



Examining brain structures associated with perceived stress in a large sample of young adults via voxel-based morphometry



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ABSTRACT

Perceived stress reflects the extent to which situations are appraised as stressful at a given point in one's life. Past brain imaging studies have examined activation patterns underlying the stress response, yet focal differences in brain structures related to perceived stress are not well understood, especially when considering gray matter (GM) and white matter (WM) structures simultaneously. In this study, voxel-based morphometry was used to investigate relations between GM/WM volume and perceived stress levels in a large young adult sample. Participants (138 men, 166 women) completed the Perceived Stress Scale (PSS; Cohen et al., 1983) and underwent an anatomical magnetic resonance imaging scan. Higher PSS scores were associated with larger GM volume in a cluster that included regions in the bilateral parahippocampal gyrus, fusiform cortex, and entorhinal cortex and smaller GM volume in a cluster that included regions of the right insular cortex. Higher PSS scores were also related to smaller WM volume in a cluster that included the body of the corpus callosum. This pattern of results remained significant even after controlling for effects of general intelligence, socioeconomic status, and depression. Together, findings suggest a unique structural basis for individual differences in perceived stress, distributed across different GM and WM regions of the brain.

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Introduction

Although people may be confronted with similar negative life events, their appraisals of the impact and severity of such events often vary (Phillips, 2012). Perceived stress refers to the degree to which situations in one's life are appraised as stressful (Cohen et al., 1983). Perceived stress reflects a global subjective evaluation of the level of stress experienced as a result of objective stressful events and their appraisal, inadequate coping resources, and perceived lack of controls (Cohen et al., 1983; Lazarus and Folkman, 1984). Previous studies have linked high perceived stress levels not only to psychiatric disturbances such as depression (Koolschijn et al., 2009), anxiety disorders (Glynn et al., 2008), alcohol and substance abuse problems (Rice and Van Arsdale, 2010) and posttraumatic stress disorder (PTSD) (Laganà and Reger, 2009), but also to physical health outcomes including increased risk of cardiovascular disease, hypertension, and stroke (Aggarwal et al., 2014; Chrousos, 2009; Ostwald et al., 2009).

Imaging and neurobiology studies have consistently implicated regions of the prefrontal cortex (PFC), insular cortex (IC), and medial temporal lobe (MTL) in determining which events are experienced as

threatening or potentially stressful (Ansell et al., 2012; McEwen, 2007; McEwen and Gianaros, 2010). For example, functional magnetic resonance imaging (fMRI) studies have directly implicated the medial PFC in combination with the anterior cingulate cortex in the regulation of the human stress response during the Montreal Imaging Stress Task (Pruessner et al., 2008) and serial subtraction stress task (Wang et al., 2005), respectively. Structural imaging research has also found greater cumulative adversity and more recent stressful life events are related to smaller gray matter volume in the medial PFC and right insular cortex (Ansell et al., 2012).

The insular cortex, which is an interface of cognitive, homeostatic, and affective systems of the human brain, also has an important role in monitoring interactions between external and internal environments (Craig, 2009; Critchley et al., 2004; Menon and Uddin, 2010). Research on socially-phobic individuals has revealed decreased brain blood flow in the insular cortex in public but not private speaking tasks compared to non-phobic controls who experience increased blood flow in the public speaking tasks (Tillfors et al., 2001). Using perfusion imaging, Wang et al. (2005) also implicated insular cortex involvement among individuals who report high levels of everyday stress. Moreover, a recent meta-analysis on affective processing emphasized the role of the insular cortex in the perception and experience of emotions (Duerden et al., 2013).

Evidence of reduced hippocampal volume has also been observed in patients with PTSD (Villarreal et al., 2002) and major depressive disorder (Koolschijn et al., 2009). To illustrate, longitudinal research found that

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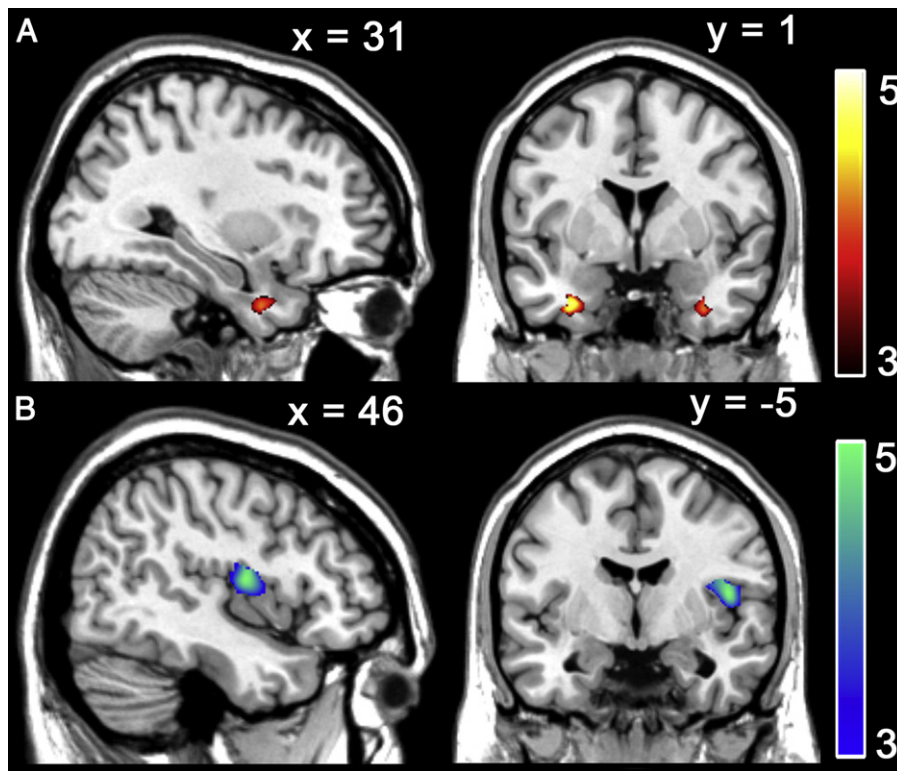


Fig. 1. Association between PSS and GMV. GMV of the bilateral parahippocampal gyrus, fusiform cortex, and entorhinal cortex was positively correlated with PSS scores (A). GMV in the right insular cortex had a significant, negative correlation with PSS scores (B). Results are shown at $p < 0.05$, corrected for multiple comparisons at the cluster-level with non-stationary correction and an underlying voxel level of $p < 0.001$, uncorrected. The color density represents the T score. PSS: Perceived Stress Scale. GMV: gray matter volume.

reports of more negative stressful life events at baseline predicted reduced hippocampal volume at a two year follow-up (Zannas et al., 2013). Finally, the parahippocampal gyrus (PHG) and amygdala, regions associated with initial stress perception and anticipation of negative events, have been linked to stress responding (McEwen and Gianaros, 2011; Ploghaus et al., 2001; Schulkin et al., 1994). For example, a prospective structural MRI study indicated that reductions in perceived stress following a stress-reduction intervention were correlated with decreased gray matter (GM) density in the right amygdala (Hölzel et al., 2010).

In large part, previous research examined activation patterns underlying the stress response. However, focal differences in brain structures, i.e., gray matter volume (GMV) and white matter volume (WMV) related to individual variability in perceived stress, are not well known in healthy samples despite their potential implications for physical and mental health. For example, studies of young adults are especially

important because this developmental period (ages 18–24) is a critical transition period (Southerland et al., 2009) characterized by higher than average stress levels than other developmental phases (Rebbeck et al., 2013). Academic overload, intimate relationship formation, competition with peers and concerns about autonomy and the future are stressors that are especially relevant to young adulthood (Vaez et al., 2006).

In addition, age-related alterations in brain structure are ongoing during young adulthood (Gogtay et al., 2004), especially in the PFC, a region crucial for self-control and stress regulation (Lebel and Beaulieu, 2011). Delayed maturation of brain structures and multiple stressors may also increase risk for mood and substance use disorders among adolescents and young adults (Paus et al., 2008). Thus, research on links between GMV/WMV and individual differences in perceived stress during young adulthood is important not only in helping to identify distinct anatomical regions associated with elevations in perceived stress

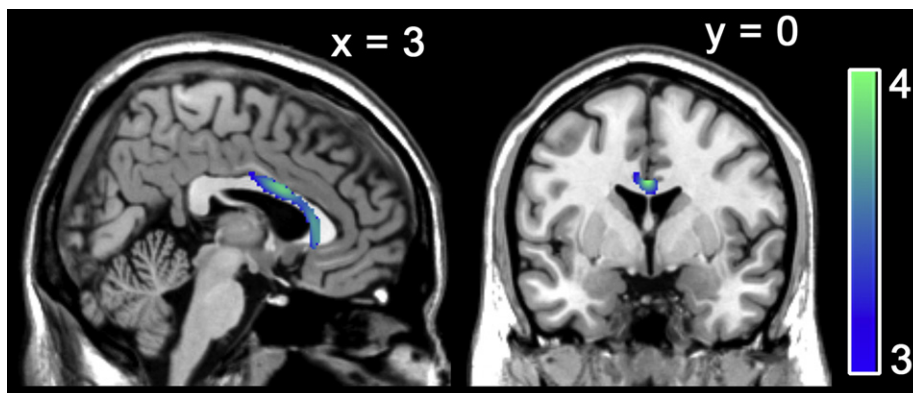


Fig. 2. Association between PSS and WMV. The corpus callosum body had a significant negative correlation with PSS scores. Results are shown at $p < 0.05$, corrected for multiple comparisons at the cluster-level, with an underlying voxel level of $p < 0.001$, uncorrected. The color density represents the T score. WMV: white matter volume; PSS: Perceived Stress Scale.

but also in explaining, at least in part, why the impact and severity of similar adverse life events vary from person to person.

Although effects of chronic stress and stress reduction interventions on structure changes (i.e., GMV) have been investigated (Gianaros et al., 2007; Hölzel et al., 2010), all such studies used region of interest (ROI)-based MRI, an approach that is subject to potential operator bias and may neglect the involvement of salient brain regions outside ROI (Abe et al., 2010; Focke et al., 2008). Voxel-based morphometry (VBM) is superior to manual ROI analysis when searching for abnormalities throughout the entire brain and is more applicable to large samples (Focke et al., 2008). VBM is also a reliable, objective method that eliminates effects of operator bias (Abe et al., 2010). In addition, while past structural MRI studies investigated GM changes after a stress-reduction intervention (Hölzel et al., 2010), effects of chronic stress over 20 years on GMV (Gianaros et al., 2007), or associations of cumulative stress and recent stress life events to GMV (Ansell et al., 2012), direct relations between perceived stress and both GMV and WMV have not been investigated in non-clinical samples of young adults.

Previous neuroimaging studies have reported a significant reduction in WMV of the corpus callosum (CC), within samples having had significant early life stress (Jackowski et al., 2011), maltreatment-related PTSD (De Bellis et al., 2002; Jackowski et al., 2008), and PTSD (Villarreal et al., 2004) compared to healthy controls. For example, Teicher et al. (2004) found that total CC area of patients who experienced childhood neglect was significantly reduced compared to psychiatric patients who had not been neglected and non-psychiatric controls. Although suggestive, it is not clear whether individual variations in perceived stress are also associated with differences in CC volume within larger general young samples reporting no history of psychiatric diagnoses.

In summary, the goals of the current research were to explore direct associations between individual differences in perceived stress and brain structure differences in both GMV and WMV using VBM. Drawing upon findings from neuroimaging studies with psychiatric samples, we posited that individual differences in perceived stress in a non-clinical sample would be associated to GMV/WMV differences in brain regions including the PFC, MTL, IC, and CC.

Methods

Participants and procedures

Participants were 304 young adults (138 men, 166 women; mean age = 19.2, SD = 1.24, age range: 17–27 years) from Southwest University (SWU), Chongqing, China who volunteered as part of an ongoing project examining associations between brain imaging, creativity and mental health. All participants were right-handed and physically healthy. None had a history of neurological or psychiatric illness. The study was approved by the SWU Brain Imaging Center Institutional Review Board.

In accordance with the Declaration of Helsinki (2008), written informed consent was obtained prior to engagement in the research tasks. First, participants underwent an MRI scan wherein they were instructed to keep their heads still and to remain awake. The scan was comprised of anatomical imaging (5 min), resting state imaging (8 min) and diffusion tensor imaging (17 min), only anatomical imaging data was used in this study. Subsequently, about half an hour after the MRI scan, all participants completed Chinese versions of the Perceived Stress Scale (PSS; Yang and Huang, 2003), Combined Raven's Test (CRT; Sun et al., 1994), Beck Depression Inventory (BDI; Beck et al., 1996), and "social ladder" assessment for subjective Socioeconomic Status (SES; Goodman et al., 2001). On average, the study took 80 min to complete. Participants were compensated 40 RMB for the MRI scan and 15 RMB for completion of self-report measures.

Measures

Perceived Stress Scale

The 14-item PSS assesses the extent to which individuals view their lives to be unpredictable, uncontrollable, and overly demanding during the past month. Items are rated on a 5-point scale from "never" (0) to "very often" (4) with higher scores representing elevations in perceived stress. Sample items include, "In the last month, how often have you felt nervous and 'stressed'?" and "In the last month, how often have you felt that things were going your way?". The PSS is a sensitive and ecologically valid measure of subjective stress levels in clinical and non-clinical samples (Cohen et al., 1983; Pbert et al., 1992). The PSS was found to be structurally-equivalent and to have a high degree of stability over two weeks ($r = 0.78$) in Chinese samples (Yang and Huang, 2003). In this study, the PSS had an acceptable internal consistency, $\alpha = 0.79$.

Combined Raven's Test

To control for individual differences in intellectual ability in analyses of relations between PSS and GMV/WMV (Haier et al., 2005; Jung and Haier, 2007), participants completed the CRT, a recognized intelligence test with a high degree of reliability and validity (Tang et al., 2012). The CRT, which includes the Raven's standard progressive matrices (C, D, E sets) and Raven's colored progressive matrices (A, B, AB sets), consists of 72 items revised for use in Chinese samples by Sun et al. (1994). Number of correct answers given in 40 min was used as a psychometric index of individual general intelligence.

Beck Depression Inventory

The BDI is a 21 item self-report questionnaire measuring severity of depressive symptoms during the past week on a four-point scale (0–3), with higher scores indicating more severe symptomatology (Beck et al., 1996). The BDI is considered to be a valid and reliable measure assessing the severity of depressive symptom in clinical and non-clinical samples (Beck et al., 1988), including those in China (Chang, 2005). In this sample, its alpha was satisfactory, $\alpha = 0.78$.

Socioeconomic status

Following previous studies (Gianaros et al., 2008; Goodman et al., 2001), subjective SES was assessed by having participants rank their parents' and their own income, education and occupational prestige levels based on their childhood and adolescence using nine-rung 'social ladders' (Goodman et al., 2001). Mother, father, and self rankings were averaged to obtain an overall perceived social status score. Past research indicates that the subjective SES is reliable and has stronger associations with stress and health-related factors (e.g. body fat, cortisol habituation to stress) than objective measures of social status do (Adler et al., 2000). In this sample, the subjective SES had an alpha of $\alpha = 0.86$.

MRI data acquisition

MR images were acquired on a 3.0-T Siemens Trio MRI scanner (Siemens Medical, Erlangen, Germany). High-resolution T1-weighted anatomical images were acquired using a magnetization-prepared rapid gradient echo (MPRAGE) sequence (TR/TE/TI = 1900 ms/2.52 ms/900 ms; Flip angle = 9°; Slices = 176; Slice thickness = 1.0 mm; Resolution matrix = 256 × 256; Voxel size = 1 × 1 × 1 mm³).

Voxel-based morphometry

MR images were processed using the SPM8 (Wellcome Department of Cognitive Neurology, London, UK) implemented in Matlab 7.8 (MathWorks Inc., Natick, MA, USA). Each image was first displayed in SPM8 to screen for artifacts or gross anatomical abnormalities. For better registration, the reorientation of the images was manually set to the anterior commissure. Segmentation of T1 weighted anatomical images into

gray matter and white matter was done using the new segmentation in SPM8. Subsequently, we performed Diffeomorphic Anatomical Registration through Exponentiated Lie (DARTEL) algebra in SPM8 for registration, normalization, and modulation (Ashburner, 2007). To ensure that regional differences in the absolute amount of GM or WM were conserved, the image intensity of each voxel was modulated by Jacobian determinants. Then, registered images were transformed to Montreal Neurological Institute (MNI) space. Finally, normalized modulated images (GM and WM images) were smoothed with a 10-mm full-width at half-maximum Gaussian kernel to increase signal to noise ratio.

Statistical analysis

Statistical analyses of GMV and WMV data were performed using SPM8. In the whole-brain analyses, we used a multiple linear regression to identify regions where regional GMV and WMV were associated with individual differences in PSS scores. In multiple linear regression analyses, PSS scores were used as the variable of interest. To control for possible confounding variables, age, sex and global volumes of GM or WM were entered as covariates within the regression model. To avoid edge effects around the borders between GM and WM, an absolute threshold masking of 0.2 was used; that is, voxels with gray matter or white matter values lower than 0.2 were excluded from analyses (Mühlau et al., 2006). For all analyses, the cluster-level statistical threshold was set at $p < 0.05$, and corrected at the non-stationary cluster correction (Hayasaka et al., 2004) with an underlying voxel level of $p < 0.001$.

Results

Perceived Stress Scale scores

The mean PSS score for the current sample was 23.10 ($SD = 6.48$), an average consistent with previous findings of Cohen et al. (1983) who reported means of 23.18 and 23.67 in two college student samples. No significant gender difference in PSS scores was found [$t(302) = -0.70$, $p = 0.48$]. PSS scores had significant relations with responses on the BDI ($r = 0.58$, $p < 0.01$) and subjective SES ($r = 0.18$, $p < 0.01$) (See Tables 1 and 2).

Correlations between GMV and PSS scores

After correcting for age, sex and global GM volumes, PSS scores had significant, positive associations with GMV in a cluster of regions that included the bilateral anterior PHG, fusiform cortex and entorhinal cortex [Left: MNI coordinate: $-32, 1, -33$; $r = 0.27$, $t = 4.83$; $p < 0.05$; Cluster size = 434; Right: MNI coordinate: $31, 3, -36$; $r = 0.25$, $t = 4.25$; Cluster size = 254; $p < 0.05$]. Furthermore, PSS scores had a significant, negative correlation with GMV in a cluster that included the right IC [MNI coordinate: $46, -5, 12$; $r = -0.29$, $t = 5.00$; Cluster size = 959; $p < 0.05$]. No other significant relations were observed. (See Fig. 1).

To examine whether these results were affected by sociodemographic factors and associated measures of emotional distress, additional models

Table 1
Descriptive statistics ($n = 304$).

variables	Means (SD)	Range	Correlation with PSS
Age	19.92 ± 1.24	17–27	/
CRT	66.31 ± 3.33	50–72	/
PSS	23.10 ± 6.48	8–44	/
BDI	5.01 ± 1.47	0–25	0.58**
SES	6.98 ± 5.30	1–8.8	-0.19**

Note: PSS, Perceived Stress Scale; CRT, Combined Raven's Test; BDI, Beck Depression Inventory; SES, Socioeconomic Status.

** $p < 0.01$.

Table 2
Brain regions with significant association between brain structures and PSS scores.

Brain regions		MNI coordination			Cluster size (mm ³)	Peak T-value
		x	y	z		
<i>Correlation between PSS and GMV</i>						
<i>Positive correlations</i>						
PHG/fusiform cortex	L	-32	1	-33	434	4.83*
cortex/entorhinal cortex	R	31	3	-36	254	4.25*
<i>Negative correlation</i>						
Insular cortex	R	46	-5	12	959	5.00*
<i>Correlation between PSS and WMV</i>						
<i>Negative correlation</i>						
Corpus callosum	L/R	0	0	30	1453	3.86*

Note: PSS, Perceived Stress Score; GMV, gray matter volume; PHG, parahippocampal gyrus.

* p (corrected) < 0.05 .

examining PSS associations with GMV were tested with CRT, subjective SES, and BDI scores as covariates. All correlations remained significant even after effects of CRT, subjective SES and BDI responses had been controlled [Left PHG: $t = 4.46$, $p = 0.068$, Cluster size = 215; Right PHG, $t = 4.42$, $p < 0.05$, Cluster size = 313; Right insular, $t = 4.95$; Cluster size = 646; $p < 0.05$]. Although there were small variations in cluster size, significant regions were identical to those identified in initial analyses.

Correlations between WMV and PSS scores

After correcting for age, sex and global WM volume, PSS scores had a significant, negative correlation with WMV in a cluster that included the body of the CC and adjacent WM regions [MNI coordinate: $0, 0, 30$; $r = -0.23$, $t = 3.86$; $p < 0.05$; Cluster size = 1453]. However, no other significant associations were found (See Fig. 2). Once again, cluster sizes changed slightly but all associations were replicated after controlling for effects of CRT, subjective SES and BDI [$t = 4.48$; $p < 0.05$; Cluster size = 1498].

Discussion

Building upon recent work linking higher self-reported levels of cumulative adversity and recent stressful life events to reduced GMV in a non-clinical sample (Ansell et al., 2012), this study is the first to identify regional variations in both GMV and WMV underlying individual difference perceived stress levels using VMB. Consistent with the general hypothesis that PSS scores would vary as a function of GMV and WMV, perceived stress was (a) positively associated with GMV in a cluster of regions that included the bilateral anterior PHG, fusiform cortex, and entorhinal cortex; (b) negatively correlated with GMV in right IC, and negatively related to WMV in a cluster that included the body of CC. All significant associations were replicated after controlling for effects of general intelligence, depression, and subjective SES levels within prediction models. These results provided direct neuroanatomical evidence for the association between perceived stress and brain regions important for the perception and experience of stress in a large non-clinical sample of young adults.

Increased GMV in a cluster involving the PHG, fusiform cortex, and entorhinal cortex was observed in participants with higher PSS scores. In concert with the hippocampus and limbic system structures, the PHG has an important role in stress and emotion regulation (Phillips et al., 2008; Ulrich-Lai and Herman, 2009), pain perception (Cheng et al., 2007), and memory consolidation (Hahn et al., 2012). PHG dysfunction has been linked to PTSD (Cooney et al., 2010), social anxiety disorder (Etkin and Wager, 2007), Alzheimer's disease and schizophrenia (Bilkey, 2004). For example, Sakamoto et al (2005) observed activation of the PHG during the presentation of masked traumatic stimuli among PTSD patients compared to healthy controls, thus implicating the

structure's involvement in the detection of stress-related stimuli among vulnerable individuals. A recent longitudinal VBM study provided further support for links between the PHG and stress responding, based on an observed association between reports of stressful life events and GM change in the PHG (Papagni et al., 2010).

On the other hand, the fusiform cortex has been implicated in the perception of emotions in facial images (Kanwisher et al., 1997; Radua et al., 2010) and, more specifically, in the association between perceived stress and human face perception (Mather et al., 2010). Psychosocial stress was also found in relation to decreased coupling between the dorsolateral PFC and fusiform cortex, both of which play important roles in flexible attentional control (Liston et al., 2009). The adjacent entorhinal cortex is considered to be an interface between the neocortex and hippocampus (Hahn et al., 2012), and may be exquisitely susceptible to stressors and glucocorticoids as a partial function of its connections with the amygdala (McGaugh, 2004). Moreover, the entorhinal cortex may be involved in preparing individuals to make adaptive response to “worst case scenarios”, including motor responses necessary for escape from environmental threats (Borras et al., 2004; Ploghaus et al., 2001). On the basis of these findings, increased GMV in regions of the PHG, fusiform cortex, and entorhinal cortex among participants with higher PSS scores may be structural markers for proneness to experiencing stress.

Reduced GMV in right IC areas was also identified among participants who had higher PSS scores. The insula is located at the interface of cognitive, homeostatic, and affective systems of the human brain (Menon and Uddin, 2010), and has been implicated in a wide range of functions including interoception, awareness of emotion, stress responses, and empathic processing (e.g., Craig, 2002, 2009). Research on clinical samples has linked IC dysfunction to major depression disorder (Sprenghelmeyer et al., 2011; Takahashi et al., 2010), pain perception (Schön et al., 2008), chronic pain (Rodriguez-Raecke et al., 2009), and anxiety disorders (Chen et al., 2006; Paulus and Stein, 2006; Tillfors et al., 2001). For example, GM density reduction in IC regions has been observed among fire survivors who had PTSD (Chen et al., 2006). Other research suggests that effects of combat stress on insula reactivity are dependent on perceived threat rather than combat exposure per se (van Wingen et al., 2011), highlighting threat appraisal as a correlate of interoceptive awareness.

In this study, higher perceived stress levels were related to lower GMV in a cluster situated in a posterior IC region, the “sensory insula”, an area considered to be critical for interoception (Paulus and Stein, 2006). Recent animal research has shown that the posterior insula modulates stress buffering effects (Christianson et al., 2008). Thus, the association between smaller GMV in the right posterior insula and elevations in perceived stress may reflect increased interoceptive awareness of stress. Tellingly, other VBM research has confirmed the positive association between increased gray matter concentrations in the IC and higher levels of experience with meditation (Hölzel et al., 2008), a popular and effective stress reduction method (Plotnikoff and Weisberg, 2013).

The negative correlation between PSS scores and insular GMV is also consistent with select findings of other recent work on non-clinical samples. Specifically, Ansell et al. (2012) found reduced GMV in the right insular and PFC corresponded to high levels of recent life events as well as the interaction of more cumulative life events and perceptions of heightened chronic stress but not major life events or chronic stress alone. Together results of the two studies suggest that individual differences in experiences of *recent* stress are especially salient to reduced right insular GMV in non-patient groups.

Notwithstanding this common result, notable differences between this research and that of Ansell et al. (2012), were also apparent. Unique to the present study, perceived stress also had positive correlations with GMV in select regions noted above. Conversely, Ansell et al.'s findings were unique in linking cumulative adversity, life trauma and/or recent stressful life events to smaller GMV in the PFC and other areas, particularly the anterior and subgenual cingulate regions. While measures of

adversity, major life events, minor life events and adversity life events all correlate with PSS scores (e.g., Cohen et al., 1983; McLaughlin et al., 2010), differences in the measurement of stress may have contributed to different results between the two studies. The use of objective and subjective stress indices as per Ansell et al. is recommended in future work to clarify how GMV and WMV are related to stressors and subjective stress responses. Variable results may have also reflected sample differences in demographics. Specifically, participants in this study were younger, had a narrower age range, and were more evenly distributed by sex compared to Ansell et al.'s sample of 103 community volunteers, half of whom were older than age 25 (range 18–48 years) and slightly over two thirds of whom were men.

Regarding WMV findings, the CC is a large bundle of nerve fibers that connects the left and right hemispheres. Because the CC connects auditory, sensory, and motor cortices as well as the superior frontal area (Pandya and Seltzer, 1986), the structural integrity of CC white matter may facilitate inter-hemispheric information processing (Bloom and Hynd, 2005). Therefore, arguably, smaller WMV in the CC body among individuals with higher PSS scores might reflect less efficient transfer and integration of information between the hemispheres which, in turn, contributes to higher perceived stress levels. The present results also dovetail with previous studies linking exposure to early life stress with reduced CC integrity via diffusion tensor imaging in healthy respondents (Paul et al., 2008). The CC is one of several regions implicated in response to traumatic events (Doctor and Shiromoto, 2009). Repeated, prolonged traumatic experiences contribute to hyper-vigilant responding to potential threats that may reduce WMV in the CC and other regions (van der Kolk, 2003). The present study suggests that decreased WMV in this area is not specifically a function of exposure to traumatic stress and may extend to members of a non-clinical sample who report high levels of perceived stress.

Notwithstanding its potential implications, the main limitations of this study should be acknowledged. First, in light of the cross-sectional research design, causal relations between perceived stress and brain structures could not be assessed. Hence, it is not clear whether GMV/WMV differences caused or resulted from high levels of perceived stress or whether causal associations are reciprocal. Longitudinal designs may be useful in assessing the status of GMV and WMV as predisposing factors that increase susceptibility for later increases in perceived stress; conversely, examining perceived stress as a risk factor for changes in GMV and WMV represents an important line of future research within non-clinical groups.

Second, whereas limiting the assessment to young adults was advantageous in examining associations between perceived stress and brain morphology independent of aging and life experience, it is not clear whether the current findings generalize to older cohorts wherein potentially unique relations between stress and structural changes may be present. For example, delayed PFC maturation (Sowell et al., 1999) may explain, in part, why young adults engage in more risky decision-making under stress than older adults do (Mather et al., 2009). Conversely, age-related decreases in GMV and WMV are also apparent (e.g., Hedden and Gabrieli, 2004; Lupien et al., 2007; Madden et al., 2009; Resnick et al., 2003), particularly between middle and late adulthood (Raz et al., 2005) and have been linked to “cascading” or cumulative effects of stress and glucocorticoids (e.g., Goosens and Sapolsky, 2010; Oitzl et al., 2010). Consequently, future research on associations between individual differences in stress and brain structures is needed, particularly in non-clinical samples over age 50.

Third, concerns that automated preprocessing procedures of VBM may result in more preprocessing errors raised in relation to other published studies (Kennedy et al., 2009) may apply to this research as well. Finally, findings should be considered provisional. While other GMV and WMV differences corresponding to varying levels of perceived stress were not revealed or did not survive corrections for multiple comparisons, replications in other large samples are needed to demonstrate the reliability of findings across groups.

In conclusion, this study directly identified associations between both GMV and WMV in particular regions and elevated levels of perceived stress levels in a non-clinical sample of young adults. Specifically, variable GMV or WMV in areas of the PHG, IC, and CC was identified as structural markers of participant differences in subjective stress levels. These findings were maintained even after controlling for individual differences on measures of general intelligence, subjective SES and depression. As such, this research demonstrated a unique structural basis for variations in perceived stress that are distributed across distinct gray and white matter areas of the brain.

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Conflict of interest

The authors declare no conflict of interest.

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