



Socioeconomic Status, Amygdala Volume, and Internalizing Symptoms in Children and Adolescents

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The associations among socioeconomic disadvantage, amygdala volume, and internalizing symptoms in children and adolescents are unclear and understudied in the extant literature. In this study, we examined associations between socioeconomic status (SES) and amygdala volume by age across childhood and adolescence to test whether socioeconomic disadvantage would be associated with larger amygdala volume at younger ages but with smaller amygdala volume at older ages. We then examined whether SES and amygdala volume were associated with children's levels of anxiety and depression. Participants were 3- to 21-year-olds from the Pediatric Imaging, Neurocognition, and Genetics study ($N = 1,196$), which included structural magnetic resonance imaging. A subsample ($n = 327$; 7–21 years of age) completed self-report measures of anxiety and depression. Lower family income and parental education were significantly associated with smaller amygdala volume in adolescence (13–21 years) but not significantly associated with amygdala volume at younger ages (3–12 years). Lower parental education, but not family income, was significantly associated with higher levels of anxiety and depression, even after accounting for family history of anxiety/depression. Smaller amygdala volume was significantly associated with higher levels of depression, even after accounting for parental education and family history of anxiety/depression. These findings suggest that associations between SES and amygdala structure may vary by age. In addition, smaller amygdala volume may be linked with an increased risk for depression in children and adolescents.

Current estimates indicate that more than one in five children in the United States grow up in poverty (U.S. Census Bureau, 2015). Although socioeconomic disadvantage is known to increase children's risk for internalizing problems (Wadsworth, Evans, Grant, Carter, & Duffy, 2016), the neural mechanisms underlying this

association are not well understood. The amygdala plays a central role in emotion processing, particularly threat detection and fear learning (Adolphs, Tranel, Damasio, & Damasio, 1995; Sergerie, Chochol, & Armony, 2008), and is vulnerable to the effects of early life stress (Tottenham & Sheridan, 2009). Although studies have demonstrated associations between socioeconomic status (SES) and amygdala volume in children, the findings have been inconclusive (Hanson et al., 2015; Luby et al., 2013; Noble, Houston, Kan, & Sowell, 2012), possibly due to differences in age or timing of exposure. Thus, the goal of the present

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research was to examine whether associations between SES and amygdala volume vary across development, and how SES and amygdala volume relate to internalizing symptoms in children and adolescents.

SES and Internalizing Problems in Children and Adolescents

Anxiety and depression are among the most common types of psychopathology during childhood and adolescence (Merikangas et al., 2010). In general, children's risk for these internalizing problems varies based on differences in temperament and environmental exposures, including poverty (Hostinar, Nusslock, & Miller, 2017; McLaughlin, 2016). Indeed, socioeconomic disadvantage, including low family income and parental educational attainment, has consistently been found to increase children's risk for internalizing problems (Wadsworth et al., 2016). For instance, in longitudinal studies, early poverty has been found to predict elevated later risk for internalizing problems, even after accounting for initial levels of symptoms (Ackerman, Brown, & Izard, 2004; Najman et al., 2010; Spence, Najman, Bor, O'Callaghan, & Williams, 2002). In addition, a longer duration of poverty has been linked with greater risk for internalizing problems (Slopen, Fitzmaurice, Williams, & Gilman, 2010). These findings raise questions about the ways in which socioeconomic disadvantage may influence brain development and in turn increase children's risk for internalizing problems.

SES and Amygdala Volume in Children and Adolescents

SES tends to reflect the quality of multiple aspects of children's environments, including their level of exposure to chronic stress. Children in lower SES families are more likely to face numerous stressors, including neighborhood violence, chaotic households, and family turmoil (Evans & Kim, 2013). It has been theorized that poverty-related stressors impact the hypothalamic-pituitary-adrenal axis stress response and alter development of brain structures with high concentrations of glucocorticoid receptors, such as the amygdala (Noble et al., 2012). Several structural neuroimaging studies have shown associations between socioeconomic factors and amygdala volume in children, but the directionality of the associations has been inconsistent. Two studies found socioeconomic disadvantage to be associated with smaller amygdala volume (Hanson et al., 2015; Luby et al., 2013), whereas another one found it to be associated with larger amygdala volume (Noble et al., 2012). Other studies have failed to find significant SES-related differences in amygdala structure in children (Hanson, Chandra, Wolfe, & Pollak, 2011; Noble et al., 2015). In particular, in a prior study using the same large sample as the one used

here, there were no significant associations between family income or parental education and amygdala volume (Noble et al., 2015). Similar discrepancies in directionality can be found in the literature linking child maltreatment and early institutionalization with altered amygdala volume (Hanson et al., 2015).

Although there are multiple possible explanations for these discrepancies, including differences in sample characteristics or other methodological factors, one intriguing possibility is that such discrepancies arose due to differences in the length of time between when the stressor was experienced and when amygdala volume was measured. One possibility, which we term the "acceleration-deceleration hypothesis," is that initial exposure to chronic stress causes accelerated growth of the amygdala, leading to increased amygdala volume relative to children of the same age. However, over time, stress-related heightened amygdala reactivity and volumetric increases may lead to cell death and slower amygdala growth, resulting in smaller amygdala volumes relative to age-matched peers (Tottenham & Sheridan, 2009). This hypothesis has been supported in animal models. For example, rodent studies have revealed that chronic stress, especially early in life, induces neuronal hypertrophy and volumetric increases in the amygdala (McEwen & Gianaros, 2010; Tottenham & Sheridan, 2009). Similarly, functional magnetic resonance imaging (MRI) studies of children exposed to early life stress have shown increased amygdala reactivity to negative emotional stimuli (Tottenham et al., 2011). Thus, long-term exposure to socioeconomic disadvantage in childhood may be ultimately linked with relatively smaller amygdala volume.

Amygdala Volume and Internalizing Symptoms in Children and Adolescents

Associations between SES and amygdala volume may be relevant for understanding socioeconomic differences in children's risk for internalizing problems. Indeed, the amygdala has long been a target of investigation for researchers seeking to understand the biological basis of internalizing disorders. However, associations between amygdala volume and internalizing problems in children and adolescents are inconsistent. Children and adolescents with anxiety disorders or major depressive disorder tend to differ in their amygdala structure compared to typically developing control children, but the directionality of these associations has been inconsistent. Some studies indicate that children and adolescents with mixed anxiety disorders (Milham et al., 2005; Mueller et al., 2013; Strawn et al., 2015) or major depressive disorder (Rosso et al., 2005) have smaller amygdala volumes. However, other studies indicated that youth with generalized anxiety disorder (De Bellis et al., 2000) and children with higher parent-reported anxiety (Qin et al.,

2014) and fearfulness (van der Plas, Boes, Wemmie, Tranel, & Nopoulos, 2010) have larger amygdala volumes. In addition, one longitudinal study found that there was increased growth of the amygdala during adolescence associated with depression in girls and decreased growth in boys (Whittle et al., 2014). Finally, other studies have not observed structural differences in the amygdala in youth with major depressive disorder (Caetano et al., 2007; MacMaster et al., 2008; Pannekoek et al., 2014) or subthreshold depression (Vulser et al., 2015), or in typically developing youth varying in parent-reported internalizing symptoms (Koolschijn, van Ijzendoorn, Bakermans-Kranenburg, & Crone, 2013).

It is not clear what explains these discrepancies, although multiple suppositions have been made, including arguments about timing. For instance, it has been noted that initial episodes of major depression may lead to increased amygdala volume and reactivity, but after repeated depressive episodes amygdala volume may start to decrease (McEwen, 2003). This pattern has been observed in the literature on major depressive disorder in adults (Campbell & MacQueen, 2006; Frodl et al., 2008a, 2008b; Schmaal et al., 2016; Sheline, 2000).

Most of this research has used a categorical approach, comparing diagnostic groups with control groups. Studies that employ a dimensional approach, examining associations of amygdala volume with continuous variability in levels of anxiety and depression in children, may complement the existing literature and help to clarify these discrepancies (Fox et al., 2015; Garvey, Avenevoli, & Anderson, 2016). A dimensional approach has been advocated in light of increasing recognition of heterogeneity and comorbidity within diagnostic categories, and the notion that a dimensional understanding may address these issues and ultimately improve treatments. In addition, recent work indicates that dimensional scaling produces measures that evidence greater estimates of reliability and validity compared to categorical scaling (Markon, Chmielewski, & Miller, 2011). In sum, there is evidence to suggest that differences in amygdala structure may be linked with continuous variability in internalizing symptoms in children, but it is difficult to specify directionality. By middle childhood through late adolescence, smaller amygdala volume may be linked with higher internalizing symptoms.

Current Study

In the current study, we investigated (a) associations between SES and amygdala volume by age and (b) associations of SES and amygdala volume with continuous variability in internalizing symptoms. The sample consisted of children and adolescents from the Pediatric Imaging, Neurocognition, and Genetics (PING) study, which included structural MRI and self-report measures of anxiety and depression (Jernigan et al., 2016). First, using the entire PING sample of 3- to 21-year-olds ($N = 1,196$), we examined whether associations between SES indices (family income, parental education) and amygdala

volume varied by age. Family income and parental education were examined separately because they represent distinct aspects of children's environments that have different roles in their development (Duncan & Magnuson, 2012). Based on a review of previous work (Tottenham & Sheridan, 2009), we hypothesized that lower SES would be associated with larger amygdala volume at younger ages (early childhood) but with smaller amygdala volume at older ages (adolescence). This study builds on previous work on SES and amygdala volume, including a study conducted on the PING sample (Noble et al., 2015), by focusing on the role of age as a moderator.

Then, using a PING subsample of 7- to 21-year-olds who completed anxiety and depression measures ($n = 327$), we examined associations of SES and amygdala volume with levels of anxiety and depression. We hypothesized that lower SES and smaller amygdala volume would be associated with higher levels of anxiety and depression. All analyses utilized a comprehensive set of covariates, including family history of anxiety/depression. Genetic factors have been found to contribute to risk for anxiety and depression and to amygdala structure (Chai et al., 2015), and thus represent a potential confound when examining associations of SES with internalizing symptoms and amygdala volume. Higher levels of internalizing problems or differences in amygdala volume may be due to a genetic predisposition rather than poverty-related factors, such as chronic stress. Yet, previous studies have not controlled for familial contributions to these outcomes. To address this, we controlled for family history of anxiety/depression in all analyses. In addition, including genetic ancestry as a covariate in analyses allowed us a precise means of controlling for the confounding of race and SES in the United States (Akshoomoff et al., 2014; Chen, Martin, & Matthews, 2006).

METHOD

Participants

As described previously (Akshoomoff et al., 2014; Jernigan et al., 2016; Noble et al., 2015), the PING study recruited 3- to 21-year-old participants through a combination of web-based and community advertising at nine university-based data collection sites in and around the cities of Los Angeles, San Diego, New Haven, Sacramento, Boston, Baltimore, Honolulu, and New York (<http://ping.chd.ucsd.edu>). Exclusionary criteria included neurological disorder; history of head trauma; preterm birth; autism spectrum disorder, bipolar disorder, schizophrenia, or intellectual disability; and contraindications for MRI. Written informed consent was provided by parents for all participants younger than 18 years of age and by the participants themselves if they were 18 years of age or older. In addition, child assent was obtained for 7- to 17-year-old participants. Each site's Institutional Review Board approved the study.

Analyses of SES by age effects utilized the whole PING sample with data on the relevant variables ($N = 1,196$ for parental education models and $N = 1,185$ for family income models). However, other analyses in this study focused on the subsample of participants who completed web-based, self-report assessments of depression and anxiety from the PhenX Toolkit (<https://www.phenxtoolkit.org>; Jernigan et al., 2016; McCarty et al., 2014; $n = 327$). Six of the nine PING sites chose to administer the PhenX assessments, and only participants 8 years of age or older completed the depression and anxiety measures. The PhenX questionnaires were often completed at a later date, after completion of neuroimaging (McCarty et al., 2014). The time between when participants completed neuroimaging to when they completed the PhenX battery ($M = 1.17$ years, $SD = .67$) was not a significant covariate in any of the analyses. Multilevel models (accounting for the nesting of participants within site) indicated that there were no significant differences in age, sex, genetic ancestry, or parental education between this subsample and the sample of participants who were eligible but did not complete the PhenX questionnaires. However, those who completed the PhenX battery came from higher income families compared to those who did not ($\beta = .21$, $p = .01$).

Full sample characteristics are provided in Table 1. The sample (52% male) ranged in age from 7 to 21 years at neuroimaging and 8 to 22 years at PhenX completion. Note

that one older 20-year-old had turned 21 by the completion of neuroimaging (Jernigan et al., 2016).

Image Acquisition and Processing

Each site administered a standardized high-resolution structural MRI protocol, using 3T scanners (see Table S1 for scanner models and parameters). Details of the image acquisition and processing protocols have been provided previously (Brown et al., 2012). At the University of California, San Diego, the protocol included a sagittal 3D inversion recovery spoiled gradient echo T1-weighted volume optimized for maximum gray/white matter contrast. Acquisition protocols with pulse sequence parameters identical or near identical to those used at the University of California, San Diego, were installed on scanners at the other eight sites. T1-weighted imaging data included in this study passed standardized quality control procedures, including visual inspection ratings by trained imaging technicians and automated quality control algorithms. Morphometric analysis of structural MRI data was performed using a specialized processing stream and FreeSurfer (<http://surfer.nmr.mgh.harvard.edu/>). 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.

TABLE 1.
Descriptive Statistics for Study Variables.

	<i>N</i>	<i>M (SD) or n (%)</i>	<i>Range</i>
Age at Neuroimaging (Years)	327	13.65 (3.62)	7.08–21.00
Age at PhenX Completion (Years)	323	14.80 (3.91)	8.25–22.67
Sex (Male)	327	171 (52%)	—
Parental Education (Years)	308	15.05 (2.26)	6.00–18.00
Family Income (U.S. Dollars)	313	104,287.54 (76,810.78)	4,500.00–325,000.00
Genetic Ancestry Factor	312		
African		.11 (.24)	0–1.00
American Indian		.06 (.14)	0–.80
Central Asian		.03 (.13)	0–1.00
East Asian		.20 (.34)	0–1.00
European		.59 (.37)	0–1.00
Oceanic		.01 (.03)	0–.23
Family History of Anxiety/Depression	326	.74 (1.30)	0–6.00
Scanner Model	296		
Philips Achieva		24 (8%)	—
GE Discovery		36 (12%)	—
GE Signa		47 (16%)	—
Siemens TrioTim		189 (64%)	—
Total Amygdala Volume (mm^3)	296	3354.89 (531.71)	2112.00–6045.00
Anxiety Symptoms	327	28.85 (17.38)	0–100.32
Depression Symptoms	327	13.55 (10.07)	0–59.00

Note: Genetic Ancestry Factor data show mean, standard deviation, and range across all subjects of the estimated proportion of genetic ancestry for each reference population. For anxiety and depression, Screen for Child Anxiety Related Emotional Disorders–Revised and Center for Epidemiologic Studies Depression Scale for Children total scores are presented. GE = General Electric.

Measures

Socioeconomic Status

The PING Study Demographics and Child Health History Questionnaire was completed by parents for participants younger than 18 years and by the participants themselves if they were 18 years or older. Via this questionnaire, the level of educational attainment was reported for parents in the home. The average parental educational attainment was used in all analyses. Total yearly family income was also reported. Both education and income data were originally collected in bins, which were recoded as the means of the bins for analysis (see Table S2). Family income was log-transformed for all analyses due to the typically observed positive skew. As expected, parental education and family income were highly correlated ($r = .56, p < .001$).

Genetic Ancestry Factor

Details of genetic ancestry assessment have been provided previously (Akshoomoff et al., 2014; Jernigan et al., 2016). In brief, genome-wide genotyping was performed on the extracted DNA using the Illumina Human660W-Quad BeadChip. Replication and quality control filters (i.e., sample call rate >99%, call rates >95%, minor allele frequency >5%) were performed (Bakken et al., 2012). To assess genetic ancestry and admixture proportions in the PING participants, a supervised clustering approach implemented in the ADMIXTURE software was used (Alexander & Lange, 2011). Using this approach, genetic ancestry factors were estimated 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. Implementation of ancestry and admixture proportions in the PING subjects is described in detail elsewhere (Fjell et al., 2012). Previous PING studies have shown strong correlations between genetically-determined and self-reported ancestry (Akshoomoff et al., 2014).

Family History of Anxiety/Depression

On the Demographics and Child Health History Questionnaire, respondents indicated whether the following family members had a history of anxiety or depression: maternal and paternal grandmother/grandfather, biological mother/father, maternal and paternal aunt/uncle, male/female sibling. These responses were summed to create a measure of the total number of family positions with a known history of anxiety or depression. This variable was log-transformed to correct for a positively skewed distribution.

Depression

Participants completed the Center for Epidemiologic Studies Depression Scale for Children (Fendrich,

Weissman, & Warner, 1990), a 20-item self-report measure. Participants rate each item in terms of frequency during the last week using a 4-point scale, ranging from 0 (*not at all*) to 3 (*a lot*). Higher scores indicate higher levels of depressive symptoms. The Center for Epidemiologic Studies Depression Scale for Children has strong psychometric properties (Myers & Winters, 2002).

Anxiety

Participants completed the Screen for Child Anxiety Related Emotional Disorders–Revised (Muris, Dreessen, Bögels, Weckx, & van Melick, 2004), a 66-item self-report measure of anxiety disorder symptoms (e.g., generalized anxiety disorder). Participants rated how frequently they experience each item on a 3-point scale, ranging from 0 (*almost never*) to 2 (*often*). Higher scores reflect higher levels of anxiety symptoms. The Screen for Child Anxiety Related Emotional Disorders–Revised has demonstrated high reliability and validity (Muris et al., 2004).

Analysis Plan

Analyses were conducted using SAS software (version 9.3). In the total PING sample ranging in age from 3 to 21 years, we examined associations between SES indices (family income, parental education) and amygdala volume by age. We used multiple linear regression to examine interactions between SES indices and age for amygdala volume. In addition, regression models were employed to examine associations between SES indices and amygdala volume separately in early childhood, middle childhood, and adolescence (3–6, 7–12, and 13–21 years, respectively), to test the hypothesis of an inverse association in early childhood and a positive association in adolescence. Using the PING subsample with anxiety and depression data (7–21 years), regression was used to examine the associations of SES indices and amygdala volume with children's levels of anxiety and depression.

Covariates

All regression analyses controlled for age, sex, and family history of anxiety/depression. In addition, all regression analyses involving amygdala volume adjusted for whole brain volume and scanner model. Genetic ancestry factors and site were not significant in any of the models and thus were not included in final models.

Past work has suggested that in certain brain regions, a quadratic term for age may be more appropriate than a linear term alone (Ostby et al., 2009). Thus, age² was included in analyses predicting amygdala volume. Note that age² did not account for significant variance in anxiety or depression and thus was not included in those models.

TABLE 2
Zero-Order Correlations for Socioeconomic Factors, Family History of Anxiety/Depression, Amygdala Volume, and Internalizing Symptoms

		1	2	3	4	5	6
1.	Family Income	—					
2.	Parental Education	.56***	—				
3.	Family History of Anxiety/Depression	.01	-.01	—			
4.	Amygdala Volume	.14***	.10***	.03	—		
5.	Anxiety	-.08	-.10	.03	-.16**	—	
6.	Depression	-.07	-.12*	.14*	-.10	.56***	—

* $p < .05$. ** $p < .01$. *** $p < .001$.

RESULTS

Descriptive statistics are provided in Table 1, and zero-order correlations are provided in Table 2. Lower family income and parental education were significantly associated with smaller amygdala volume. Lower parental education, but not family income, was significantly associated with higher levels of depression symptoms. Smaller amygdala volume was significantly associated with higher levels of anxiety symptoms.

Associations Between SES and Amygdala Volume by Age

Regression analyses using the entire sample (age range = 3–21 years) indicated that interactions between SES indices and age were not significant for amygdala volume. Results for associations between SES and amygdala volume within each age group (early childhood, middle childhood, and adolescence) are shown in Table 3 and Figure 1. As shown in Figure 1, for all participants, amygdala volume tended to increase with age until adolescence when it began to plateau, consistent with previous reports (Ostby et al., 2009). The pattern of results for associations between SES and amygdala volume was partially consistent with our expectations. During early childhood (3–6 years), associations between SES indices and amygdala volume were not significant. During adolescence (13–21 years), lower family income ($p < .05$) and parental education ($p < .01$) were significantly associated with smaller amygdala volume.

For the family income models, the regression coefficients for early childhood ($\beta = -.05$) versus adolescence ($\beta = .04$) differed significantly, $t(715) = 2.50$, $p = .01$. For the parental education models, these regression coefficients ($\beta = .03$ and $.06$, respectively) did not differ significantly, $t(729) = .67$, $p = .50$.

Associations Between SES and Internalizing Symptoms

Lower parental education (but not family income) was significantly associated with higher anxiety ($p = .03$) and

depression ($p = .03$) in children and adolescents (7–21 years) after accounting for age, sex, and family history of anxiety/depression (see Table 4). Thus, we controlled for parental education in the following analyses examining associations of amygdala volume with internalizing symptoms.

Associations Between Amygdala Volume and Internalizing Symptoms

Smaller amygdala volume was significantly associated with higher levels of depressive symptoms ($p = .03$), but not anxiety symptoms, after adjusting for parental education, whole brain volume, age, sex, family history of anxiety/depression, and scanner model (see Table 5). Parental education was no longer significant in either regression model after amygdala volume was added. These results remained unchanged when analyses were run without controlling for family history of anxiety/depression or parental education.

We ran parallel analyses with the hippocampus as a check for specificity. Unlike in the amygdala, we found no differences in SES associations with hippocampal volume by age. Further, although both lower parental education ($\beta = -.12$, $p = .04$) and lower hippocampal volume ($\beta = -.16$, $p = .04$) were associated with increased symptoms of depression, both of these variables remained significant in the model, consistent with the possibility that hippocampal differences were not fully accounting for socioeconomic differences in depressive symptoms.

DISCUSSION

The goals of this study were to examine (a) associations between SES and amygdala volume by age and (b) associations of SES and amygdala volume with internalizing symptoms. To our knowledge, this is the first study to address this set of questions. Some previous studies have linked lower SES with smaller amygdala volume (Hanson et al., 2015; Luby et al., 2013) whereas others have linked lower SES with larger amygdala volume (Noble et al., 2012). In this study, we tested whether these discrepancies may be due to age differences, as

TABLE 3
Associations of Family Income and Parental Education With Amygdala Volume in Early Childhood, Middle Childhood, and Adolescence

	3–6 Years		7–12 Years		13–21 Years	
	β	<i>p</i>	β	<i>p</i>	β	<i>p</i>
Model 1:						
Whole Brain Volume	.46	< .0001	.47	< .0001	.45	< .0001
Age	-.86	.6363	.11	.4661	.01	.9834
Age ²	-.59	.3887	-.17	.3998	.01	.9257
Sex	-.16	.0272	-.08	.1163	-.17	.0013
Family History of Anxiety/Depression	-.03	.3025	-.02	.3979	.02	.3002
Family Income	-.05	.1706	-.004	.8758	.04	.0444
Model 2:						
Whole Brain Volume	.43	< .0001	.48	< .0001	.44	< .0001
Age	-.55	.7633	.12	.4425	.01	.9579
Age ²	-.49	.4728	-.12	.5669	-.01	.9630
Sex	-.19	.0107	-.09	.1162	-.18	.0007
Family History of Anxiety/Depression	-.02	.4580	-.01	.5167	.03	.2010
Parental Education	.03	.4627	-.01	.6823	.06	.0060

Note: These regression analyses also adjusted for scanner model. Sample sizes for family income models were 218, 466, and 501, respectively. Sample sizes for parental education models were 220, 463, and 513, respectively.

previously theorized (Tottenham & Sheridan, 2009). Specifically, we tested the a priori hypothesis of an inverse association between SES and amygdala volume in early childhood and a positive association between SES and amygdala volume in adolescence. Interactions between SES indices (family income, parental education) and age were not significant, possibly because of the truncated age range of the sample (i.e., not including children younger than 3 years) or to a

threshold effect (e.g., step function) at a certain age. We then conducted separate regression analyses by age group. Results indicated nonsignificant associations between SES indices and amygdala volume in early and middle childhood (3–12 years) and significant positive associations in adolescence (13–21 years). These results suggest that adolescents from disadvantaged families may have smaller amygdala volumes than their peers from more advantaged families.

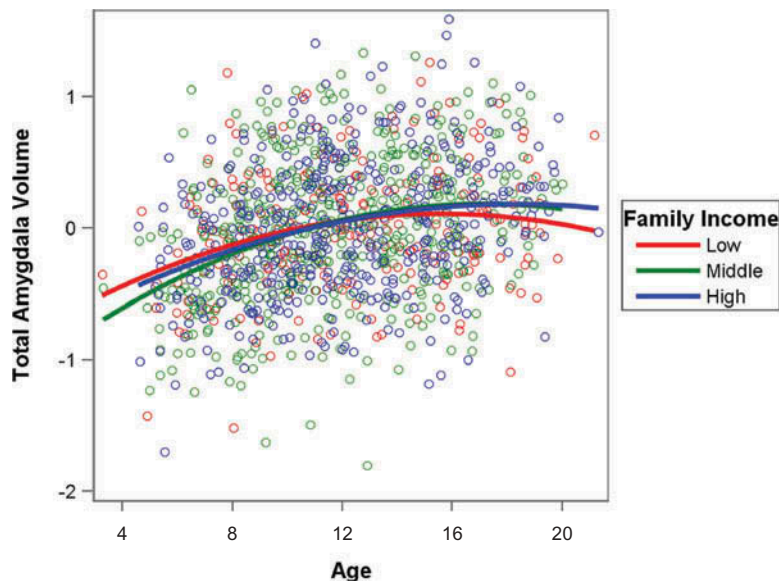


FIGURE 1 Partial regression plot showing association between age and total amygdala volume by family income, controlling for whole brain volume, sex, and scanner model. Lower family income was significantly associated with smaller amygdala volume during adolescence (see Table 3). For interpretation purposes, the tick marks for age display ages in years corresponding to the standardized residuals for age. Family income was a continuous variable in analyses but is displayed in ecologically valid family income groups (low = \$4,500–\$25,000, middle = \$35,000–\$75,000, high = \$125,000–\$325,000).

TABLE 4
Associations of Family Income and Parental Education With Internalizing Symptoms.

	<i>Anxiety</i>			<i>Depression</i>		
	β	<i>t</i>	<i>p</i>	β	<i>t</i>	<i>p</i>
Model 1						
Age	-.08	-1.30	.1932	.07	1.06	.2892
Sex	.37	3.35	.0009	.17	1.54	.1241
Family History of Anxiety/Depression	.04	.74	.4575	.16	2.85	.0046
Family Income	-.09	-1.47	.1428	-.07	-1.11	.2660
Model 2						
Age	-.09	-1.33	.1842	.07	1.14	.2549
Sex	.40	3.59	.0004	.18	1.58	.1159
Family History of Anxiety/Depression	.05	.88	.3804	.15	2.73	.0067
Parental Education	-.13	-2.24	.0258	-.13	-2.18	.0298

Note: Sex: 1 = female, 0 = male.

TABLE 5
Associations of Amygdala Volume With Internalizing Symptoms.

	<i>Anxiety</i>			<i>Depression</i>		
	β	<i>t</i>	<i>p</i>	β	<i>t</i>	<i>p</i>
Whole Brain Volume	.19	2.01	.0452	.21	2.31	.0218
Age	-.04	-.63	.5261	.05	.81	.4209
Sex	.53	3.76	.0002	.20	1.39	.1645
Family History of Anxiety/Depression	.03	.53	.5982	.16	2.73	.0068
Parental Education	-.09	-1.54	.1237	-.11	-1.91	.0576
Amygdala Volume	-.15	-1.39	.1670	-.23	-2.12	.0347

Note: These regression analyses accounted for scanner model.

Sex: 1 = female, 0 = male.

Disadvantaged environments are often characterized by chronic stressors, including crowding/noise, dangerous neighborhoods, household chaos and unpredictability, and lower parental responsiveness (Evans & Kim, 2013). Stressors such as these may have a particularly strong impact on the amygdala, which is closely involved in fear processing, detecting perceived threats, and triggering the hypothalamic-pituitary-adrenal axis stress response (McEwen & Gianaros, 2010; Tottenham & Sheridan, 2009). In the context of chronic stress, the amygdala may initially increase and show greater reactivity but then begin to diminish in size with continued exposure over time (Tottenham & Sheridan, 2009). Thus, amygdala hyperactivity may lead to this pattern of “acceleration” followed by “deceleration.” Initial exposure to chronic stress may lead to amygdala hyperactivity and neuronal hypertrophy (e.g., increased dendritic arborization), but after prolonged exposure (by adolescence), chronic hyperactivity might lead to excitotoxic changes and amygdala atrophy (Nacewicz et al., 2006). Adolescents from disadvantaged environments may have accrued histories of long-term exposure to chronic

stress, which explains their smaller amygdala volume, relative to their more advantaged peers. Longitudinal studies are needed to formally test this hypothesis and to elucidate the way in which SES may modify trajectories of amygdala development during childhood and adolescence.

In a subsample of 7- to 21-year-olds for whom anxiety and depression data were available, lower parental education, but not family income, was associated with higher levels of anxiety and depression. These associations remained significant even after accounting for family history of anxiety/depression, lending some support to the notion that SES-related factors, such as chronic stress, may be driving these results. Family income and parental education may reflect distinct aspects of children’s environments. Family income may more directly reflect the material resources available to the family, whereas parental education may more directly reflect parenting style and the quality of parent–child interactions (Duncan & Magnuson, 2012).

Findings also indicated that smaller amygdala volume was significantly associated with higher levels of depression in children and adolescents, even after accounting for

parental education and family history of anxiety/depression. The association of *smaller* amygdala volume with elevated depressive symptoms was consistent with some prior studies (Milham et al., 2005; Mueller et al., 2013; Rosso et al., 2005; Strawn et al., 2015) but not others (De Bellis et al., 2000; Qin et al., 2014). It is possible that due to the older age of the sample (7–21 years), participants had experienced these symptoms for a prolonged period, leading to relatively reduced rather than increased amygdala volume (McEwen, 2003). Most of the previous studies have focus on diagnostic groups. This study provides insight into these associations for dimensionally scaled anxiety and depression.

Taken together, these findings are consistent with the hypothesis that differences in amygdala development may partially explain the higher levels of depressive symptoms often found among children from disadvantaged families, consistent with a recent functional neuroimaging study (Barch et al., 2016). However, longitudinal studies are needed to formally test such a mediation model (Cole & Maxwell, 2003; Maxwell & Cole, 2007). In terms of clinical implications, it is possible that early preventative interventions targeting emotion management techniques may lead to a reduced risk of internalizing problems among children from disadvantaged families. Because socioeconomic disadvantage may alter brain development prior to the onset of observable internalizing problems, prevention efforts provided early in childhood and potentially targeting reductions in exposure to poverty-related stressors and training in emotion regulation may be very important.

Results from this study should in no way be interpreted to mean that structural differences in the amygdala represent a full explanation for the link between socioeconomic disadvantage and increased risk for internalizing problems in children. We did not test for regional specificity and thus cannot say whether differences in the amygdala would emerge above and beyond all other brain regions. The amygdala is likely part of a larger neural network (e.g., hippocampus, medial prefrontal cortex) that is impacted by early exposure to socioeconomic disadvantage and implicated as a mechanistic pathway in internalizing problems. Research is needed to further identify the ways in which structural and functional connectivity with the amygdala may be altered by socioeconomic disadvantage and linked with higher internalizing symptoms during childhood. For instance, less efficient prefrontal cortex regulation of the amygdala has been found in adults who grew up in poverty (Kim et al., 2013).

This study had a number of strengths, including a large sample size and a comprehensive statistical approach, which included a broad set of covariates. In addition, the use of the PING sample increases the generalizability of these findings. There were also limitations to this study that should be taken into account when interpreting the findings. This was a cross-sectional, correlational study, and such research designs do not allow inferences about developmental trajectories or causality. Also, the anxiety and depression data

were only collected for a subsample. In addition, data were not available on variability in exposure to specific poverty-related stressors (e.g., neighborhood violence, family turmoil), and thus we cannot specify which SES-related risk factors might be driving these associations. Given that anxiety and depression were measured solely via self-report, we were unable to examine consistency in reporting across multiple informants (De Los Reyes et al., 2015). Although it is possible that the nonsignificant associations between SES and amygdala volume for younger children reflect age-related differences in technical artifacts (e.g., differences in the quality of FreeSurfer segmentation, greater registration error in younger children), it is important to note that a rigorous quality control protocol was employed in the PING study (Jernigan et al., 2016). Also, although we took care to limit the number of comparisons and tested a priori hypotheses, it should be noted that results were not strictly corrected for multiple comparisons. Finally, although this was not a clinical sample, it is possible that medication use (e.g., antidepressants) was ongoing in some of the participants in this sample.

In this study, socioeconomic disadvantage was linked with smaller amygdala volumes in adolescents but not children between 3 and 12 years of age, consistent with the notion that these associations may differ by timing or duration of exposure. Lower parental education, but not family income, was associated with higher levels of anxiety and depression, even after accounting for family history of anxiety/depression. Smaller amygdala volumes were significantly associated with higher levels of depressive symptoms, even after accounting for parental education and family history of anxiety/depression. Prevention efforts that combat economic inequality and reduce children's exposure to poverty-related stressors may reduce their risk for internalizing problems and improve their chances of healthy emotional and behavioral development.

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