Perceived stress is associated with smaller hippocampal volume in adolescence

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Abstract
Perceived stress has been associated with decreased hippocampal, amygdala, and prefrontal cortex volume, as well as decreased memory and executive functioning performance in adulthood. Parents’ perceived stress has been linked to decreased hippocampal volume in young children. However, no studies have investigated the links between self-perceived stress and brain structure or function in adolescents. Additionally, findings from previous research with younger or older samples are inconsistent, likely in part due to inconsistencies in participants’ age range. In this study, we investigated the associations among self-perceived stress, family socioeconomic factors (family income, parental education), subcortical (hippocampus, amygdala) volumes, prefrontal cortical thickness and surface area, and memory and executive functioning performance in adolescents. One hundred and forty-three participants (12–20 years old) were administered a cognitive battery, a questionnaire to assess perceived stress, and a structural MRI scan. Higher levels of perceived stress were associated with decreased adolescent hippocampal volume. This study provides empirical evidence of how experience may shape brain development in adolescence—a period of plasticity during which it may be possible to intervene and prevent negative developmental outcomes.

KEYWORDS
adolescence, amygdala, hippocampus, perceived stress, prefrontal cortex, stress

1 | INTRODUCTION

Although acute stress is an adaptive response to real or perceived threats, chronic exposure to stress may have deleterious effects on brain structure, cognition, and mental health (McEwen, 1998b, 1999, 2001, 2006). Among the factors contributing to chronic stress are adverse socioeconomic circumstances, as well as exposure to traumatic events, abuse, and neglect (for a review, see Blair & Raver, 2016; Tottenham & Sheridan, 2010). Exposure to chronic stress has been associated with physiological and neuroendocrine dysregulation of stress response mechanisms (Evans & Kim, 2007; Lupien, King, Meaney, & McEwen, 2000, 2001; Lupien, Ouellet-Morin, Herba, Juster, & McEwen, 2016; McEwen, 1998a; Whittle et al., 2011). Higher levels of stress have been related to functional and structural alterations in areas of the brain that regulate stress hormones (Pruessner et al., 2008), including the hippocampus, amygdala, and prefrontal cortex (Blair & Raver, 2016; Hanson et al., 2015; McEwen & Gianaros, 2010; Romeo, 2017; Tottenham & Sheridan, 2010). Together, this network is considered critical for the functioning of memory (McEwen & Gianaros, 2010) and self-regulation (Gianaros et al., 2007; McEwen & Gianaros, 2010).

The perception of stress may drive these physiological consequences. Evidence from previous research examining the associations between perceived stress and brain structure varies, depending in part on analysis techniques, brain regions evaluated, and the gender and age of the sample. For
example, studies with older samples (including postmeno-
pausal women) have reported that higher perceived stress is
associated with decreased gray matter volume in the hippo-
campus (Gianaros et al., 2007; Lindgren, Bergdahl, &
Nyberg, 2016; Pagliaccio et al., 2014; Zimmerman et al.,
2016), amygdala (Hölzel et al., 2009), and prefrontal cortex
(Gianaros et al., 2007; Moreno, Bruss, & Denburg, 2017), as
well as with deleterious effects on cognitive outcomes
(Aggarwal et al., 2014; Korten, Comijs, Penninx, & Deeg,
2017; Munoz, Sliwinska, Scott, & Hofer, 2015; Rubin et al.,
2015). Additionally, stressful life events reported by parents
have been associated with decreased hippocampal volume in
their children (Luby et al., 2013; Pagliaccio et al., 2014), as
well as with reductions in children’s prefrontal cortical vol-
ume (Buss, Davis, Muftuler, Head, & Sandman, 2010) and
reduced performance in executive function measures in child-
hood (Blair et al., 2011; Merz, Harle, Noble, & McCall,
2016). However, the link between perceived stress and chil-
ren’s amygdala volume is less clear, with some work report-
ing that increased perceived stress is associated with smaller
amygdala volume in children (Pagliaccio et al., 2014), other
work reporting that stress is associated with larger amygdala
volume in children (Tottenham et al., 2010), and still other
work finding no association between stress and amygdala vol-
ume (Luby et al., 2013).

In adolescents, we have the unusual ability to inquire
about the individual’s own perception of stress relatively
early in life. However, the effects of self-perceived stress on
the structure of the adolescent brain are largely unknown.
This represents a key gap in the literature, as stress response
mechanisms are still undergoing development during the ado-
lescent period (Hollenstein, McNeely, Eastabrook, Mackey,
& Flynn, 2012; Romeo, 2010) and may result in different
neural consequences during adolescence as compared to other
life stages (Lupien, McEwen, Gunnar, & Heim, 2009). Due
to pubertal changes in gonadal hormones and sensitivity of
the hypothalamic-pituitary-adrenal axis (HPA), adolescents
are highly vulnerable to the consequences of stress that can
persist into adulthood as potentiation or incubation effects
(Lupien et al., 2016). Moreover, adolescence is marked by
intense neurobiological and cognitive changes related to the
maturational alterations in the brain structure (Spear, 2000),
representing an important opportunity to intervene and pre-
vent negative developmental outcomes.

In this study, we asked whether adolescents’ own percep-
tion of stress would be associated with brain structure and
memory and executive functioning performance. We investi-
gated the associations among perceived stress, family socioe-
omic factors (family income, parental education), subcortical volumes (hippocampus, amygdala), prefrontal
cortical thickness and surface area, and memory and execu-
tive functioning performance in adolescents. Based on previ-
ous research with younger (Luby et al., 2013; Pagliaccio
et al., 2014) and older participants (Aggarwal et al., 2014;
Gianaros et al., 2007; Hölzel et al., 2009; Lindgren, Berg-
dahl, & Nyberg, 2016; Moreno et al., 2017; Munoz, Sliwin-
ski, Scott, & Hofer, 2015; Pagliaccio et al., 2014; Zimmer-
man et al., 2016), we hypothesized that higher per-
ceived stress in adolescence would be associated with reduc-
tions in hippocampal volume, amygdala volume, prefrontal
cortical thickness and surface area, and memory and execu-
tive functioning performance. Finally, we explored whether
socioeconomic factors may moderate these associations,
given that socioeconomic circumstance has been related to
stress (Blair & Raver, 2016; Tottenham & Sheridan, 2010)
and may moderate links with brain structure and function
(Brito, Piccolo, & Noble, 2017; Noble, McCandliss, &
Farah, 2007; Merz, Tottenham, & Noble, 2017; Noble et al.,
2012; Piccolo, Merz, He, Sowell, & Noble, 2016).

2 | METHOD

2.1 | Participants

This study included 143 participants from the multisite Pedi-
atric Imaging, Neurocognition, and Genetics (PING) study
(http://ping.chd.ucsd.edu). Participants were included if they
had complete data available for the following measures: Per-
ceived Stress Scale (PSS-10), parental education, family
income, age, gender, genetic ancestry factor (GAF), scanner
serial number, hippocampus volume, amygdala volume, pre-
frontal cortex morphometry (including volume, surface area,
and cortical thickness of inferior frontal gyrus [IFG], middle
frontal gyrus [MFG], and anterior cingulate cortex [ACC], as

<table>
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<th>TABLE 1 Sample demographics</th>
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<tr>
<td>$M$ (SD) or $n$ (%)</td>
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<tr>
<td>Age in years</td>
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<tr>
<td>Sex</td>
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<tr>
<td>Female</td>
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<tr>
<td>Male</td>
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<tr>
<td>SES</td>
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<tr>
<td>Parental education in years</td>
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<tr>
<td>Family income in U.S. dollars</td>
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<tr>
<td>Genetic ancestry factor (GAF)</td>
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<tr>
<td>African</td>
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<td>Central Asian</td>
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<tr>
<td>East Asian</td>
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<td>European</td>
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</table>

$N = 143$. |
well as executive functioning measures (see Table 1 for sample demographics). Participants from the PING study were recruited at nine university-based data collection sites in the cities of Los Angeles, Davis, New Haven, Sacramento, San Diego, Boston, Baltimore, Honolulu, and New York. Exclusion criteria involved report of history of neurological, psychiatric, medical, or developmental disorders. All participants and their parents gave their informed written consent/assent to participate in all study procedures. Each data collection site’s Office of Protection of Research Subjects and Institutional Review Board approved the study.

2.2 | Instruments and procedures

2.2.1 | PSS-10

This self-administered scale was used to measure an individual’s level of perceived stress and has been widely used to measure chronic stress (Cohen, Kamarck, & Merelstein, 1983). The PSS-10 includes 10 questions about the person’s feelings and thoughts during the past month. The response options for each feeling or thought indicate the frequency with which it occurred: 0 = never, 1 = almost never, 2 = sometimes, 3 = fairly often, and 4 = very often, with higher scores indicating higher levels of chronic stress (in this sample, $M = 15.25$, $SD = 6.26$). Although not designed to be a diagnostic instrument, the scale has good reliability and validity and has been used in many settings.

2.2.2 | Socioeconomic status (SES)

Parents reported the total yearly family income and their level of educational attainment. Parental education was measured by averaging maternal and paternal years of education. Both parental education and family income data were collected in bins, which were recoded as the means of the bins for analysis (Noble et al., 2015). Family income was natural log-transformed, as it was positively skewed. Parent education and income were highly correlated ($r = .525$, $p < .001$).

2.2.3 | Structural MRI

Detailed information about the standardized structural MRI protocol administered in each site and the pre- and postprocessing techniques were reported previously (Fjell et al., 2012). In this study, the MRI protocol was performed at six different sites: Los Angeles ($N = 20$), San Diego ($N = 44$), Honolulu ($N = 29$), New Haven ($N = 14$), New York ($N = 26$), and Baltimore ($N = 10$). High-resolution structural MRI included a three-dimensional T1-weighted scan. A modified Freesurfer software suite (http://surfer.nmr.mgh.harvard.edu/) was used to analyze the images and obtain the measures of cortical and subcortical volume, and vertexwise cortical thickness and surface area. Subcortical structures were labeled using an automated, atlas-based, volumetric segmentation procedure (Fischl et al., 2002). Volumes in mm$^3$ were calculated for each structure. All MRI data passed a standardized quality-image check (see Jernigan et al., 2016, for details).

2.2.4 | GAF

A complete description of the genetic ancestry of the PING sample is presented elsewhere (Akshoomoff et al., 2014; Fjell et al., 2012). Briefly, saliva samples were analyzed in the Scripps Translational Research Institute. Genomic DNA was genotyped with Illumina Human660W-Quad BeadChip, and replication and quality control filters (sample call rate $> 99$, call rates $> 95\%$, minor allele frequency $> 5\%$) were performed (Bakken et al., 2012). A supervised clustering approach implemented in the ADMIXTURE software was used to assess genetic ancestry and admixture proportions in the PING participants (Alexander & Lange, 2011). Through this approach, a GAF was developed for each participant, representing the proportion of ancestral descent for each of six major continental populations: African, Central Asian, East Asian, European, Native American, and Oceanic.

2.2.5 | Cognitive measures

Performance on episodic memory, working memory, inhibition, and cognitive flexibility tasks were evaluated using the NIH Toolbox Cognitive Function Battery (Weintraub et al., 2013), as described below.

Picture Sequence Memory Test

The task evaluated episodic memory and involved recalling increasingly lengthy series of illustrated objects and activities that were presented one at a time in the center of the computer screen. The stimuli were presented in a fixed order, with corresponding audio-recorded brief definitions of its contents. The participants were asked to recall the sequence of pictures, by moving each picture from the center to its correct location to replicate the correct sequence. Three test trials were administered to each participant with the level of difficulty adjusted for different age ranges. One point was computed for each adjacent pair of pictures correctly placed. Final scores corresponded to the number of correct adjacent pairs reproduced (Akshoomoff et al., 2014; in this sample, $M = 33.17$, $SD = 8.34$).

List Sorting Working Memory Test

This test requires immediate recall and sequencing of different pictures of different foods and animals displayed on the computer screen visually (object) and orally (spoken name), one at a time. Participants were asked to order stimuli by size, from smallest to largest (Tulsky et al., 2013). The test
was divided into the one-list (one category) and two-list conditions (two categories). In the one-list condition, all stimuli come from one category (food or animals) and in the two-list condition, stimuli are presented from two categories (food and animals, mixed). The participant must report first all stimuli from one category, then from the other, in order of size within each. Working memory scores consisted of combined total items correct on both one-list and two-list conditions, with a maximum of 28 points (in this sample, $M = 21.08$, $SD = 2.63$).

**Flanker Inhibitory Control Test**
This test required the participant to focus on a given stimulus while inhibiting attention to stimuli flanking it. The test consisted of a block of 25 fish trials and a block of 25 arrow trials, with 16 congruent and 9 incongruent trials in each block, presented in pseudorandom order in the center of a computer screen. On congruent trials, all the stimuli were pointing in the same direction. On the incongruent trials, the flanker fish/arrow was pointing in the opposite direction of the central fish/arrow. Congruent and incongruent trials were intermixed in the block of standard trials. The accuracy score was based on performance on both congruent and incongruent trials. A two-vector method was used that incorporated both accuracy and reaction time for participants who maintained a high level of accuracy (>80% correct) and accuracy only for those who did not meet these criteria. Each vector score ranged from 0 to 5, for a maximum total score of 10 (in this sample, $M = 8.78$, $SD = .58$).

**Dimensional Change Card Sort Cognitive Flexibility Task (DCCS)**
The DCCS is a measure of cognitive flexibility. Two target pictures were presented, one on each side of the screen and

<table>
<thead>
<tr>
<th></th>
<th>PSS</th>
<th>Income</th>
<th>PED</th>
<th>PSMT</th>
<th>WM</th>
<th>Flanker</th>
<th>DCCS</th>
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<tr>
<td><strong>Income</strong></td>
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<td>.525**</td>
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<tr>
<td><strong>WM</strong></td>
<td>-.015</td>
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<td>.240**</td>
<td>.385**</td>
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<td></td>
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</tr>
<tr>
<td><strong>Flanker</strong></td>
<td>.006</td>
<td>.086</td>
<td>.072</td>
<td>.221**</td>
<td>.143</td>
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<tr>
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<td>.104</td>
<td>.270**</td>
<td>.295**</td>
<td>.683**</td>
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<td>.103</td>
<td>-.019</td>
<td>.208*</td>
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<td>.158</td>
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<tr>
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<td>-.047</td>
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<td>.085</td>
<td>.040</td>
<td>.158</td>
<td>.102</td>
<td>.172*</td>
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<tr>
<td><strong>R_Hippo</strong></td>
<td>-.038</td>
<td>.155</td>
<td>.121</td>
<td>.007</td>
<td>.200*</td>
<td>.092</td>
<td>.184*</td>
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<tr>
<td><strong>R_Amyg</strong></td>
<td>-.048</td>
<td>.178*</td>
<td>.091</td>
<td>.055</td>
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<tr>
<td><strong>L_Hippo</strong></td>
<td>-.119</td>
<td>.183*</td>
<td>.076</td>
<td>-.043</td>
<td>.198*</td>
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<td>.117</td>
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<tr>
<td><strong>L_Amyg</strong></td>
<td>-.042</td>
<td>.184*</td>
<td>.072</td>
<td>.019</td>
<td>.181*</td>
<td>.106</td>
<td>.198*</td>
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<tr>
<td><strong>MFG CT</strong></td>
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<td>-.009</td>
<td>.026</td>
<td>-.094</td>
<td>-.022</td>
<td>-.236**</td>
<td>-.189*</td>
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<td><strong>IFG CT</strong></td>
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<td>.054</td>
<td>.116</td>
<td>-.022</td>
<td>.036</td>
<td>-.279**</td>
<td>-.175*</td>
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<tr>
<td><strong>ACC CT</strong></td>
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<td>-.006</td>
<td>-.030</td>
<td>-.010</td>
<td>-.090</td>
<td>-.239**</td>
<td>-.173*</td>
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<td>-.095</td>
<td>.099</td>
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<td>.035</td>
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<td>.130</td>
<td>.009</td>
<td>.111</td>
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<tr>
<td><strong>ACC SA</strong></td>
<td>.075</td>
<td>.171</td>
<td>.069</td>
<td>-.016</td>
<td>.191*</td>
<td>.080</td>
<td>.182*</td>
</tr>
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</table>

*Note. PSS = Perceived Stress Scale; PED = parental education; PSMT = Picture Sequence Memory Test; WM = List Sorting Working Memory Test; DCCS = Dimensional Change Card Sort Cognitive Flexibility Task; R_Hippo = right hippocampus volume; R_Amyg = right amygdala volume; L_Hippo = left hippocampus volume; L_Amyg = left amygdala volume; MFG = medium frontal gyrus; IFG = inferior frontal gyrus; ACC = anterior cingulate cortex; CT = cortical thickness; SA = surface area.

*p < .05. **p < .01.
varying along two dimensions (e.g., shape and color). Participants were asked to match a series of bivalent test pictures (e.g., yellow balls and blue trucks) to the target pictures, first according to one dimension (e.g., color) and then after a number of trials, according to the other dimension (e.g., shape). In the “switch” trials, the participant must change the dimension being matched. Scoring is based on a combination of accuracy and reaction time for participants who maintained a high level of accuracy (> 80% correct) and accuracy only for those who did not meet this criterion. Each vector score ranged from 0 to 5, for a maximum total score of 10 (in this sample, M = 8.59, SD = .64).

3.3 | Statistical analyses

Descriptive statistics (Table 1) and Pearson correlations (Table 2) were analyzed to describe the sample and to explore the relationship between the variables. Linear multiple regressions were used to investigate the associations between perceived stress; socioeconomic factors (family income, parental education); left and right hippocampus; left and right amygdala; IFG, MFG, and ACC structure (volumes, surface area, cortical thickness); and cognitive measures, controlling for age, age squared, sex, scanner site, and GAF. In the models using hippocampus or amygdala volumes as outcomes, whole brain volume was additionally included as a covariate. The regression models were performed by adding all control variables in a first step and then adding perceived stress to the models. Scanner site, sex, and GAF were entered as dummy variables. Analyses were performed using SPSS version 23, and moderation models were tested using PROCESS (Hayes, 2015). Multiple comparisons were verified using false discovery rate analyses.

3 | RESULTS

3.1 | Bivariate correlations

Bivariate correlations (see Table 2) showed that perceived stress was not correlated with socioeconomic factors, brain structure, or cognitive measures. Family income was positively correlated with left hippocampus (r = .18, p = .029), left amygdala (r = .18, p = .028), right amygdala (r = .18, p = .033), and ACC volume (r = .17, p = .04). Family income (r = .22, p = .007) and parental education (r = .24, p = .004) were correlated with working memory task performance.

3.2 | Perceived stress associated with hippocampal volume

Greater perceived stress was associated with smaller total hippocampal (β = -.17, p = .017, adjusted [adj.] R² = .45) and left hippocampal size (β = -.22, p = .003, adj. R² = .41), controlling for age, age squared, sex, GAF, scanner site, and whole brain volume (Figure 1). This relationship remained significant when controlling for parental education (total hippocampal volume: β = -.18, p = .014, adj. R² = .45; left hippocampus: β = -.23, p = .003, adj. R² = .41) or family income (total hippocampal volume: β = -.17, p = .018, adj. R² = .45; left hippocampus: β = -.22, p = .004, adj. R² = .41). No statistically significant association was found between perceived stress and right hippocampus volume, left/right amygdala volume, IFG, MFG, or ACC cortical thickness or surface area. Perceived stress was not significantly associated with any socioeconomic factors or cognitive measures. Socioeconomic factors did not moderate the association between perceived stress and brain structures.
DISCUSSION

Several recent studies in adults have reported that higher perceived stress levels are associated with smaller hippocampal volumes (Gianaros et al., 2007; Lindgren et al., 2016; Romeo, 2017; Zimmerman et al., 2016), a structure sensitive to the experience of stress (McEwen, 2001). Similarly, recent work has reported that increased parental perceptions of stress are associated with smaller hippocampal volumes in young children (Luby et al., 2013; Pagliaccio et al., 2014). This study extends this work by examining the association between perceived stress and brain structures earlier in development—specifically during adolescence, a unique time period in which we can reliably investigate an individual’s own perception of stress relatively early in life. Because adolescence is marked by intense hormonal, neurobiological, and cognitive changes, adolescents are highly vulnerable to the consequences of stress (Lupien et al., 2016).

Previous research into the associations among perceived stress, SES, and brain structure and function have been mixed, depending in part on the sample age range and gender, analysis method, brain measures, and control variables. Our findings are in accordance with results from some previous findings, but contrary to others. We discuss these differences below.

The association between higher levels of perceived stress and decreased total hippocampal volume is broadly consistent with the literature (Lindgren et al., 2016; Luby et al., 2013; Zimmerman et al., 2016). However, while studies in young children must rely either on parental report of stress or physiological measures (e.g., Luby et al., 2013), here we found that higher levels of adolescents’ self-perceived stress were associated with reduced hippocampal volume. This finding suggests that the effect of perceived stress on brain structure may be similar to physiological stress effects.

Animal research has consistently demonstrated that the wear and tear produced by repeated stressful situations may result in damage to the HPA axis and resultant reductions in hippocampal volume (McEwen, 2001; McEwen, Nasca, & Gray, 2016; Romeo, 2017). However, the extent to which this effect is lateralized is controversial. In line with our findings, one other study found a specific association between stressful life events (reported by the parents) and decreased left (but not right) hippocampal volume in young children (Luby et al., 2013). Another study reported a link between perceived stress and left hippocampal size, but only for individuals with certain genetic profiles (Pagliaccio et al., 2014). On the other hand, Gianaros and colleagues (2007) found that higher perceived stress was associated with a smaller right (but not left) hippocampal volume in postmenopausal women. Variations in the age range and sex of participants across these studies may have driven these differences.

Additionally, Gianaros and colleagues speculated that the morphology of the right hippocampus and networked brain areas may be more closely related than left hippocampus areas to indicators of moderate perceived stress. In supplementary analyses, the same authors reported a reduction in left hippocampal gray matter volume as a function of high levels of perceived stress (Gianaros et al., 2007). In fact, adolescents participating in our research reported relatively high mean scores of perceived stress ($M = 15.25$, $SD = 6.26$) when compared to the mean scores from Gianaros and colleagues’ study ($M = 8.75$; $SD = 2.44$), and similar mean scores when compared to the PSS-10 original studies (Cohen et al., 1983; Cohen & Janicki-Deverts, 2012; $M = 14.54$; $SD = 5.95$), supporting Gianaros’s hypotheses.

We did not find associations between adolescents’ perceived stress and amygdala or prefrontal cortical volumes in this sample, similar to some previous research findings (Luby et al., 2013; Pagliaccio et al., 2014), but in contrast to others (Gianaros et al., 2007; Hölz et al., 2009; Moreno et al., 2017). These disparities may reflect differences in analysis techniques, for example, evaluating amygdala gray matter density rather than volume (Hölz et al., 2009) or studying postmenopausal women or older adults rather than adolescents (Gianaros et al., 2007; Moreno et al., 2017). We additionally did not find associations between perceived stress and cognitive measures, similar to some previous research (Ronnlund, Sundstrom, Sorman, & Nilsson, 2013; Zimmerman et al., 2016), but distinct from other work (Aggarwal et al., 2014; Boals & Banks, 2012; Korten et al., 2017; Munoz, Sliwinski, Scott, & Hofer, 2015; Rubin et al., 2015). Each of these studies examined adults or elderly individuals; none included adolescents in the sample.

In the present study, although family income was positively correlated with hippocampal, amygdala, and ACC volumes, we did not find a significant link between socioeconomic factors and adolescents’ perceived stress. Previous work has shown that socioeconomically disadvantaged children are more likely to be exposed to stressful environments (Blair & Raver, 2016; Evans, 2004), and are more likely to exhibit dysregulation of physiological and neuroendocrine mechanisms responsible for stress response modulation (Evans & Kim, 2007; Hair, Hanson, Wolfe, & Pollak, 2015; Lupien et al., 2000, 2001, 2016; Sripada, Swain, Evans, Welsh, & Lib erzon, 2014). However, socioeconomic disparities in parental reports of perceived stress have been mixed (Ursache, Merz, Meyer, & Noble, 2017; Ursache, Noble, & Blair, 2015). One possibility is that adolescents’ perception of their stressful experiences may reflect relationships with peers or teachers that are not captured by the family-level socioeconomic indicators used in this study.

This study has several limitations. First, this is a cross-sectional and correlational study, and as such we are unable to interpret our findings in terms of the direction of causality. One possibility is that higher levels of perceived stress cause...
reduced hippocampal volume (Conrad, LeDoux, Magarinos, & McEwen, 1999; Isogor, Kabbaj, Akil, & Watson, 2004; Sapolsky, 1996; Tottenham & Sheridan, 2010). Alternatively, smaller hippocampal volume may increase vulnerability for stress perception (Gilbertson et al., 2002; Kasai et al., 2008). Indeed, some studies have suggested that smaller hippocampal volume may precede dysfunctional stress responses (Gilbertson et al., 2002; Kasai et al., 2008; Kremen, Koenen, Afari, & Lyons, 2012; Lindgren et al., 2016; van Rooij et al., 2015). Longitudinal studies may answer developmental questions more precisely (Mills & Tannies, 2014). Additionally, the development of subcortical brain structures depends on other unmeasured biological processes, such as genetic influence (Hibar et al., 2015). Finally, although restricted to adolescence, the sample’s age range was relatively wide. Pubertal status should be considered in future studies and, as such, our results should be interpreted with caution.

Nonetheless, this study contributes to the emerging literature investigating the effects of stress on brain structure and function in adolescence, by providing empirical evidence of how experience may shape brain development. Fortunately, the effects of psychosocial stress on neural processes may be reversible (Liston, McEwen, & Casey, 2009). Nurturing environments may minimize the negative consequences of biologically and psychologically toxic events (Biglan, Flay, Embry, & Sandler, 2012). In this sense, the neural plasticity of adolescence may represent an opportunity to propose interventions focusing on stress reduction in order to promote healthy brain development.

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