medial surfaces of the frontal lobes, crossing the midline through the genu of the corpus callosum (Schmahmann and Pandya, 2006; Wakana et al., 2004). The wide distribution of the effects suggests that general rather than regionally specific processes are driving the effects, and further emphasizes the importance of collecting WM integrity measures throughout the brain. One previous study has investigated the relations between DTI derived WM integrity and FFM, demonstrating decreased WM integrity manifested as increased MD with increasing neuroticism in multiple WM tracts (Xu and Potenza, 2012). In the present study, we not only provide a replication of these findings, but also extend previous findings by documenting associations between neuroticism and FA and RD. It is likely that the discrepancy between studies is related to the increased power to detect subtle differences in the present study.

In addition, besides our previous findings of reduced WM integrity in major WM tracts with higher harm avoidance (Westlye et al., 2011), a recent study provides developmental support to these findings by showing that harm avoidance during childhood is negatively related to FA in the uncinate fasciculus in adolescent (Taddei et al., 2012). Notably, a recent study of a sample comprising 110 participants contrasts the present findings showing positive correlations with trait anxiety and FA in several WM tracts connecting the hippocampus with various brain regions (Montag et al., 2012). Although a relatively new and emerging field of research, the first few DTI reports on anxious and neurotic personality dimensions provide converging evidence of altered WM microstructure in widespread anatomical brain regions. This is also consistent with findings of abnormalities of the structural integrity in various anxiety disorders (reviewed in Ayling et al., 2012). The inconsistency of findings illustrates the need for more investigations to disentangle the connections between WM integrity and negative emotionality.

Extraversion

Higher scores on extraversion were associated with thinner cortex in left ventrolateral prefrontal regions sometimes referred to as the inferior frontal gyrus (IFG). This area corresponds to Broca's area mostly known for its important role in language production (Dronkers et al., 2007). In addition, this area seems to be implicated in general inhibitory processes including risk aversion, where increased activation in fMRI studies (Christopoulos et al., 2009) and suppressed excitability by transcranial magnetic stimulation is associated with riskier choices (Knoch et al., 2006). Most studies emphasize left IFG involvement in language comprehension and the right side for inhibitory processes (Aron et al., 2004; Fecteau et al., 2007; Knoch et al., 2006). However, results are ambiguous and recent findings in patients with left side IFG lesions have indicated that also left hemisphere is critical for inhibitory processes (Swick et al., 2008).

Extroverts tend to be outgoing and highly talkative persons seeking excitement whereas introverts are timid around unfamiliar people, and show less need for excitement. It is tempting to speculate that a thinner IFG reflects a structural correlate of this tendency for extroverts to be less inhibited in speech and more daring than their introvert opposites. Consistent with this hypothesis facet analyses revealed that excitement seeking is the major contributor to the extraversion-thickness associations. A previous study reported thinner right side IFG cortex with higher extraversion scores (Wright et al., 2006). Moreover, a PET study demonstrated increased resting state blood flow bilaterally in this region in introverts (Johnson et al., 1999), adding to the hypothesis that structural and functional properties of this region reflect individual differences in extraversion.

Conscientiousness

A negative relationship was found between conscientiousness and arealization of the posterior part of the left superior temporal gyrus continuing into supramarginal gyrus coinciding with the temporoparietal junction and the Wernicke's area, and the observed effects were mainly driven by the order, achievement striving and self-discipline facets. Recently, in a study investigating neuroanatomical correlates of personality change in patients with frontotemporal dementia, conscientiousness was negatively associated with relative gray matter preservation in the left superior temporal sulcus and superior temporal gyrus (Mahoney et al., 2011). Whereas these studies support a role for superior temporal cortices in regulating conscientious behavior most studies fail to find brain correlates of this personality trait or report results that do not resemble these findings (DeYoung et al., 2010; Jackson et al., 2011). The current findings must therefore be interpreted with caution and should be replicated in future studies before drawing conclusions about brain structure association with conscientiousness. Moreover, it is important to bear in mind that the association between brain structure and function is far from simple, and speculations about possible relations based purely on structural associations remain hypothetical retrospective constructions.

Directions for future work

There are limitations to this study that should be addressed in future work. In particular, whereas this study has some intriguing findings indicative of preexisting associations between neuroticism and brain structure resembling brain correlates of PTSD, the study design do not allow conclusions about the etiology of these relations. For instance, we do not know to what degree the brain–personality relationships primarily are the results of developmental processes during childhood, or whether they are strengthened during adult life. The youngest participants in the present study was 20 years of age and even if strict health screening procedures were applied, excluding individuals with sign of previous or current psychopathology, it is possible that the negative associations between neuroticism and brain structure are caused by chronic stress-induced remodeling of neural circuitry, instead of early neurodevelopmental determinants as we have proposed. Moreover, this is an emerging field of research and whereas some of our findings replicate previous reports, others are inconsistent with previous studies. Large-scale studies are necessary in order to establish distinct brain correlates of human personality. Prospective studies combining genetic and structural brain metrics including children and adolescents are warranted to provide insight about the temporal dynamics of the reported associations.

Moreover, the choice of personality inventory is not obvious. While the FFM has provided a personality assessment standard it is based on adjective descriptors of personality (Allport and Odbert, 1936) and factor analyses (Cattell, 1947). It might be argued that neurobiologically based self-report inventories such as the Temperament and Character Inventory by Cloninger (1986), the Behavioral Activation and Behavioral inhibition Scales by Carver and White (1994), or the more recently developed Affective Neuroscience Personality Questionnaire by Davis and Panksepp (Davis and Panksepp, 2011; Davis et al., 2003) may be more sensitive to the structural imaging parameters included in the present study.

Conclusively, by using multimodal imaging in a large healthy sample we show associations between brain structure and variations in personality. Neuroticism was the trait most clearly linked to brain structure, indicating that higher neuroticism including anxiety, depression and vulnerability to stress was associated with reductions in total brain volume, WM microstructure in large anatomical regions, and frontotemporal surface arealization. The results provide insight into the associations between brain structure and personality dimensions related to emotional instability and trait anxiety, and support that multimodal structural imaging markers represent promising biomarkers for delineating the brain structural substrate for human personality and for identifying individuals with increased susceptibility to psychiatric disease.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.neuroimage.2012.10.009.

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