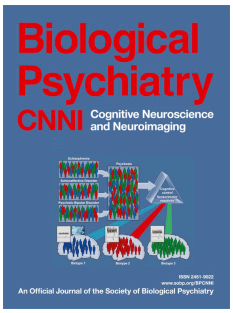

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Timing and Type of Early Psychopathology Symptoms Predict Longitudinal Change in Cortical Thickness from Middle Childhood into Early Adolescence

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Short Title: Early Adversity and Cortical Thickness Development

Keywords: Cortical Thickness, Development, Preschool, Adolescent, Poverty, Anxiety, Externalizing

Abstract

Background – Early life experiences have profound effects on functioning in adulthood. Altered cortical development may be one mechanism through which early life experiences, including poverty and psychopathology symptoms, impact outcomes. However, there is little prospective research beginning early in development that combines clinician rated psychopathology symptoms and multi-wave MRI to examine when these relationships emerge.

Methods – Children from the Preschool Depression Study who completed diagnostic interviews at three different developmental stages (preschool, school-age, early adolescent) and up to three MRI scans beginning in middle childhood participated in the current study (N=138). Multilevel models were used to calculate intercepts and slopes of cortical thickness within *a priori* cortical regions of interest (Sotiras et al., PNAS 2017). Linear regressions probed how early life poverty and psychopathology (depression, anxiety, and externalizing symptoms at separate developmental periods) related to intercept/slope.

Results – Collectively experiences during the preschool period predicted reduced cortical thickness, either via reduced intercept or accelerated thinning (slope). Early life poverty predicted intercepts within sensory and sensory-motor integration regions. Beyond poverty, preschool anxiety symptoms predicted intercepts within insula, subgenual cingulate, and inferior parietal cortex. Preschool externalizing symptoms predicted accelerated thinning within prefrontal and parietal cortices. Depression and anxiety/externalizing symptoms at later ages were not significant predictors.

Conclusions – Early childhood is a critical period of risk, experiences at this developmental stage specifically have the potential for prolonged influence on brain development. Negative early experiences collectively predicted reduced cortical thickness, but the specific neural systems impacted aligned with those typically implicated in these individual disorders/experiences.

Keywords: Anxiety, Externalizing, Preschool, Adolescence, Cortical Thickness

1 Introduction

Negative early life experiences, including poverty and experience of psychopathology, have long-term impacts on adaptive functioning in adulthood (1, 2). Emerging evidence suggests that altered brain development may be a critical part of this risk pathway (3), particularly when these experiences occur early in life (4, 5). However, as the majority of this literature is either cross-sectional or captures symptoms later in the course of development (e.g., school-age and adolescence), it is unclear whether earlier (e.g., preschool) versus later (school-age, adolescence) timing of these experiences have differential impacts on brain development. Understanding whether developmental timing of adversity impacts brain outcomes is important for informing whether there are key periods when prevention or protection from adversity might be most critical (4). There is also emerging evidence that different domains of psychopathology (e.g., externalizing versus internalizing symptoms – note some studies use a more general 'internalizing' symptom measure and others specifically isolate effects of depression and anxiety) impact cortical thickness development within dissociable neural systems during adolescence (6, 7). For example, when considered as independent predictors of cortical thickness development, internalizing symptoms relate to limbic regions and externalizing symptoms relate to control and motor regions (6, 7). However, in the past studies tended to focus on a single disorder or symptom dimension when examining relationships with brain development, but more recently this idea of examining multiple dimensions of psychopathology in the same study to isolate unique effects of different disorders/symptom domains has become more prominent (8). This is an important methodological consideration, particularly given the high rates of

comorbidity across disorders (9), which will help identify how common and dissociable neural correlates of different symptom domains emerge across development. Such information will be important for future understanding of the developmental etiology and consequences of these symptoms.

There is a growing consensus that cortical thickness declines from early childhood through young adulthood in normative development (10-12). This thinning is thought to be driven by both synaptic pruning and myelination processes (13-15). However, the rate and timing of these thinning processes differ across cortex – these differences are driven in part by patterns of gene expression and relate to the evolutionary expansion of cortex (16, 17). For example, lower-order sensory areas, such as primary somatosensory or visual cortices, show less age-related change across adolescence (indicating earlier development) than higher-order association cortex, which show later onset of thinning and more pronounced changes over adolescence (18). This meaningful regional variation in cortical thickness can be used to define data-driven networks of regions that show coordinated cortical thickness development. Using these networks for investigations of brain behavior relationships is fundamentally similar to adopting a region of interest (ROI) approach except here covariation patterns of cortical thickness data are used to define the ROI instead of gyri and sulci. Non-negative matrix factorization (NMF) is one analytical technique for identifying such networks, often termed components. NMF is conceptually similar to a principal components analysis, but where only positive loadings of voxels onto component(s) are allowed(19). Importantly, NMF has been applied in a large community sample of adolescents to characterize which parts of cortex show similar thickness properties. Like

with functional connectivity networks, these structural networks or ‘components’ tend to show related function or evolutionary development and thickness in these components differs with adolescent development (16) and with psychopathology (8).

Anxiety, depression, and externalizing symptoms have all *separately* been linked to reduced cortical thickness (5, 20-22). However, given that there is often significant comorbidity between disorders in childhood and adolescence (23), recent work has focused on the *unique* relationships between different trans-diagnostic dimensions of psychopathology and cortical thickness. Notably, a recent cross-sectional paper utilizing NMF techniques and a bi-factor model of psychopathology highlighted relationships between reduced thickness across a large portion of cortex with increased fear symptoms, above and beyond general psychopathology and other orthogonal symptom domains, which included anxious-misery, psychosis, and behavioral dysfunction (8). However, another longitudinal study focusing on more general internalizing symptoms versus externalizing symptoms, reports that these symptom domains relate to cortical thickness trajectories within separable networks of regions that are commonly implicated in that type of psychopathology – e.g., internalizing symptoms predicting thickness within limbic regions and externalizing symptoms predicting thickness within postcentral gyrus (6). Such approaches, using separable domains of psychopathology as simultaneous predictors of cortical thickness development, highlight important differences in neural correlates across domains of psychopathology. Such findings may yield critical information regarding the specific neurodevelopmental mechanisms of these disorders, as well as the timing of when these symptoms/disorders might have their most powerful influence on neurodevelopment.

Cortical development is also related to exposure to poverty early in life (24). In particular, reduced thickness is routinely observed within sensory integration networks when poverty is experienced in childhood. Important emerging work suggests that relationships between early poverty and later academic/cognitive functioning are explained in part by the impact of poverty on cortical development (25, 26). Critically, although poverty and psychopathology are related (27), studies investigating effects of psychopathology on cortical development do not always include measures of poverty or socio-economic status in models. As such, it is unclear to what extent relationships between psychopathology and cortical development are explained by poverty and correlated risk factors, particularly when experienced early in development.

To address these gaps in the literature, we capitalize on a rich longitudinal dataset where cortical thickness was assessed repeatedly beginning in middle childhood and psychopathology was assessed via semi-structured clinical interviews beginning in preschool and continuing through adolescence. These data allow for examining three key questions; 1) whether relationships between early life experiences, including poverty and psychopathology symptoms (externalizing, anxiety, and depression), and cortical thickness are already observable by middle childhood or emerge across adolescent development, 2) whether relationships between these experience types and cortical development are dissociable across both experience type and brain region/system, and 3) whether timing of experience (e.g., symptoms experienced in preschool versus school-age or adolescence) relates to brain development in different ways.

In the current study, we build on previous work showing the utility of using NMF as a data driven data-reduction tool that facilitates examining the unique relationships of different dimensions of psychopathology to cortical thickness across development (8, 16). In our unique dataset – where early poverty was assessed alongside psychopathology symptoms (beginning in preschool and continuing through adolescence) and cortical thickness trajectories (beginning at school age and continuing through adolescence) – we can prospectively examine the importance of early versus later childhood life experiences in relation to cortical thickness development. We hypothesize that early life is a sensitive period, such that experience of poverty and psychopathology symptoms at this period will show the strongest relationships with cortical thickness. We further hypothesize that adversity (either financial or experience of psychopathology symptoms) will predict reduced cortical thickness, either at baseline (intercept) or through accelerated thinning trajectories (slope). Finally, there is evidence for both widespread thinning of cortex with increased fear symptoms in cross sectional work (8) and more regionally specific effects of different types of psychopathology symptoms in longitudinal work (6). However, given the similarity in sample ages and longitudinal design between our study and Whittle et al., 2020 (6), we also hypothesize that different symptom domains will predict thickness within dissociable sets of regions which have been functionally related to that domain – e.g., limbic regions involved in affective processing (insula and subgenual anterior cingulate) will relate specifically to anxiety and/or depression, whereas regions involved in executive function (dorsolateral prefrontal cortex) will relate specifically to externalizing symptoms.

2 Methods and Materials

2.1 Participants. Children/adolescents from the Preschool Depression Study (PDS); who both completed at least one MRI scans between during middle childhood/ early adolescence and diagnostic interviews beginning in preschool participated (N=138). The majority of participants (n=125) completed three MRI scans. See Table 1 for demographic and symptom descriptive statistics.

The PDS is a longitudinal study at Washington University School of Medicine (WUSM) in St. Louis where children aged 3.0-5.11 years old were recruited from primary caregivers, daycares, and preschools oversampling for depression using the Preschool Feelings Checklist (PFC; (28)). The PFC is sensitive to screen for preschool depressive symptoms but, due to comorbidities, also identifies children with other disorders, including anxiety and externalizing disorders (29). Children with either elevated PFC scores (≥3) or scores of 0 (presumed healthy) were contacted for participation. Children with Autism Spectrum disorder, chronic illness, clinically significant speech, language or cognitive delays or neurological disorders were excluded. Diagnostic assessments were conducted approximately annually over the next 12-15 years – these data were used to create dimensional symptom scores at specific developmental stages (more detail below). MRI was added to the PDS protocol in middle childhood, when children were aged 6-12 years. An additional two scans were administered at the next two in-person follow-up sessions. Details of the PDS and MRI exclusions have been reported elsewhere (5, 30).

Caregivers completed informed consent and child verbal/written assent was obtained before study participation. WUSM institutional review board approved all procedures.

2.2 Measures.

2.2.1 Early Life Psychopathology. Dimensional depression, anxiety, and externalizing severity scores were created using diagnostic interviews of caregivers. The Preschool-Age Psychiatric Assessment (PAPA; (31)) through age 7 and the caregiver and child report were obtained. The Childhood and Adolescent Psychiatric Assessment (CAPA; (32) was obtained from ages 8 and older. Anxiety severity scores include symptoms from anxious affect, worries, life events, post-traumatic stress disorder, somatization, separation anxiety, and sleep modules. Externalizing symptom severity scores include items from the attention deficit hyperactivity disorder, oppositional defiant disorder, and conduct disorder modules. Depression symptom severity scores include items that went into the major depressive disorder (MDD) diagnosis/severity score from the MDD, food, sleep, and hyperactivity modules.

To create symptom scores specific to each developmental epoch, means for each symptom dimension were calculated using all diagnostic interviews conducted when participants were within each of the following age ranges: preschool age = <6.0 years, school age = 6.0- 9yrs, 11months, early adolescence = 10-14years, 11months. Notably, MRI scans occurred during the school age and early adolescent epochs (Supplemental Figure 1), meaning that preschool symptoms preceded all scan waves whereas scanning was underway during school age and early adolescent symptom assessment.

2.2.2 Early Life Income to Needs Ratio. At baseline caregivers reported on family income. Income-to-needs ratio was calculated as total family income divided by federal poverty level, based on family size at time of collection (33). A family with income to needs ratio of 1 is at the federal poverty level.

2.3 MRI Data Collection and Processing

At each of the three scanning waves participants underwent neuroimaging with a magnetic resonance imaging scanner (model 3.0-T Tim Trio; Siemens Healthcare GmbH) which included two magnetization-prepared, rapid acquisition gradient-echo (MPRAGE) T1-weighted images with the following parameters: 1mm isotropic resolution; TR 2.4 ms; TE 3.16 ms; 160 slices; FOV 256 × 256 × 224 mm; flip angel 8°; matrix 256 × 224 mm. The 2 MPRAGE scans were assessed visually, and the best one was selected for further processing by blinded raters (see Supplemental Methods for greater detail). The longitudinal Freesurfer processing stream (version 5.3, http://surfer.nmr.mgh.harvard.edu/) was used on the selected MPRAGE (see (5) for further details) to generate cortical thickness maps. Cortical thickness maps were spatially normalized to fsaverage5 template and smoothed using an isotropic Gaussian filter kernel with full width at half maximum (FWHM) size of 20mm. The 18-component solution from Sotiras et al, 2017 (Table 3; Supplemental Figure 2) was applied to this data and thickness for each component was extracted for each participant from each scan. See supplemental methods for explanation of NMF.

2.4 Statistical Analyses

2.4.1 Longitudinal multilevel linear models. Longitudinal multilevel linear models (MLM) were implemented in SAS, version 9.3. Each of the 18 components growth curve model included both random intercept and random slope components (with either a variance components or autoregressive covariance matrix between the 2 components, depending on best model fit) – model fit did generally improve when slope was modeled as a fixed effect, but modeling slope as a random effect is essential for asking questions about individual differences in thickness trajectories. Time was coded as age. Models included age (centered at mean = 12 years) and female sex – model fit improved for two components, 5-superior frontal cortex and 9-ACC, with inclusion of quadratic effect of age and thus, age^2 was also included for these components. Intercepts and slopes from these MLMs as the dependent variables in further analyses. Relationships between poverty/psychopathology and intercepts would indicate that these vulnerabilities impact cortical thickness similarly across development, whereas relationships with slope would indicate vulnerabilities' impact on cortical thickness emerges from middle childhood into adolescence.

2.4.2 Regressions predicting brain development. Regressions for each of the 18 components (intercept and slope DVs for separate tests) were conducted with income to needs ratio, PS depression, SA depression, EA depression, PS anxiety, SA anxiety, EA anxiety, PS externalizing, SA externalizing, EA externalizing as predictors of interest. Sex (male=1, female =2) and age in months at scan 1 were included as covariates (age at scan 3 also included for slope regressions as time between scan1 and 3 varied across participants). Prior to conducting these regressions, data were checked for multivariate outliers using mahalanobis distances – two sets of distances

were calculated using the independent variables predicting intercepts or slopes. No individuals were identified as significant multivariate outliers, p>0.001 for all individuals for both sets of predictors.

Bivariate correlations between significant predictors of interest and components are reported in Table S3 and multicollinearity statistics are reported in Table S4.

2.4.3 Multiple Comparisons Correction. A false discovery rate (FDR) correction (q=.05) was applied across the 18 components for a particular effect, e.g. preschool anxiety. This means that for each dependent variable we corrected across the 18 parallel regressions (one for each component). This approach has been used previously (8).

3 Results

3.1 Relationships between poverty and psychopathology domains across development. Correlations between predictors are reported in Figure 1 – symptoms were positively related within and across domains, whereas higher income to needs ratio (i.e., greater advantage) was related to reduced symptoms across domains. Of particular note, externalizing symptoms showed the strongest within symptom domain relationships across the three developmental periods, followed by depression symptoms and then anxiety symptoms, which were only moderately related across time with r ~.4. Depression and externalizing symptoms also showed the strongest relationship between symptoms at a given point in development – this was true across developmental periods. Relationships between anxiety and the other symptoms dimensions strengthened over development, but these relationships remained modest in size and were not a source of problematic collinearity (Table S4). Finally, income to

needs ratio showed strongest relationships to preschool externalizing and early adolescent depression symptoms.

3.2 Longitudinal MLMs. All regions showed a significant negative slope indicating cortical thinning from middle childhood through early adolescence (Table S1; Supplemental Figure 3). As expected, older age predicted thinner cortex intercepts. Sex was not a significant predictor of any component's intercept/slope.

3.3 Early Poverty And Anxiety, But Not Depression Or Externalizing Symptoms, Predict Reduced Cortical Thickness Intercepts

3.2.1 Income to needs ratio. Low income to needs ratio, i.e., increased poverty, early in life predicted reduced cortical thickness intercepts within several components that include regions of parietal and occipital cortices and primary motor/somatosensory cortices (Table 3, Figure 2, Supplemental Figure 4), but did not predict slopes of any components.

3.2.2 Anxiety symptoms. Anxiety symptoms specifically experienced during the preschool period (3-5 years) predicted reduced cortical thickness intercepts within several components that include regions implicated in affective function including the insula, subgenual ACC, and inferior lateral parietal cortex (Table 3, Figure 2, Supplemental Figure 4). Notably, both early poverty and preschool anxiety were unique predictors of cortical thickness within occipital and superior parietal cortices. Anxiety symptoms experienced at school age (7-9 years) and early adolescence (10-14 years) did not significantly predict intercept or slope for any component above and beyond other symptom and demographic measures (Table S2).

3.4 Early Externalizing, But Not Early Poverty, Depression, Or Anxiety Symptoms, Predicts Accelerated Cortical Thinning

Externalizing symptoms specifically experienced during the preschool period (3-5 years) predicted accelerated thinning in components that include the DLPFC, superior PFC, association and motor/somatosensory cortices (Table 3, Figure 2, Supplemental Figure 4). Note, preschool externalizing symptoms did not significantly predict intercept for any component (Table S2). Externalizing symptoms experienced at other developmental stages did not significantly predict intercept or slope for any component above and beyond other symptom and demographic measures (Table S2).

4 Discussion

Here we capitalize on a rich prospective dataset where both semi-structured clinician-rated psychopathology and brain development were assessed longitudinally beginning early in development. This allowed for an investigation of whether different symptom dimensions, experienced at key periods in development, as well as early poverty might uniquely relate to longitudinal change in cortical thickness. We observed reduced cortical thickness in children who experienced greater adversity (including poverty and psychopathology). However, the pattern of reduced thickness – either reduced thickness consistently observed over development (intercept effects) and/or more rapid thinning over development (slope effects) – as well as the neural systems impacted (limbic, sensory-motor, versus prefrontal) showed important differences across domains of adversity and psychopathology. Finally, across poverty and symptom domains, relationships between the developmental timing of those experiences and neural outcomes suggest that early childhood is a critical period, as adversity

experienced specifically during the preschool years predicted adverse neural outcomes, some of which worsened over time.

We observed reduced thickness (intercept) for children experiencing increased anxiety symptoms during the preschool period and those experiencing poverty early in life. Previous work using similar NMF methods and contrasting different dimensions of psychopathology in a large cross-sectional sample of adolescents reported specific relationships between 'fear' symptoms and reduced cortical thickness; this effect was observed broadly but was strongest in the posterior cingulate cortex and temporoparietal junction (8). Interestingly, in the current work, thickness within these regions was predicted by early life poverty, rather than anxiety symptoms. Poverty was not included in Kaczkurkin et al., 2019. Our finding that poverty predicted reduced cortical thickness within regions of parietal and occipital cortices and primary motor/somatosensory cortices is similar to other work focusing on poverty (25, 34). These results also suggest that the relationship between poverty and the brain emerges early – greater income to need ratio early in life predicted greater cortical thickness at baseline (intercept) but did not predict the trajectory of thinning over development (slope). Although this conclusion is common in the literature (26, 35), with effects of poverty on brain development observed in infancy (3, 36), here we extend this literature to identify *unique* effects of early poverty, independent of psychopathology. This is an important addition to the literature as psychopathology and poverty are often related (27) but are less frequently used as independent predictors of brain outcomes. Given this known relationship and the similar direction of poverty and anxiety effects reported

here, future work investigating cortical thickness correlates of early anxiety or other psychopathology should aim to also account for early life poverty.

Anxiety symptoms experienced in preschool predicted reduced intercepts within the subgenual anterior cingulate, insula, and inferior parietal cortex – all regions functionally implicated in affective disorders (37) and where fear symptoms predicted reduced thickness in Kaczkurkin et al., 2019. Although there were differences between our two studies, we both attempted to isolate the unique relationships between different symptom domains and cortical thickness. Kaczkurkin et al., 2019 used a bi-factor modeling approach to create orthogonal symptom dimensions, as well as a general psychopathology or p-factor, and included all factors as simultaneous predictors of thickness. In this data-driven bi-factor model, items that traditionally fall under ‘anxiety’ broadly were assigned to either a ‘fear’ factor or to ‘anxious-misery’, which also included traditional ‘depression’ items. We also included different symptom domains as simultaneous predictors of thickness in our work, although we used more traditional anxiety, depression, and externalizing symptom scores. Given this approach, and that Kaczkurkin et al., 2019 also found relationships between thickness in these regions and anxiety specific (i.e. ‘fear’ factor) versus internalizing more broadly (i.e. anxious-misery factor), the similarity in findings’ specificity to anxiety symptoms is quite striking. However, our data are also able to provide critical within-subject developmental context not available in prior work. In fact, our results suggest that relationships between anxiety and reduced thickness within these systems is evident relatively early in development, rather than emerging over adolescence. Future work is still needed to investigate whether these relationships are observed even earlier, for example in preschool.

Externalizing symptoms, specifically those experienced in preschool, predicted accelerated thinning from middle childhood through early adolescence within the prefrontal cortex, somatosensory and motor cortices, as well as the precuneus and superior parietal cortex. These PFC and parietal regions in particular have been implicated in cognitive control and decision-making – processes known to be impacted in externalizing disorders (38). Although less longitudinal work has focused on relationships between externalizing symptoms and longitudinal change in cortical thickness, our results do largely fit within the extant literature. For example, reduced thickness within the prefrontal and parietal cortices is predicted by impulsivity (but not depression) in adolescence (7), ADHD in adults (39), and ADHD in children/adolescents (40). However, some studies report attenuated cortical thinning, or more protracted neurodevelopment, in externalizing psychopathology/symptoms (22, 41). The inconsistency in this literature may relate to sample sizes, ages of participants, or other comorbidities. These findings underscore the need to attend to externalizing symptoms arising in the preschool period to prevent deleterious effects on brain development.

Notably, we did not observe any significant relationships between depression symptoms and cortical thickness. This may seem to stand in contrast to our previous work demonstrating links between early depression symptoms, but not trauma or familial depression, and accelerated whole-brain cortical thinning (5). However, it is important to note that these analyses focused on the *relative* impact of different domains of psychopathology and early poverty on regional cortical thickness (not whole brain). Another caveat is that our analyses focused on cortex. There is a long-established literature linking depression to alterations in subcortical volume, particularly

the putamen (42, 43). It may be that the relative effects of depression, versus anxiety and externalizing symptoms, are maximal in subcortex or relate to volume rather than cortical thickness.

Although this study has many strengths, there are also limitations. Multicollinearity is always a concern when correlated measures are included in the same model, as multicollinearity can impact the precision of estimated coefficients and the reliability of associated p-values. All significant relationships identified in regression analyses were also evident in bivariate correlations, and the variance inflation factor (VIF) was tolerable for all variables of interest. However, symptom measures were correlated across domain and developmental stage and this may have influenced their estimated effects on cortical thickness – future studies may use other factoring approaches to minimize correlation between symptom domains. A further limitation is the generalizability of these findings given that this sample was enriched for early depression which, because of comorbidity, also increased the incidence of preschool anxiety and externalizing symptoms at preschool. Because of the heightened early symptoms, there was a general regression to the mean – i.e., an improvement in symptoms over time. Although this increased variation in early symptoms likely improves our ability to detect relationships with brain development, it may reduce the application of our findings to the population at large and findings need to be replicated in community samples. However, the lack of depression effects somewhat mitigates this limitation. Finally, non-linear relationships between symptoms and thickness were not considered, but should be investigated in future studies.

In conclusion, we observed that negative early experiences (externalizing, anxiety, poverty) predicted thinner cortex either through reductions in thickness early in life or accelerated thinning trajectories across adolescence. However, the neural systems impacted differed depending on symptom dimension and align with neural systems traditionally implicated in these disorders. Our findings further suggest that early childhood is a critical period of risk, experiences at this developmental stage specifically have the potential for prolonged influence on brain development.

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Table 1. Descriptive statistics

		Mean	SD	Min	Max	N
Externalizing symptoms - mean PS		6.78	6.31	0	31	
Externalizing symptoms - mean SA		6.00	5.77	0	27	
Externalizing symptoms - mean EA		4.44	5.30	0	25	
Anxiety symptoms - mean PS		2.17	2.63	0	12.5	
Anxiety symptoms - mean SA		1.43	2.11	0	10	
Anxiety symptoms - mean EA		0.67	1.40	0	9.5	
Depression symptoms - mean PS		2.44	1.65	0	7	
Depression symptoms - mean SA		2.32	1.49	0	6.67	
Depression symptoms - mean EA		2.30	1.57	0	8	
Baseline income to needs ratio		2.07	1.15	0	3.93	
Age at Scan 1 (years)		9.80	1.31	6	12	138
Age at Scan 2 (years)		11.30	1.15	9	14	135
Age at Scan 3 (years)		12.58	1.26	10	15	127
Parent report of child sex	male	73 (52.9%)				
	female	65 (47.1%)				
Parent report of child race	Black	48 (34.8%)				
	white	76 (55.1%)				
	other	14 (10.1%)				

Note: PS = preschool (ages 3.0-5.11 years.months); SA= school-age (ages 6.0-9.11 years.months); EA = early adolescent (ages 10.0-14.11 years.months)

Component	Label	PS Anx	Inc/ Need	PS Extl
1	Anterior PFC	-0.242 (0.056)	-0.068 (0.813)	**-0.419 (0.036)**
2	Inferior lateral parietal ctx	**-0.32 (0.018)**	0.137 (0.337)	-0.34 (0.108)
3	sgACC, entorhinal ctx and medial temporal pole	**-0.302 (0.018)**	*-0.048 (0.88)*	0.151 (0.513)
4	Occipital ctx	**-0.31 (0.018)**	**0.215 (0.042)**	-0.134 (0.525)
5	Superior frontal ctx	-0.166 (0.142)	0.017 (0.906)	**-0.570 (0.009)**
6	Superior parietal ctx	**-0.317 (0.018)**	**0.225 (0.042)**	**-0.503 (0.018)**
7	TPJ	-0.213 (0.077)	**0.249 (0.036)**	-0.021 (0.902)
8	Primary motor ctx	-0.05 (0.624)	**0.293 (0.018)**	**-0.473 (0.027)**
9	Cingulate Ctx	-0.082 (0.475)	0.040 (0.881)	-0.277 (0.188)
10	Inf and ant m temporal lobe	-0.254 (0.056)	-0.035 (0.88)	-0.101 (0.581)
11	primary somatosens ctx	-0.229 (0.056)	**0.226 (0.042)**	-0.121 (0.534)
12	lingual gyrus	-0.231 (0.056)	**0.274 (0.018)**	-0.295 (0.173)
13	DLPFC	-0.171 (0.138)	-0.031 (0.88)	**-0.591 (0.018)**
14	L posterior middle and superior temporal lobe	-0.184 (0.114)	0.078 (0.813)	-0.134 (0.525)
15	Insula	**-0.308 (0.018)**	-0.008 (0.927)	-0.197 (0.394)
16	Precuneus	-0.203 (0.091)	0.074 (0.813)	**-0.422 (0.036)**
17	Inferior frontal ctx	-0.204 (0.091)	-0.019 (0.927)	-0.151 (0.513)
18	Right lateral frontal ctx, inferior temporal ctx	-0.19 (0.111)	0.032 (0.88)	-0.191 (0.394)

Table 2. Standardized betas and FDR corrected p-values from regressions predicting either thickness intercept (PS Anx, Inc/Need) or slope (PS Extl) for each structural component. Effects where FDR corrected p<.05 are bolded. PS=preschool, Anx= anxiety, Extl= externalizing, PFC=prefrontal cortex, sgACC=subgenual anterior cingulate cortex, ctx=cortex, m=middle, TPJ=temporal-parietal junction, DLPFC=Dorsolateral PFC

Figure Captions

Figure 1. Bivariate correlations between symptom measures and demographic variables. Bivariate correlations for all predictors of interest. Those relationships that were associated at an uncorrected p-value of 0.05 are shown in color. The darkness of color indicates strength of relationship (darker color = stronger) and the hue indicates direction of relationship (blue=negative, red=positive). PS=preschool, SA=school-age, EA=early adolescent

Figure 2. Components showing significant relationships between early life experiences and the components' intercept or slope. Baseline poverty (income to needs ratio) and preschool anxiety symptoms predicted intercepts only whereas preschool externalizing symptoms predicted slopes only. Components numbered according to Table 3.