# Social support, stress and the aging brain

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## Abstract

Social support benefits health and well-being in older individuals, however the mechanism remains poorly understood. One proposal, the stress-buffering hypothesis states social support 'buffers' the effects of stress on health. Alternatively, the main effect hypothesis suggests social support independently promotes health. We examined the combined association of social support and stress on the aging brain. Forty healthy older adults completed stress questionnaires, a social network interview and structural MRI to investigate the amygdala-medial prefrontal cortex circuitry, which is implicated in social and emotional processing and negatively affected by stress. Social support was positively correlated with right medial prefrontal cortical thickness while amygdala volume was negatively associated with social support and positively related to stress. We examined whether the association between social support and amygdala volume varied across stress level. Stress and social support uniquely contribute to amygdala volume, which is consistent with the health benefits of social support being independent of stress.

**Key words**: aging; social support; psychological stress; amygdala

## Introduction

Elderly adults benefit physically and mentally from the social support of friends and family members (Berkman *et al*., 2000). Previous work indicates older adults who receive support have lower blood pressure (Birditt *et al*., 2012), reduced mortality rates (Holt-Lunstad *et al*., 2010), and higher cognitive functioning (Gow *et al*., 2013). One prominent hypothesis is that the positive physical and mental effects result from the role social support can play in stress management. This has been referred to as the stress-buffering hypothesis (SB; Cohen and Wills, 1985; Antonucci, 2001). A contrasting hypothesis, referred to as the 'main effect' hypothesis (House *et al*., 1988), contends that social support, in and of itself, benefits health regardless of stress level by enhancing feelings of well-being.

One way to explore the mechanism by which social support influences physical and mental health is to examine whether it has a mediating effect on the relationship between stress and the brain. Considerable research has revealed that stress has dramatic effects on the brain across the lifespan.

The amygdala-medial prefrontal cortex (mPFC) circuitry, which has been strongly implicated in emotional and social processing across the lifespan (Shin *et al*., 2005; Urry, 2006; Liao *et al*., 2010; Hahn *et al*., 2011; Holmes *et al*., 2012), has been an important focus of this work. Previous studies established that stress inversely affects the structural integrity of both the mPFC and the amygdala (for review see: Davidson and McEwen, 2012) which has significant consequences for psychological well-being including affect regulation and increased susceptibility to mental disorders (Holmes *et al*., 2012). In the mPFC, acute and chronic stress cause a decrease in dendritic materials (Radley *et al*., 2004; Cook and Wellman, 2004; Liston, 2006; Arnsten, 2009; Holmes and Wellman, 2009). Previous work in humans suggests that stressful environments are linked to smaller prefrontal cortices (Hanson *et al*., 2012) and greater social difficulties (Hanson *et al*., 2010). In contrast, dendrites in the amygdala reliably increase in the face of stress (Vyas *et al*., 2002). Results from some human studies are consistent with these findings, suggesting that larger amygdala volume is associated with higher stress levels (Mehta *et al*., 2009; Lupien *et al*., 2011), poor emotion

regulation, increased anxiety (Tottenham *et al.*, 2010) and the recent-onset of major depressive disorder (Lange *et al.*, 1999). The outcome of a human intervention study demonstrated that stress reduction led to a decline in amygdala volume (Holzel *et al.*, 2010). Together past research demonstrates that the volume of the amygdala increases with stress exposure while the mPFC decreases. Since the structural integrity of the amygdala-mPFC circuitry is negatively impacted by stress (Davidson and McEwen, 2012), we focused our exploration on how social support is related to these brain regions in elderly individuals.

The goal of this study was to investigate the combined influence of social support and stress on the morphometry of the amygdala and mPFC in a cross-sectional sample of elderly adults. Given prior research demonstrating the effects of stress on the amygdala-mPFC circuitry, we hypothesized that greater social support would be associated with greater cortical thickness in mPFC and smaller amygdala volumes. We then tested statistical models to determine if there was any evidence that social support buffers the relationship between stress and differences in the amygdala-mPFC circuitry (SB hypothesis) or if these relationships are independent (ME hypothesis).

## Materials and methods

### Participants

Forty-one right-handed older adults participated in this research study. Interested members of the Austin community responded to physical or online advertisements posted at recreational centers, educational programs and social groups. These participants were recruited for this study and a second study that examined the neurocognitive relationship between sleep patterns and memory. The sleep and memory data will be reported in an unrelated manuscript. One participant was dropped due to missing data from the stress questionnaires. Based on previous studies of brain-behavior relationships in aging, we decided to include a sample size of 40 (27 females, mean age $= 67.2 \pm 5.1$, age range $= 60$–78 years). All participants provided written informed consent that was approved by the Institutional Review Board at the University of Texas at Austin.

Participants were excluded if they reported a medical history of heart conditions or vascular disease, including hypertension and elevated body mass index (BMI greater than 30). Cardiovascular exclusions are important because increased cardiovascular risk has been associated with significant neurological changes from middle age on (Salat *et al.*, 2011; Haley, 2014). Additionally, participants were excluded for any history of neurological injury or disorder, arthritis, diabetes, current psychiatric disorder, major depression within the past five years or a score greater than 15 on the Geriatric Depression Scale (GDS), current sleep disorder or a score greater than 8 on Pittsburg Sleep Quality Index (PSQI), cancer in the last three years, or current medications that affect the central nervous system.

After the initial screening and consent, elderly participants underwent a battery of neuropsychological tests to verify normal cognitive functioning, including the WAIS-IV Vocabulary and Digit Span subtests (Wechsler, 2008), California Verbal Learning Test (CVLT), Trails A & B, Controlled Oral Word Fluency Task (COWAT) and the WMS-IV Logical Memory I & II (Wechsler, 2009). All older adults included in the study were within 1 s.d. of normal performance on memory and executive function composite scores as well as the Vocabulary subtest of the WAIS-IV.

### Behavioral measures

Following the neuropsychological assessment, participants completed a structured interview to measure the size, complexity and quality of social networks (Fingerman and Charles, 2010; Fingerman *et al.*, 2012). This included an assessment of social support across four domains: companionship, advice, emotional support, and practical support. Participants were asked to report the frequency they were given and received support from each domain over the past 12 months on the following scale: 1 (*daily*), 2 (*a few times a week*), 3 (*weekly*), 4 (*at least once every two weeks*), 5 (*a few times a month or monthly*), 6 (*a few times a year*), 7 (*once a year*), 8 (*less than once a year or never*). Social network size was evaluated using the Social Network Index (SNI) which assesses the number of regular social engagements with a spouse, friends and family members as well as the number of people one is in contact with at least once every two weeks (Cohen *et al.*, 2003). The interview also included the positive and negative affect scale (PANAS; Watson *et al.*, 1988), questions regarding the frequency of social activities and a three-question measure of loneliness adapted from the UCLA Loneliness Scale (Hughes *et al.*, 2004).

Additionally, participants completed the online versions of the Perceived Stress Scale—10 (PSS-10; Cohen, *et al.*, 1983) and the Social Readjustment Rating Scale (SRRS; Holmes and Rahe, 1967) within one year of the social support network interview. The PSS-10 includes 10 questions to assess an individual's perception of their stress over the past month. For each question, participants indicated the frequency of perceived stress on a scale from never (0) to very often (4). The SRRS includes a list of 43 life events and asks the participant to indicate which events have occurred within the last 12 months. Each event is assigned a weight, which represents the potential stress that life event caused. The weights are summed to get a total life stress score. Higher scores indicate a greater likelihood of stress negatively impacting health. In addition, participants reported basic demographic information including household income.

### Structural image acquisition

Participants underwent structural magnetic resonance imaging (MRI) on a 3T Siemens Skyra MRI scanner with a 32-channel phase array head coil at the University of Texas at Austin Imaging Research Center. Two high-resolution T1-weighted MPRAGE scans (TR $= 2.53$, TE $= 3.37$, flip angle $= 7°$, 1 mm slice thickness, 176 slices, FOV $= 256 \times 256\,\mathrm{mm}^2$) were collected. The T1 scans were motion corrected and averaged to optimize the signal and contrast for analysis.

### Structural analysis

Cortical thickness, subcortical volumes and gray matter volumes were computed using FreeSurfer software package (http://surfer.nmr.mgh.harvard.edu). The technical details have been previously explained in a number of publications (Dale *et al.*, 1999; Fischl *et al.*, 2002, 2004). Two T1-weighted images were analyzed for each participant. Computations followed reconstruction of the cortical surface. The cortical reconstruction involves intensity normalization, stripping non-brain tissue and segmentation, which utilize intensity and continuity constraints to label white matter. An algorithm was implemented to assign neuroanatomical labels to each voxel. This algorithm was based on a probabilistic atlas of class statistics derived from a manually labeled training set (Fischl *et al.*, 2002). Cortical thickness was measured using intensity and continuity

information to determine the gray/white matter and gray/CSF boundaries to generate surface models (Dale *et al*., 1999; Akirav and Maroun, 2007). The distance between the surfaces was calculated as the measure of cortical thickness (Fischl and Dale, 2000). Volumetric measurements were calculated automatically by counting the number of voxels within each label. These procedures have been shown to closely resemble results from histological analysis (Rosas *et al*., 2002) and manual labeling (Kuperberg *et al*., 2003). The automated segmentation technique is valid and reliable across different populations (Kuperberg *et al*., 2003; Salat, 2004) and sequence parameters (Wonderlick *et al*., 2009). The results from FreeSurfer's automated segmentation and parcellation were visually inspected. All results were determined to be accurate and did not require manual editing.

Given our hypotheses concerning the associations between social support and the structural integrity of the amygdala and mPFC, we conducted analyses on the volumetric segmentation (Fischl *et al*., 2002) of the left and right amygdala and cortical thickness which resulted from surface-based analyses of the right and left medial orbitofrontal region labeled by Desikan *et al*. (2006). Amygdala volume was corrected for head size by dividing gray matter volume by the total intracranial volume (Buckner *et al*., 2004; Wright *et al*., 2005; O'Brien *et al*., 2006).

## Results

### Overview

*Behavioral measures.* The answers from the social support questions were reverse coded and averaged so that larger numbers indicated a higher frequency of support. Only the frequency of receiving social support was examined given that the stress-buffering hypothesis pertains to receiving support not giving (Cohen and Wills, 1985). (Social support received [$M = 5.1$, s.d. $= 1.6$] and given [$M = 5.5$, s.d. $= 1.5$] were very highly correlated, $r = .91$, CI [0.84, 0.95], $P < .00001$). Receiving more social support was associated with a lower score on the UCLA Loneliness Scale ($r = -0.47$, CI [$-0.68$, $-0.19$], $P = 0.002$) and a higher frequency of social activities ($r = 0.34$, CI [0.04, 0.59], $P = 0.03$). The amount of social support received (hereafter referred to as social support) was not associated with household income, WAIS-IV vocabulary z scores, or social network size (SNI; all $P$'s $> 0.05$). Nor did scores differ between males and females, $F < 1$. Social support was marginally associated with age ($r = 0.30$, CI [$-0.01$, 0.56], $P = 0.06$) suggesting that older participants reported receiving more support.

Neither measure of stress was associated with social support (perceived stress: $r = -0.19$, CI [$-0.48$, 0.13], $P = 0.23$; SRRS: $r = 0.07$, CI [$-0.24$, 0.38], $P = 0.65$). The scores from the perceived stress scale ($M = 9.53$, s.d. $= 5.20$) and the SRRS ($M = 114.13$, s.d. $= 97.58$) were not correlated, $r = .18$, CI [$-0.14$, 0.46], $P = 0.28$. The perceived stress scale was positively associated with negative affect ($r = 0.56$, CI [0.31, 0.74], $P = 0.0002$) and negatively associated with positive affect ($r = -0.32$, CI [$-0.58$, $-0.01$], $P = 0.04$) from the PANAS. Additionally, both measures of stress were not related to age, WAIS-IV vocabulary z scores, nor did they vary by sex (all $P$'s $> 0.05$).

*Neural measures.* Sex, WAIS-IV vocabulary z scores and social network size were not associated with mPFC (right: $M = 2.26$, s.d. $= 0.14$; left: $M = 2.39$, s.d. $= 0.15$) or amygdala volume ($M = 0.097$, s.d. $= 0.012$), all $P$'s $> 0.05$. Furthermore, amygdala volume was not correlated with cortical thickness of right or left mPFC ($r = 0.02$, CI [$-0.30$, 0.33], $P = 0.92$; $r = 0.01$, CI [$-0.30$, 0.32],

$P = 0.96$, respectively). Since age was marginally associated with right mPFC thickness ($r = 0.30$, CI [$-0.01$, 0.56], $P = 0.06$,) and amygdala volume ($r = -0.33$, CI [$-0.58$, $-0.02$], $P = 0.04$) it was included in the analyses below as a covariate.

### Social support

*Medial PFC.* Linear regression analyses using social support to predict right mPFC cortical thickness revealed that greater cortical thickness in right mPFC was associated with higher social support, ($\beta = 0.42$, CI [0.12, 0.72], $t(38) = 2.83$, $P = 0.007$; Figure 1). This relationship remained significant after adjusting for age ($\beta = 0.36$, CI [0.05, 0.67], $t(37) = 2.34$, $P = 0.02$, $\Delta R^2 = 0.05$). Cortical thickness of left mPFC was not associated with social support ($\beta = 0.13$, CI [$-0.20$, 0.45], $t(38) = 0.77$, $P = 0.44$).

*Amygdala.* In contrast to cortical thickness, linear regression analyses using social support to predict amygdala volume revealed that amygdala volume was inversely related to social support ($\beta = -0.43$, CI [$-0.72$, $-0.13$], $t(38) = -2.90$, $P = 0.006$; Figure 2A). This relationship remained significant after adjusting for age ($\beta = -0.36$, CI [$-0.67$, $-0.05$], $t(37) = -2.37$, $P = 0.02$, $\Delta R^2 = 0.06$). When analyzing left and right amygdala volume separately, the results held suggesting that the relationship between volume and social support was not lateralized.

### Stress

*Medial PFC.* Cortical thickness in right or left mPFC was not associated with scores from the PSS-10 (right: $\beta = -0.02$, CI [$-0.35$, 0.31], $t(38) = -0.14$, $P = 0.88$; left: $\beta = -0.09$, CI [$-0.41$, 0.24], $t = -0.53$, $P = 0.60$) or scores from the SRRS (right: $\beta = 0.02$, CI [$-0.31$, 0.34], $t = 0.10$, $P = 0.92$; left: $\beta = -0.04$, CI [$-0.36$, 0.29], $t(38) = -0.22$, $P = 0.82$).

*Amygdala.* In line with previous work, larger amygdala volumes were related to higher perceived stress ($\beta = 0.36$, CI [0.05, 0.66], $t(38) = 2.36$, $P = 0.02$; Figure 2B). When analyzing left and right amygdala volume separately, the results were significant for both volumes suggesting that this effect is not lateralized. The relationship remained significant after adjusting for age ($\beta = 0.31$, CI [0.004, 0.61], $t(37) = 2.05$, $P = 0.05$, $\Delta R^2 = 0.03$). In contrast, life stress (SRRS) was not associated with amygdala volume ($\beta = -0.11$, CI [$-0.44$, 0.22], $t(38) = -0.68$, $P = 0.50$).

### Whole brain analysis

While the number of participants in this study is not ideal for a whole brain examination of brain/behavioral relationships, we nevertheless conducted an exploratory whole brain surface-based analysis to examine the associations between social support and cortical thickness across the cortex. There were no regions that were significantly associated with social support after performing a cluster-wise correction for multiple comparisons ($P < 0.05$; Hagler *et al*., 2006). When using a more liberal uncorrected threshold of $P < 0.001$, social support was significantly associated with only a region of right medial prefrontal cortex and a region of right insula. Follow up ROI analyses of the full structures revealed that the cortical thickness of the right insula was not associated with social support ($\beta = 0.07$, CI [$-0.26$, 0.40], $t = 0.44$, $P = 0.66$) while the thickness of the right mPFC was ($\beta = 0.42$, CI [0.12, 0.72], $t(38) = 2.83$, $P = 0.007$). Therefore, it is unlikely that this study is obscuring any false-negative relationships between cortical thickness and social support.
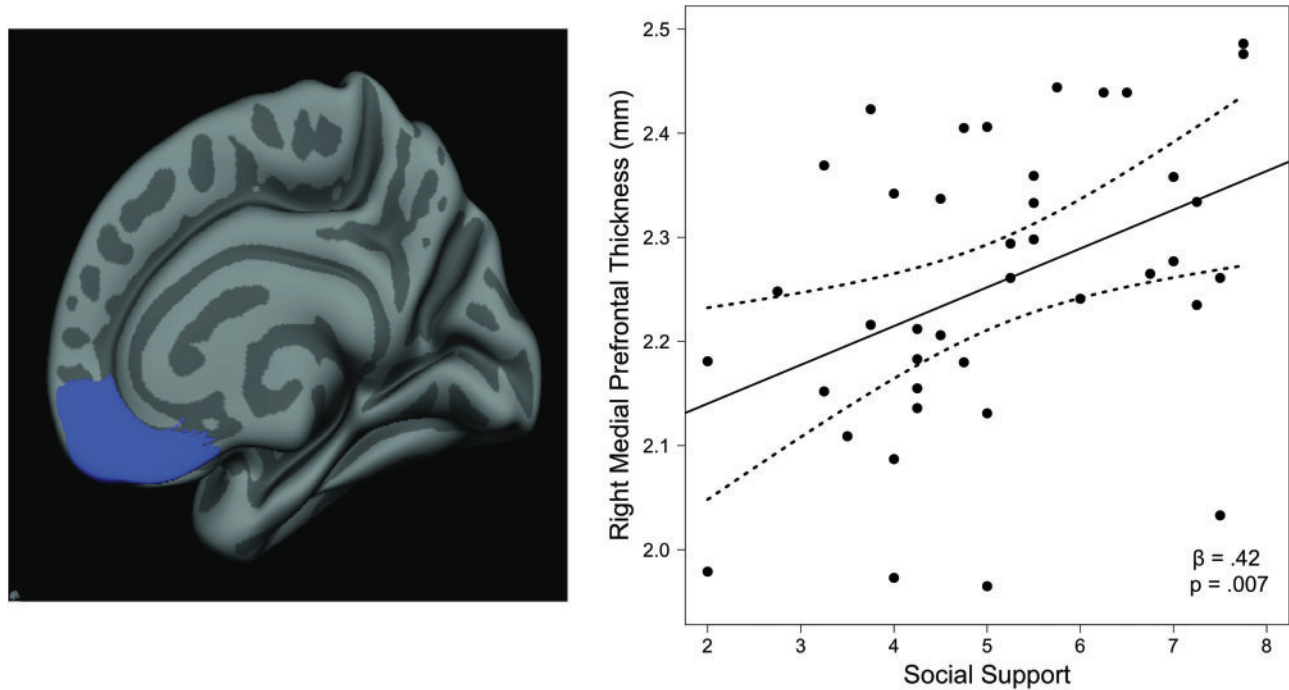
**Fig. 1.** Right medial prefrontal cortical thickness is positively associated with social support. The region displayed is the medial orbitofrontal label from the Desikan Atlas (Desikan et al., 2006). The dotted lines represent 95% confidence intervals.
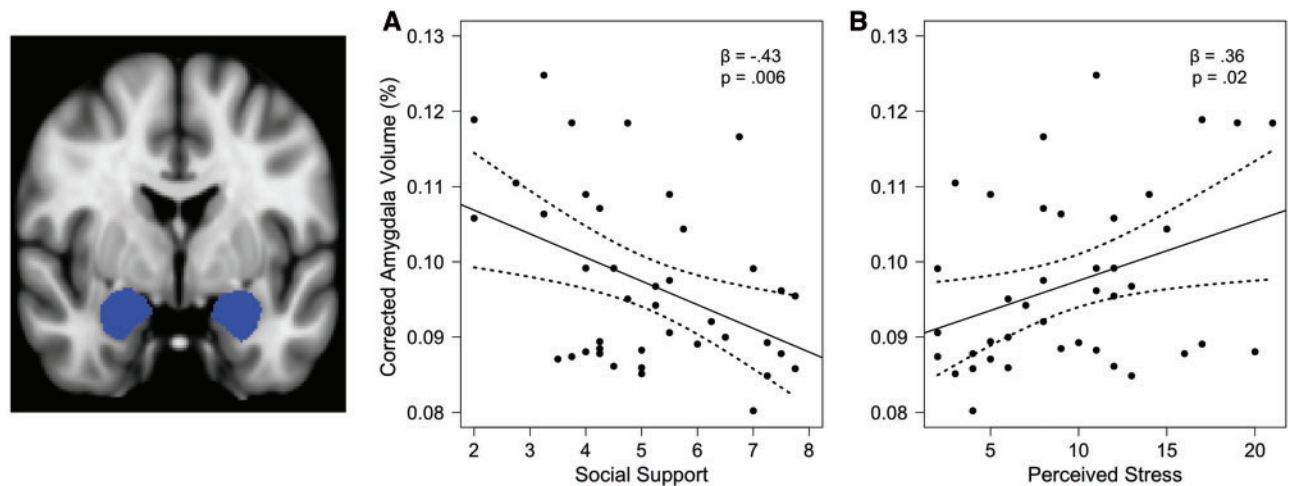


**Fig. 2.** The relationships between amygdala volume (divided by intracranial volume and multiplied by 100), social support, and perceived stress are depicted. Panel A illustrates that higher social support is associated with lower amygdala volume. In contrast, panel B shows the positive relationship between amygdala volume and perceived stress from the Perceived Stress Scale-10 (Cohen et al., 1983). Higher stress scores indicate greater perceived stress. The dotted lines represent 95% confidence intervals.

In summary, right mPFC cortical thickness is positively associated with social support and not associated with stress. This is the only region of the cerebral cortex that reliably revealed this relationship. Moreover, amygdala volumes were negatively correlated with social support and positively associated with perceived stress level.

### Testing stress-buffering and main effect hypotheses

Since amygdala volume was associated with both perceived stress and social support, we used the amygdala volume results in order to test whether our data support the main effect hypothesis or the stress-buffering hypothesis. We conducted a linear regression analysis with social support and perceived stress as the predictors and amygdala volume as the outcome variable; see Figure 3C.

To test the stress-buffering hypothesis, we examined whether the relationship between social support and amygdala volume depended (e.g. 'buffered') on stress level. Social support did not significantly interact with perceived stress suggesting that the relationship between social support and amygdala volume did not vary across stress scores; see Figure 3C. Subsequently we assessed whether perceived stress and social support uniquely contributed to amygdala volume. Consistent with the main effect hypothesis, we demonstrated that amygdala volume was differentially related to social support and
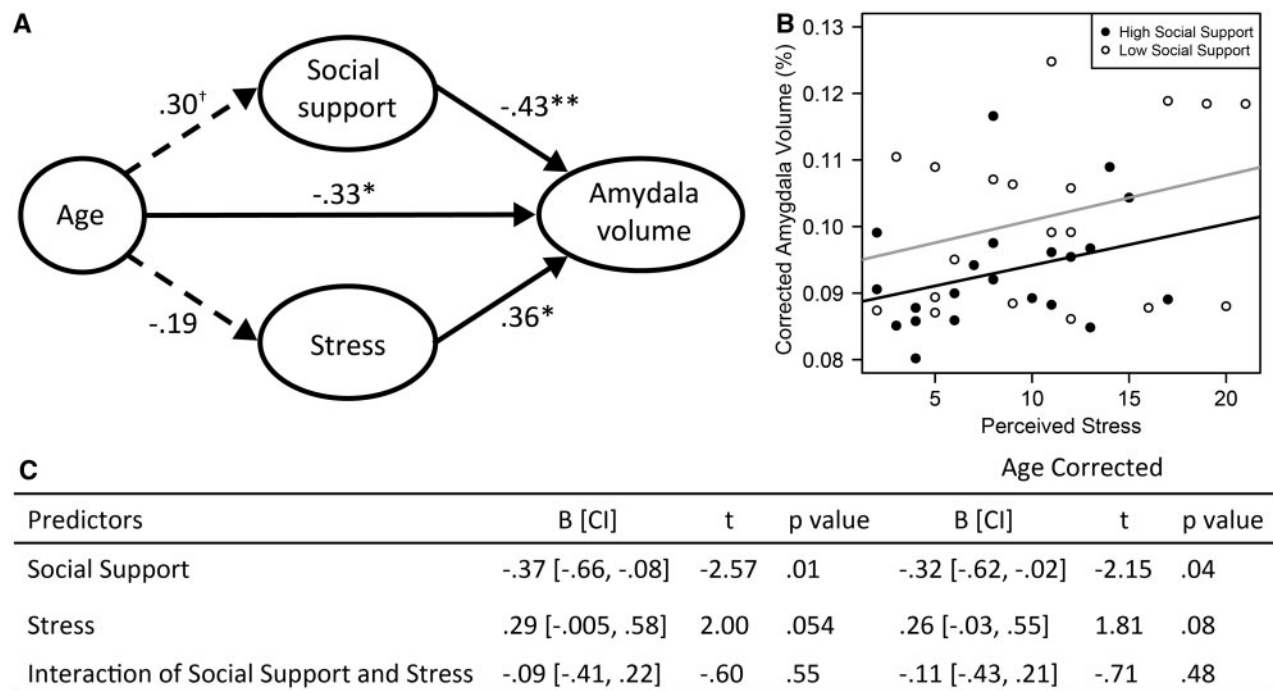
**Fig. 3.** Panel A illustrates the associations among age, social support, stress, and amygdala volume. Standardized beta values (*β*) were calculated for each pathway. The dotted lines represent non-significant pathways. Panel B shows that the association between social support and amygdala volume does not vary across different levels of stress. More perceived stress is associated with larger amygdala volume while more social support is correlated with smaller amygdala volume. A median split was performed on social support so that the black dots represent high social support and the white dots represent low social support. The gray line is the regression line for low social support and the black line is the regression line for high social support. Panel C includes the results of the linear regression analyses using social support and stress to predict amygdala volume. †$P < 0.10$, *$P < 0.05$, **$P < 0.01$.

perceived stress; see Figure 3B. Specifically amygdala volume was negatively associated with social support and marginally positively associated with perceived stress; see Figure 3C. When adjusting for age, the main effect of social support remained significant but the main effect of perceived stress did not, see Figure 3C. This demonstrated that the association between perceived stress and amygdala volume could partially be accounted for by age.

## Discussion

This study examined associations between social support and stress on amygdala-medial prefrontal cortex circuitry in healthy older adults. To our knowledge, this is the first study to examine the patterns of brain morphometry associated with social support, but more importantly, whether those patterns differ depending on varying levels of stress. Our results illustrated that social support was positively associated with cortical thickness of the right mPFC and negatively correlated with amygdala volume. In addition to these important new findings, we found that, consistent with previous research in animals and human adults, amygdala volume was positively associated with stress level. When modeling the combined relationship between social support and stress on amygdala volume, it was revealed that social support and stress *uniquely and differentially* relate to amygdala volume. Therefore, our findings are more consistent with the main effect hypothesis because social support was *directly* associated with brain circuitry that has been implicated in psychological well-being. These results provide early, but compelling evidence for a link between amygdala-medial prefrontal cortex circuitry and social support. The current findings advance our understanding of how supportive relationships are

critically linked to brain circuitry that has been implicated in emotional and social processing.

Due to the cross-sectional nature of the current work, it is not possible to make strong conclusions about the causal direction of our results demonstrating that social support is positively associated with right mPFC cortical thickness and negatively associated with amygdala volume. One possibility is that over the course of the adult lifespan receiving support and experiencing stress causes structural changes in the amygdala-mPFC circuitry. This possibility has support from previous work showing that greater reduction in stress following an 8-week mindfulness-based stress reduction program in middle-aged adult humans led to greater declines in amygdala volume (Holzel *et al.*, 2010). In addition, stress exposure caused increased amygdala volume in rats (Vyas *et al.*, 2002). Many argue that initially stress causes amygdala hyperactivity, which in turn increases volume but after prolonged periods of hyperactivity, amygdala volume decreases. Consequently, more stress is associated with larger amygdala volume in healthy populations and smaller amygdala volume in clinical populations (Tottenham, 2009; Davidson and McEwen, 2012; Holmes *et al.*, 2012). Although no one has looked at the effects of social support on this circuitry longitudinally, changing social support through interventions has been shown to impact both physical and mental health in specific populations (Constantino *et al.*, 2005). Young to middle-aged victims of domestic violence participated in an 8-week intervention program to boost social support. At the end of the intervention, victims had reduced self-reported psychological distress and a decreased need for medical resources due to poor health.

Contrasted with the potential that social support and stress could differentially impact the course of brain aging, it is also

possible that innate differences in the amygdala-mPFC circuitry shape engagement of social support and responses to stress levels over time. This is in line with work showing that the amount of social support people receive is typically fairly stable across the lifespan (Ertel *et al.*, 2009). Therefore we may hypothesize that any changes in social support may be partly a reflection of pre-existing individual differences in functional and structural brain characteristics. Evidence for this may be found in genetic vulnerabilities such as carriers of the short allele in the serotonin transporter gene, who show increased susceptibility to stress (Holmes, 2008; Lee *et al.*, 2005). In addition, short allele carriers have been shown to have altered functional and structural connectivity between the amygdala and mPFC that may result in emotional dysfunctions (Heinz *et al.*, 2004; Pezawas *et al.*, 2005; Pacheco *et al.*, 2009; Volman *et al.*, 2013). Future research should determine the causal direction of the relationships among social support, stress and the amygdala-medial prefrontal cortex circuitry across the lifespan.

In this study, we used two questionnaires to measure stress, the Perceived Stress Scale (PSS-10) and the Social Readjustment Rating Scale (SRRS). Our analyses revealed that amygdala volume was associated with stress measured by the PSS-10 but not the SRRS. Furthermore, the PSS-10 and the SRRS were not correlated, meaning that life-changing events within the past year did not appear to match current perceived stress levels. While experiencing more life-changing events is generally associated with higher perceived stress (Monroe, 2008) the relationship is weaker in older individuals (Cohen *et al.*, 1983). In contrast to the SRRS, the PSS-10 asks individuals how they perceive their global stress level, which may include stress about future events or events not traditionally thought to induce stress. The PSS-10 includes stress pertinent to the individual therefore it may be a better predictor of health outcomes than the number of stressful life events (Cohen *et al.*, 1983). These results suggest that perceived stress levels are reflected in brain circuitry independent of social support.

Due to the cross-sectional nature of our study, we were unable to directly determine the influence of chronic stress across the lifespan, which has been shown to significantly impact brain structures including the amygdala (Lupien *et al.*, 2009). As an indirect measure, the SRRS evaluates probable life stressors, which could serve as a proxy for chronic stress. However, this measure was associated with neither the critical brain circuitry examined here nor the social support measures. Considerable research has revealed that the psychological and physiological reactions to daily stress (i.e. stress reactivity) better predicts mental and physical health rather than the number of possible stressful events (Almeida *et al.*, 2011). Therefore, the lack of a relationship between the SRRS and brain circuitry likely reflects the fact that counting stressful events is not the critical variable with respect to the health effects of stress. Examining individual differences in stress reactivity over time would be an important next step in understanding the relationship between stress, social support and brain circuitry.

Although other human studies have examined the influence of social support on brain function (Eisenberger *et al.*, 2007; Hyde *et al.*, 2011; Bickart *et al.*, 2012) to our knowledge only two previous studies examined the relationship between social support and brain structure in humans (Bickart *et al.*, 2011; Che *et al.*, 2014). Neither study found a relationship between perceived social support and amygdala volume. Che and colleagues (2014) examined a young adult sample and did not include any measures of affect, stress, or mental health outcomes, which greatly limited their ability to explore the associations between social

support and affect-related brain circuitry. In contrast to the current study, Bickart *et al.* (2011) examined 58 participants across a broad age range—from 19 to 83 years old. Only 35 of the participants were defined as older adults ranging from 46 to 83 years old. The current study included 40 individuals ranging from 60 to 78 years old. Our homogeneous older sample may have allowed us to detect and better isolate these relationships. In addition, we found no association between social support and social network size. This is in line with previous work suggesting that social support is distinct from social network size (Berkman *et al.*, 2000). Social network size includes social ties that place demands on individuals, whereas social support comes from social partners who provide help with life tasks that may improve well-being (Antonucci, 2001).

Our novel findings demonstrating that social support was independently associated with affect-related brain circuitry provide evidence consistent with the main effect hypothesis. One recent theory, the Relational Regulation Theory (RRT), postulates a clear mechanism for the main effect hypothesis (Lakey and Orehek, 2011). Unlike the stress-buffering hypothesis, which suggests social support benefits health only during times of stress, the RRT states that social support continually benefits health through daily social interactions. For example, social support provides a sense of belonging, companionship (Thoits, 2011) and encourages individuals to adopt healthy lifestyle behaviors (Thoits, 2011; Karelina and DeVries, 2011). The benefits of active social relationships promoting healthy lifestyles likely contribute to better physical and mental health (Thoits, 2011). In contrast, there are consistent findings illustrating that low social support is linked to poor mental health including major depressive disorder (Lakey and Cronin, 2008) and psychological distress (Finch *et al.*, 1999). Given the important role that the amygdala-mPFC circuitry plays in affect and social processing, ongoing social ties may support the structural integrity of these regions directly, or at the very least delay changes that may occur during the aging process.

There were several limitations with the current study that should be addressed in future work. First, the cross-sectional nature of this study did not allow us to determine the causal direction of these brain/behavior relationships. Nevertheless we uncovered novel associations between supportive relationships, psychological stress and brain circuitry that can guide future work on this topic. Additionally the cross-sectional design did not allow us to measure chronic stress. Future work applying state of the art longitudinal methods will be required to differentiate the influence of chronic from current stress to aid our understanding of how prolonged stress is related to social ties and brain circuitry. Another potential limitation is that our sample included a subset of older individuals that were selected to be in good physical and mental health and therefore is not fully representative of the elderly population at large. Moreover, there were more women than men who participated in this study. While we found no gender differences in amount of social support, stress, mPFC cortical thickness, or amygdala volume, future studies should continue to explore the interaction between social support, stress and brain aging in gender balanced and more diverse samples of elderly adults.

Our study contributes to a growing body of work exploring how social support benefits heath. We have added a unique finding demonstrating how social support is related to a critical emotional regulation circuit in the brain. Moreover, we are able to provide evidence suggesting that the associations between social support and brain structures are independent of stress.

Further research will be needed in order to determine whether these results are from differential effects across the developmental lifespan or reflect preexisting differences in brain circuitry.

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## Funding

## References

Akirav, I., Maroun, M. (2007). The role of the medial prefrontal Cortex-Amygdala Circuit in stress effects on the extinction of fear. *Neural Plasticity*, **2007**, 1–11.

Almeida, D.M., Piazza, J.R., Stawski, R.S., Klein, L.C. (2011). The speedometer of life: Stress, Health and Aging. In: Schaie, K.W., Willis, S.L. editors. *Handbook of the Psychology of Aging*, 7th edn, San Diego, CA: Academic Press.

Antonucci, T.C. (2001). Social relations: an examination of social networks, social support, and sense of control. In: Schaie, K.W. editors. *Handbook of the Psychology of Aging*, 5th edn, pp. 427–453. San Diego, CA: Academic Press

Arnsten, A.F.T. (2009). Stress signalling pathways that impair prefrontal cortex structure and function. *Nature Reviews Neuroscience*, **10**, 410–22.

Berkman, L.F., Glass, T., Brissette, I., Seeman, T.E. (2000). From social integration to health: Durkheim in the new millennium. *Social Science & Medicine*, **51**, 843–57.

Bickart, K.C., Hollenbeck, M.C., Barrett, L.F., Dickerson, B.C. (2012). Intrinsic Amygdala-Cortical functional connectivity predicts social network size in humans. *Journal of Neuroscience*, **32**, 14729–41.

Bickart, K.C., Wright, C.I., Dautoff, R.J., Dickerson, B.C., Barrett, L.F. (2011). Amygdala volume and social network size in humans. *Nature neuroscience*, **14**(2), 163–4.

Birditt, K.S., Newton, N., Hope, S. (2012). Implications of marital/partner relationship quality and perceived stress for blood pressure among older adults. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*. doi:10.1093/geronb/gbs123.

Buckner, R.L., Head, D., Parker, J., *et al.* (2004). A unified approach for morphometric and functional data analysis in young, old, and demented adults using automated atlas-based head size normalization: reliability and validation against manual measurement of total intracranial volume. *NeuroImage*, **23**, 724–38.

Che, X., Wei, D., Li, W., *et al.* (2014). The correlation between gray matter volume and perceived social support: A voxel-based morphometry study. *Social Neuroscience*, **9**, 152–9.

Cohen, S., Wills, T.A. (1985). Stress, social support, and the buffering hypothesis. *Psychological Bulletin*, **98**, 310.

Cohen, S., Doyle, W.J., Turner, R., Alper, C.M., Skoner, D.P. (2003). Sociability and Susceptibility to the Common Cold. *Psychological Science*, **14**, 389–95.

Cohen, S., Kamarck, T., Mermelstein, R. (1983). A global measure of perceived stress. *Journal of Health and Social Behavior*, **24**, 385–396.

Constantino, R., Kim, Y., Crane, P.A. (2005). Effects of a social support intervention on health outcomes in residents of a domestic violence shelter: a pilot study. *Issues in Mental Health Nursing*, **26**, 575–90.

Cook, S.C., Wellman, C.L. (2004). Chronic stress alters dendritic morphology in rat medial prefrontal cortex. *Journal of Neurobiology*, **60**, 236–48.

Dale, A.M., Fischl, B., Sereno, M.I. (1999). Cortical surface-based analysis: I. Segmentation and surface reconstruction. *NeuroImage*, **9**, 179–94.

Davidson, R.J., McEwen, B.S. (2012). Social influences on neuroplasticity: stress and interventions to promote well-being. *Nature Neuroscience*, **15**, 689–95.

Desikan, R.S., Ségonne, F., Fischl, B., *et al.* (2006). An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. *NeuroImage*, **31**, 968–80.

Eisenberger, N.I., Taylor, S.E., Gable, S.L., Hilmert, C.J., Lieberman, M.D. (2007). Neural pathways link social support to attenuated neuroendocrine stress responses. *NeuroImage*, **35**, 1601–12.

Ertel, K.A., Glymour, M.M., Berkman, L.F. (2009). Social networks and health: A life course perspective integrating observational and experimental evidence. *Journal of Social and Personal Relationships*, **26**, 73–92.

Finch, J.F., Okun, M.A., Pool, G.J., Ruehlman, L.S. (1999). A comparison of the influence of conflictual and supportive social inter- actions on psychological distress. *Journal of Personality*, **67**, 581–621.

Fingerman, K.L., Charles, S.T. (2010). It Takes Two to Tango: Why Older People Have the Best Relationships. *Current Directions in Psychological Science*, **19**, 172–6.

Fingerman, K.L., Cheng, Y.P., Birditt, K.S., Zarit, S. (2012). Only as happy as the least happy child: multiple grown children's problems and successes and middle-aged parents' well-being. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, **67B**, 184–93.

Fischl, B., Dale, A.M. (2000). Measuring the thickness of the human cerebral cortex from magnetic resonance images. *Proceedings of the National Academy of Sciences*, **97**, 11050–5.

Fischl, B., Salat, D.H., Busa, E., *et al.* (2002). Whole brain segmentation: automated labeling of neuroanatomical structures in the human brain. *Neuron*, **33**, 341–55.

Fischl, B., Salat, D.H., van der Kouwe, A.J.W., *et al.* (2004). Sequence-independent segmentation of magnetic resonance images. *NeuroImage*, **23**, S69–84.

Gow, A.J., Corley, J., Starr, J.M., Deary, I.J. (2013). Which social network or support factors are associated with cognitive abilities in old age? *Gerontology*, **59**, 454–63.

Hagler, D.J., Jr, Saygin, A.P., Sereno, M.I. (2006). Smoothing and cluster thresholding for cortical surface-based group analysis of fMRI data. *NeuroImage*, **33**, 1093–103.

Hahn, A., Stein, P., Windischberger, C., *et al.* (2011). Reduced resting-state functional connectivity between amygdala and orbitofrontal cortex in social anxiety disorder. *NeuroImage*, **56**, 881–9.

Haley, A.P. (2014). Vascular functions and brain integrity in midlife: effects of obesity and metabolic syndrome. *Advances in Vascular Medicine*, **2014**, 1–7.

Hanson, J.L., Chung, M.K., Avants, B.B., *et al.* (2012). Structural variations in prefrontal cortex mediate the relationship between early childhood stress and spatial working memory. *Journal of Neuroscience*, **32**, 7917–25.

Hanson, J.L., Chung, M.K., Avants, B.B., *et al.* (2010). Early stress is associated with alterations in the orbitofrontal cortex: a tensor-based morphometry investigation of brain structure and behavioral risk. *Journal of Neuroscience*, **30**, 7466–72.

Heinz, A., Braus, D.F., Smolka, M.N., *et al.* (2004). Amygdala-prefrontal coupling depends on a genetic variation of the serotonin transporter. *Nature Neuroscience*, **8**, 20–1.

Holmes, A. (2008). Genetic variation in cortico-amygdala serotonin function and risk for stress-related disease. *Neuroscience and Biobehavioral Reviews*, **32**, 1293–314.

Holmes, A.J., Lee, P.H., Hollinshead, M.O., *et al.* (2012). Individual differences in Amygdala-Medial prefrontal anatomy link negative affect, impaired social functioning, and polygenic depression risk. *Journal of Neuroscience*, **32**, 18087–100.

Holmes, A., Wellman, C.L. (2009). Stress-induced prefrontal reorganization and executive dysfunction in rodents. *Neuroscience and Biobehavioral Reviews*, **33**, 773–83.

Holmes, T.H., Rahe, R.H. (1967). The social readjustment rating scale. *Journal of Psychosomatic Research*, **11**, 213–8.

Holt-Lunstad, J., Smith, T.B., Layton, J.B. (2010). Social relationships and mortality risk: a meta-analytic review. *PLoS Medicine*, **7**, e1000316.

Holzel, B.K., Carmody, J., Evans, K.C., *et al.* (2010). Stress reduction correlates with structural changes in the amygdala. *Social Cognitive and Affective Neuroscience*, **5**, 11–17.

House, J.S., Landis, K.R., Umberson, D. (1988). Social relationships and health. *Science, New Series*, **241**, 540–5.

Hughes, M.E., Waite, L.J., Hawkley, L.C., Cacioppo, J.T. (2004). A short scale for measuring loneliness in large surveys: Results from two population-based studies. *Research on Aging*, **26**, 655–72.

Hyde, L.W., Gorka, A., Manuck, S.B., Hariri, A.R. (2011). Perceived social support moderates the link between threat-related amygdala reactivity and trait anxiety. *Neuropsychologia*, **49**, 651–6.

Karelina, K., DeVries, A.C. (2011). Modeling Social Influences on Human Health. *Psychosomatic Medicine*, **73**, 67–74.

Kuperberg, G.R., Broome, M.R., McGuire, P.K., *et al.* (2003). Regionally localized thinning of the cerebral cortex in schizophrenia. *Archives of General Psychiatry*, **60**, 878–88.

Lakey, B., Cronin, A. (2008). Low social support and major depression: Research, theory and methodological issues. In: Dobson, K.S., Dozois, D. editors. *Risk factors for depression*, pp. 385–408. San Diego, CA: Academic Press.

Lakey, B., Orehek, E. (2011). Relational regulation theory: a new approach to explain the link between perceived social support and mental health. *Psychological Review*, **118**, 482–95.

Lange, C., Irle, E. (1999). Enlarged amygdala volume and reduced hippocampal volume in young women with major depression. *Psychological Medicine*, **34**, 1059–64.

Lee, H.J., Lee, M.S., Kang, R.H., *et al.* (2005). Influence of the serotonin transporter promoter gene polymorphism on susceptibility to posttraumatic stress disorder. *Depression and Anxiety*, **21**, 135–9.

Liao, W., Qiu, C., Gentili, C., *et al.* (2010). Altered effective connectivity network of the Amygdala in social anxiety disorder: a resting-state fMRI study. *PLoS ONE*, **5**, e15238.

Liston, C. (2006). Stress-induced alterations in prefrontal Cortical Dendritic Morphology predict selective impairments in perceptual attentional set-shifting. *Journal of Neuroscience*, **26**, 7870–4.

Lupien, S.J., McEwen, B.S., Gunnar, M.R., Heim, C. (2009). Effects of stress throughout the lifespan on the brain, behaviour and cognition. *Nature Reviews Neuroscience*, **10**, 434–45.

Lupien, S.J., Parent, S., Evans, A.C., *et al.* (2011). Larger amygdala but no change in hippocampal volume in 10-year-old children exposed to maternal depressive symptomatology since birth. *Proceedings of the National Academy of Sciences of the United States of America*, **108**, 14324–9.

Mehta, M.A., Golembo, N.I., Nosarti, C., *et al.* (2009). Amygdala, hippocampal and corpus callosum size following severe early institutional deprivation: the English and Romanian Adoptees Study Pilot. *Journal of Child Psychology and Psychiatry*, **50**, 943–51.

Monroe, S.M. (2008). Modern approaches to conceptualizing and measuring human life stress. *Annual Review of Clinical Psychology*, **4**, 33–52.

O'Brien, L.M., Ziegler, D.A., Deutsch, C.K., *et al.* (2006). Adjustment for whole brain and cranial size in volumetric brain studies: a review of common adjustment factors and statistical methods. *Harvard Review of Psychiatry*, **14**, 141–51.

Pacheco, J., Beevers, C.G., Benavides, C., McGeary, J., Stice, E., Schnyer, D.M. (2009). Frontal-limbic white matter pathway associations with the serotonin transporter gene promoter region (5-HTTLPR) polymorphism. *Journal of Neuroscience*, **29**, 6229–33.

Pezawas, L., Meyer-Lindenberg, A., Drabant, E.M., *et al.* (2005). 5-HTTLPR polymorphism impacts human cingulate-amygdala interactions: a genetic susceptibility mechanism for depression. *Nature Neuroscience*, **8**, 828–34.

Radley, J.J., Sisti, H.M., Hao, J., *et al.* (2004). Chronic behavioral stress induces apical dendritic reorganization in pyramidal neurons of the medial prefrontal cortex. *Neuroscience*, **125**, 1–6.

Rosas, H.D., Liu, A.K., Hersch, S., *et al.* (2002). Regional and progressive thinning of the cortical ribbon in Huntington's disease. *Neurology*, **58**, 695–701.

Salat, D.H. (2004). Thinning of the cerebral cortex in aging. *Cerebral Cortex*, **14**, 721–30.

Salat, D.H., Williams, V.J., Leritz, E.C., *et al.* (2012). Inter-individual variation in blood pressure is associated with regional white matter integrity in generally healthy older adults. *Neuroimage*, **59**(1), 181–92.

Shin, L.M., Wright, C.I., Cannistraro, P.A., *et al.* (2005). A functional magnetic resonance imaging study of amygdala and medial prefrontal cortex responses to overtly presented fearful faces in posttraumatic stress disorder. *Archives of General Psychiatry*, **62**, 273.

Steptoe, A., Kivimäki, M. (2013). Stress and cardiovascular disease: an update on current knowledge. *Annual Review of Public Health*, **34**, 337–54.

Thoits, P.A. (2011). Mechanisms linking social ties and support to physical and mental health. *Journal of Health and Social Behavior*, **52**, 145–61.

Tottenham, N. (2009). A review of adversity, the amygdala and the hippocampus: a consideration of developmental timing. *Frontiers in Human Neuroscience*. doi:10.3389/neuro.09.068.2009.

Tottenham, N., Hare, T.A., Quinn, B.T., *et al.* (2010). Prolonged institutional rearing is associated with atypically large amygdala volume and difficulties in emotion regulation. *Developmental Science*, **13**, 46–61.

Urry, H.L. (2006). Amygdala and ventromedial prefrontal cortex are inversely coupled during regulation of negative affect and predict the diurnal pattern of cortisol secretion among older adults. *Journal of Neuroscience*, **26**, 4415–25.

Volman, I., Verhagen, L., den Ouden, H.E.M., *et al.* (2013). Reduced serotonin transporter availability decreases prefrontal control of the amygdala. *Journal of Neuroscience*, **33**, 8974–9.

Vyas, A., Mitra, R., Rao, B.S., Chattarji, S. (2002). Chronic stress induces contrasting patterns of dendritic remodeling in hippocampal and amygdaloid neurons. *The Journal of Neuroscience*, **22**, 6810–18.

Watson, D., Clark, L.A., Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: the

PANAS scales. *Journal of Personality and Social Psychology*, **54**, 1063.

Wonderlick, J.S., Ziegler, D.A., Hosseini-Varnamkhasti, P., *et al.* (2009). Reliability of MRI-derived cortical and subcortical morphometric measures: effects of pulse sequence, voxel geometry, and parallel imaging. *NeuroImage*, **44**, 1324–33.

Wright, C.I., Williams, D., Feczko, E., *et al.* (2005). Neuroanatomical correlates of extraversion and neuroticism. *Cerebral Cortex*, **16**, 1809–19.

Wechsler, D. (2008). *Wechsler adult intelligence scale*, 4th edn. San Antonio, TX: NCS Pearson.

Wechsler, D. (2009). *Wechsler Memory Scale*, 4th edn. San Antonio, TX: Pearson.