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Cumulative Trauma, Adversity and Grief Symptoms associated with Fronto-temporal Regions in Life-course Persistent Delinquent Boys

Amy E. Lansing^{a,c,*}, Agam Virk^a, Randy Notestine^a, Wendy Y. Plante^{a,c}, and Christine Fennema-Notestine^{a,b}

^aDepartment of Psychiatry, University of California, San Diego, La Jolla, CA, USA

^bDepartment of Radiology; University of California, San Diego, La Jolla, CA, USA

^cDepartment of Sociology, San Diego State University, San Diego, CA, USA

Abstract

Delinquent youth have substantial trauma exposure, with life-course persistent delinquents [LCPD] also demonstrating elevated cross-diagnostic psychopathology and cognitive deficits. Because adolescents remain in the midst of brain and neurocognitive development, tailored interventions are key to improving functional outcomes. This structural magnetic resonance imaging study compared neuroanatomical profiles of 23 LCPD and 20 matched control adolescent boys. LCPD youth had smaller overall gray matter, and left hippocampal, volumes alongside less cortical surface area and folding within the left pars opercularis and supramarginal cortex. LCPD youth had more adversity-related exposures, and their higher Cumulative Trauma, Adversity and Grief [C-TAG] symptoms were associated with less surface area and folding in the pars opercularis and lingual gyrus. Neuroanatomical differences between LCPD and control youth overlap with data from both maltreatment and antisocial literatures. The affected left frontal regions also share connections to language- and executive-related functions, aligning well with LCPD youths' cognitive and behavioral difficulties. These data also dovetail with research suggesting the possibility of neurodevelopmental delays or disruptions related to cumulative adversity burden. Thus, concurrent treatment of LCPD youths' C-TAG symptoms and, cognitive deficits with overlapping neuroanatomical bases, may be most effective in improving outcomes and optimizing neurodevelopmental trajectories.

*Corresponding Author: Amy E. Lansing, Ph.D., 8950 Villa La Jolla Drive, Suite A109, University of California, San Diego, La Jolla, CA 92037, Phone: (858) 534 – 5557, Fax: (858) 534 – 7778, alansing@ucsd.edu.

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Contributors

Contributors AL and CFN were responsible for the study concept and design. AL, WYP, RN, and CFN contributed to the acquisition of MRI data. AL was responsible for all screening and psychiatric data collection. RN and CFN performed image analysis. AL, AV, WYP, and CFN performed statistical analyses and developed data presentation.

All authors contributed to the interpretation of findings and critically reviewed content and approved final version for publication.

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Keywords

Structural magnetic resonance imaging; Cumulative adversity; Complex trauma; Grief; Loss; Life-course Persistent Delinquent youth; Fronto-temporal regions

1. Introduction

Over 1.3 million youth are arrested annually in the United States (Puzzanchera, 2014), and each delinquent youth costs \$2.5–\$3.9 million (Cost adjusted, 2015) in their lifetime (Cohen, 1998). Substantial costs derive from their functional impairments in educational, occupational and social competence, which intensify with increased autonomy and responsibilities during young adulthood. Unfortunately, maltreatment increases the risk for delinquency, adult criminality, violence, cognitive deficits and poor functional outcomes (Cisler et al., 2012; van der Kolk et al., 2001; Widom et al., 1996). In turn, delinquent youth demonstrate significant cognitive deficits (Lansing, et al., 2014), psychiatric impairment (Teplin et al., 2002), and cumulative childhood adversities (total accumulated adversity burden, with poorer mental health among those experiencing the most severe adversities, Lloyd and Turner, 2003; Schilling et al., 2008). “Adversities” experienced by delinquent youth include exposure to multiple traumatic events (e.g., poly-victimization; Abram et al., 2013; Baglivio et al., 2014; Duke et al., 2010), losses (Perkins-Dock, 2001), deprivation (e.g., neglect), and complex trauma; which is defined as typically severe (direct harm), interpersonal (involving betrayal often by caregivers), repetitive and/or pervasive traumas occurring during development, such as ongoing childhood maltreatment (Ford and Courtois, 2013). This is especially true for Life-Course Persistent Delinquents [LCPD], who exhibit early onset disruptive behavior and engage persistently in antisocial behavior (Moffitt, 1993; Moffitt, 2006). Notably, these youth remain in the midst of continued brain and neurocognitive development (Geidd et al., 2010; Lenroot et al., 2006; Lebel et al., 2011; Giedd et al., 2015); therefore, adversity during early life may cause or exacerbate brain abnormalities, including delayed or disrupted development of myelination and cortical maturation.

Adversity exposure and trauma disorders among delinquents are up to eight times higher than in community youth, and high density housing with other delinquents and separation from family can result in re-traumatization and exacerbation of symptoms (Abram et al., 2004 and 2013; Arroyo, 2001; Cauffman et al., 1998; Hennessey et al., 2004; Holman and Ziedenberg, 2006; Wolpaw and Ford, 2004). LCPD youth are at particular risk for poor lifespan outcomes (Piquero et al., 2007) and intensive mental health and education service needs, yet are unlikely to receive traditional health services (Liebenberg & Ungar, 2014), emphasizing the need for a more sophisticated nosology and treatment strategies. The Adverse Childhood Experiences [ACE] (Anda et al., 2006; Baglivio et al., 2014) studies assess ten factors, including childhood abuse (physical, sexual, emotional); physical and emotional neglect; and parental distress (incarceration, mental illness, substance use; maternal-directed domestic violence); however, there is a clear need to address a broader range of adversities common among delinquents (Child Protective Services [CPS] removal; living in violent communities; Perkins-Dock, 2001). To provide effective programs, reduce

academic disengagement, improve functional outcomes and prevent delinquency escalation, we must better understand early adversity, along with the associated neurodevelopmental (neurological, psychiatric, cognitive) sequelae, among high-risk populations.

Neuroimaging research in criminally-engaged populations mainly focuses on violent and/or psychopathic adults; psychopathic youth (a theoretically controversial pathology for children; Blair 2010); or youth seen in mental health settings (Conduct Disorder; Kruesi et al., 2004) rather than justice-involved youth. These data indicate smaller prefrontal gray matter (Raine et al., 2000) and reduced frontal functional activation (Blair 2010), as well as smaller temporal lobe, particularly amygdala, volumes, and abnormal amygdalar activation (Kruesi et al., 2004; Blair 2010). Studies of adult and adolescent incarcerated psychopaths suggest less gray matter and abnormal functional connectivity in limbic and paralimbic areas (hippocampus, amygdala, cingulate, prefrontal cortex; Ermer et al., 2012), with cortical thinning among adults (Ly et al., 2012), and paralimbic involvement among adolescents (Ermer et al., 2012). Meta-analysis implicates less gray matter or lower functional activation in orbitofrontal, dorsolateral frontal and anterior cingulate cortex in a range of antisocial, violent and psychopathic adults (Yang and Raine, 2009). Compared to controls, Conduct Disordered youth demonstrate cortical thinning in the superior temporal gyrus and, both childhood- and adolescence-onset conduct disordered youth demonstrate reduced surface area in the orbitofrontal cortex (Fairchild et al., 2015). While these findings provide insight supporting critical associations with temporal and frontal areas, little is known about LCPD youth, not all of whom are psychopathic (Dembo et al., 2007), or the role of dimensions of early adversity exposure in brain development among delinquents.

Given the range of adversities experienced among delinquents (e.g., ACEs, deaths of loved ones, neighborhood violence), findings from maltreatment and post-traumatic stress disorder [PTSD] studies are additionally informative. Maltreatment studies suggest smaller intracranial vaults [ICV] and cerebral brain volumes, frontal and limbic abnormalities including both smaller structural estimates and abnormal functional activation patterns (DeBellis et al. 2002; Fennema-Notestine et al., 2002; Hart and Rubia, 2012; Kelly et al., 2013; Kelly et al. 2015), supporting the potential influence of trauma on the brain in LCPD youth. Early childhood adversity is associated with cognitive, psychiatric and neurologic sequelae that persist into adulthood (Fennema-Notestine et al., 2002; Hart and Rubia, 2012; McCrory et al., 2010; Sheriday et al., 2012), and the impact of stress on the brain has been associated with hippocampus, amygdala, cingulate, and prefrontal cortex abnormalities in children and adults (Bremner, 2006; DeBellis, 2005; Hart and Rubia, 2012; McCrory et al., 2010; Robinson and Shergill, 2011; Kelly et al., 2013; Kelly et al., 2015). Among adult males, data specifically indicate that higher cumulative adversity exposure is associated with reduced gray matter volume in prefrontal and limbic regions (Ansell, et al, 2012). Structural estimates are also typically smaller in maltreatment and stress-related cohorts (although one reported greater amygdala volume, Karl et al., 2006). The separate study of cortical thickness and surface area, both components of cortical volume, is critical, particularly within developing populations, as these aspects are driven by separate underlying genetic influences (Panizzon et al., 2009) and have varied developmental trajectories over time (Raznahan et al., 2011). Indeed, there is recent evidence for thinner cortex and smaller estimates of surface area and folding in distinct areas of the brain in maltreated youth,

particularly frontal regions (e.g., anterior cingulate, lingual gyrus, and pars opercularis (Kelly et al., 2013)).

In addition to the neural abnormalities consistently noted in the maltreatment and delinquency literatures, cognitive deficits among these populations suggest a clinical relevance to these neural findings. First, child maltreatment, early adversity and PTSD, are associated with cognitive deficits in executive, intellectual (especially Verbal IQ), memory and academic performance (e.g., Beers and De Bellis, 2002; see review Wilson et al., 2011) and other psychiatric/neurologic sequelae that may result from delayed or disrupted neurodevelopment and persist into adulthood (e.g., Perry et al., 2008). Second, delinquents exhibit prominent verbal and intellectual deficits, alongside verbal memory, early-onset visual-spatial and mixed executive deficit findings (Lansing, et al., 2014; Moffitt & Caspi, 2001; Morgan & Lilienfeld, 2000; Raine et al., 2005). This cognitive dysregulation, alongside behavioral and affective dysregulation observed among delinquents, may be linked to noted brain abnormalities, driven by the neurodevelopmental consequence of their increasingly well-documented early adversity exposure (Abram et al., 2013; Baglivio et al., 2014). In line with evidence related to the developmental impact of complex trauma (Pyne, et al., 1995; Cloitre et al., 2009) on emotion regulation and symptom complexity (Cloitre et al., 2009; Shipman et al., 2000, 2005), Moffitt (1993) proposed a developmental taxonomy for early-onset and persistent delinquency, suggesting that the interaction of cognitive deficits and adverse environments across development result in pathological behavior. Moffitt's later work (Koenen, et al., 2006), implicating children's externalizing behavior and family stress (maternal distress, loss of a parent) in the developmental roots of PTSD, further aligns with these concepts. Despite the strong evidence of the developmental impact of adversity on cognitive, neural, and psychiatric functioning and delinquency, no neuroimaging studies have specifically characterized adversity-related symptomatology among LCPD youth.

Therefore, we aimed to compare the neuroanatomical profiles of LCPD youth with matched controls, and to characterize the associations among neuroanatomical effects and adversity and resulting symptomatology in LCPD boys. Our investigation focused on brain regions implicated in both the antisocial and maltreatment/adversity literatures (e.g., frontal cortex, hippocampus, amygdala), reviewed above, and on sensitive metrics previously shown to elucidate neuroanatomical differences in childhood development (e.g., surface area, cortical folding; Kelly et al., 2013). We hypothesized that LCPD youth may have smaller hippocampal and amygdala volumes, alongside evidence of smaller frontal cortices. Considering reported structural and functional effects in frontal regions alongside the ongoing neurodevelopment in these areas within LCPD youth, we also proposed that, in addition to thinner cortex, we may see smaller surface areas and less folding indicative of stunted or delayed development in frontal cortex. Finally, we propose that the measures of regional frontal cortical surface area and folding may be strongly associated with cumulative adversities and resulting symptoms. These findings ultimately will facilitate the development of more informed preventive measures and better-targeted interventions for high-risk youth.

2. Methods

2.1 Subjects

We studied 23 LCPD adjudicated males, 16–18 years old, and 20 male control participants matched on age, race/ethnicity and household characteristics (e.g., single head of household, family resources, neighborhood; Table 1). LCPD youth were recruited from the San Diego County Probation Department's [SDCPD] Camp Barrett, a post-adjudication placement with similar age, offense and racial/ethnic minority distributions as those nationwide (Sickmund and Puzzanchera, 2014). Boys were selected from the three primary ethnic groups represented in this setting (Latino, African American and Caucasian; Keaton et al., 2008). Controls were recruited through flyers placed in communities where LCPD boys resided and research advertisements.

Eligibility included right handedness, English fluency; an IQ ≥ 70 ; and MRI safety eligibility for 3T MRI. Exclusions included color blindness; moderate to severe head injuries which are more consistently linked to neuroanatomical abnormalities (Faul et al., 2010; Silver et al., 2005) (e.g., Glasgow Coma Score ≤ 12 , abnormal neuroimaging); or psychotic symptoms interfering with informed consent/decisional capacity. LCPD-specific requirements included: disruptive behavior symptoms by age 10 and multiple adjudications. Psychopathy was assessed but not part of the eligibility criteria. Control-specific exclusions included: arrest, incarceration and/or CPS contact histories or Conduct Disorder. Imaging data were acquired at the University of California, San Diego [UCSD] Center for Functional MRI. All youth were interviewed by female interviewers with degrees in psychology or psychiatry, experience interviewing at-risk youth, and ≥ 3 months of training. Interviews were reviewed and supervised, or administered by a clinician.

2.2 Screening and Consenting Procedures

Research involving incarcerated youths requires special procedures because they are legal wards of the Juvenile Court who may not have a legal guardian to provide consent. Staff had SDCPD background clearance. A Juvenile Court Order allowed access to official records and incarcerated youth. All youth provided voluntary consent/assent.

A race/ethnicity stratified random sampling method was used with LCPD boys (random number generator and last digit of Probation ID within each racial/ethnic group). Potential controls responded to recruitment efforts by phone or email for screening: nine were ineligible due to neurological conditions ($n=2$), daily substance use precluding MRI acquisition ($n=1$), prior arrest/incarceration ($n=1$) or match incompatibility with LCPD youth (e.g., different age, race/ethnicity, $n=5$).

Eligible LCPD boys signed a study assent (<18 years) or consent (≥ 18 years) form. Consistent with federal regulations, the UCSD Institutional Review Board [UCSD-IRB], Centers for Disease Control and Prevention IRB, and the US Office of Protection from Research Risks [US OPRR] waived parental consent, although it was obtained when possible. Youths' assent was overseen by a participant-advocate who represented the youths' interests and ensured understanding of the study and consent forms. Study methods and consent forms were approved by the UCSD-IRB, US OPRR, and Department of Health and

Human Services which provides guidance on the involvement of prisoners in research (HHS regulations at 45 CFR part 46, subpart C). Controls provided screening assent/consent verbally by phone. If they were <18 years old, parents' verbal consent was obtained first. If eligible, written assent/consent was obtained from the youth. Written parental consent was obtained for controls <18 years old.

2.3 Measures

2.3.1 Structured Clinical Interview for Trauma and Loss Spectrum (SCI-TALS, Dell'Osso et al., 2008)—This 116-item interview uses a dichotomous response-structure (yes/no) to assess nine lifetime Domains: Loss Events (I); Grief Reactions (II); Trauma Events (III); Reactions to Losses/Upsetting Events (IV); Re-experiencing/Intrusion (V), Avoidance and Numbing (VI) and Arousal/Reactivity (VIII) symptoms in response to any endorsed loss and/or trauma; loss/trauma-related Maladaptive Coping (reckless/destructive behaviors) (VII); and Personal Risk-Factors (characteristics, such impulsivity, conceptualized to confer risk for stress-spectrum disorders but not queried in response to endorsed stressors) (IX). The SCI-TALS has acceptable reliability and validity (Dell'Osso et al., 2008). All Chronbach alphas showed acceptable internal reliability for symptom Domains (0.729).

In the present study, we explored both event-types and adversity-related symptom responses. ACE studies demonstrate graded negative health outcomes to higher ACE event-type exposures (Anda et al., 2006), which include trauma-type (physical abuse) and loss-type (parental divorce) events. First, Loss Events (e.g., death of a loved one, unwanted separations, miscarriages) capture negative experiences which may cause grief responses, including complicated bereavement, intrusion, avoidance, re-experiencing, guilt/self-blame, increased emotionality, and failure to adapt (Horowitz et al., 2003; Prigerson et al., 1999). Second, Trauma Events include traditional traumas (e.g., rape, physical abuse) and potentially traumatic experiences (e.g., bullying). Consistent with ACE studies, event-types represent only the number of exposure types, not number of total events experienced (i.e., any physical abuse represents an exposure to physical abuse, but not frequency of abuse), event severity or resulting symptomatology. Figure 1 describes event-types queried.

Third, unlike the more traditional PTSD symptom Domains in the SCI-TALS (e.g., Re-experiencing/intrusion), the Grief Reactions Domain II includes both *grief symptoms* (II-A), queried directly in response to losses (excessive longing, feeling life is purposeless), and theorized “*personality characteristics*” (II-B) (difficulty asking for help; needing to be a caregiver) which could represent grief-related risk-factors, symptoms or impairments but are queried without reference to losses (“Are you the type of person who forms very close attachments...”). To capture only symptomatology rather than theoretical risk-factors, we separated out the loss-specific grief symptoms (Cumulative Grief [C-G] Symptom-Index). Fourth, we captured the sum of Re-experiencing/intrusion, Avoidance/numbing and Arousal/ reactivity symptoms in response to all traumas and losses with a single score (Cumulative Trauma and Adversity [C-TA] Symptom-Index). Fifth, we created a single symptom score (Domains II-A, V, VI, VIII), with the Cumulative Trauma, Adversity and Grief [C-TAG] Symptom-Index’.

2.3.2 Life Event Checklist (LEC; Gray et al., 2004)—The LEC self-report: 1) separated events collapsed (“physical or sexual abuse”) on the SCI-TALS; 2) incorporated additional precipitating events; and 3) clarified event-exposure (directly experienced, witnessed, heard about). Modifications included: 1) familial separations (CPS removals); suicide attempts; and teen dating violence; 2) separating familial from community assault experiences; 3) expanding perpetration events (forced injury to others) if upsetting; 4) assessing age of trauma-exposures (age of onset variables); and 5) clarifying caregiver/living arrangement (placements) status.

2.3.3 Wechsler Abbreviated Scale of Intelligence [WASI]—The WASI is a four subtest measure of general intellectual abilities (Vocabulary, Block Design, Similarities, Matrix Reasoning) designed to provide an abbreviated measure of intellectual functioning, correlates well with other full measures of intelligence, and has acceptable reliability and validity (Wechsler, 1999).

2.3.4 Early Disruptive Behavior Scale (DSM-IV-TR, 2000)—Youth were asked about the presence or absence of Oppositional Defiant and Conduct Disorder symptoms before age 10.

2.3.5 Youth Psychopathic trait Inventory [YPI]—The YPI is 50-item self-report for adolescents tapping personality traits without reference to antisocial behavior (Andershed et al., 2002). The YPI measures three core dimensions of psychopathy with a 4-point scale (1=does not apply at all to 4=applies very well). The Grandiose-Manipulative dimension (20 items: range 20–80) addresses Dishonest Charm, Lying, Grandiosity, and Manipulation. The Callous-Unemotional dimension (15 items: range 15–60) addresses Callousness, Unemotionality and Remorselessness. The Impulsive-Irresponsible dimension (15 items: range 15–60) addresses Impulsiveness, Irresponsibility, and Thrill-seeking. All three factors showed acceptable internal reliability (Chronbach alpha range: 0.756–0.906, total reliability alpha = 0.940).

2.3.6 Substance Use Screen—Youth's age of first, weekly and daily use for illegal substances, over-the-counter and prescription drug abuse were queried. The Customary Drinking and Drug Use Record Form provided additional data on substance use, dependence and withdrawal (Brown et al., 1998).

2.3.7 Traumatic Brain Injury (TBI)—While we excluded youth with moderate to severe TBI, we characterized mild TBI using a 7-point severity scale derived from extensively queried self-report details capturing associated features (e.g., presence and length of loss of consciousness, confusion or amnesia; headache; nausea; ear-ringing/tinnitus; CDC, 2003). These methods stem from our extensive prior work characterizing TBI and evaluating the neurobehavioral sequelae of pediatric TBI and stroke (Lansing et al., 2004; Max et al., 2001; Max et al., 2004).

2.3.8 Family Resource Scale (Dunst and Leet, 1987)—This 31-item self-report assesses family resources (food, shelter, financial, transportation, healthcare, time for self

and family, and childcare), using a 5-point scale (1=not at all adequate to 5=almost always adequate).

2.3.9 Structural MRI—Neuroimaging methods provided gray and white matter volume, cortical surface area, thickness, and folding. MRI scans were acquired on a 3.0T GE MR750 scanner at the UCSD Keck Center for fMRI using an 8-channel head coil with three anatomical sequences: 3D sagittal T1 and 2D coronal T2 and proton density [PD] volumes. *T1*: IR-FSPGR, slice thickness=1.2mm, flip angle=8degrees, Multivariate Segmentation: TI=640ms, matrix 256×192; FreeSurfer TI=900ms, matrix 256×256. *T2*: TR=4600ms, ETL=16, matrix 256×256; and *PD*: TE=minimum full, TR=3000ms, matrix 256×192 with *T2* & *PD*: FOV=24cm, frequency encoding S/I direction, rbw=15.63, slice thickness=2.0mm. All image volumes were visually reviewed for motion, artifacts, and technical accuracy.

First, a multivariate tissue segmentation technique that employs the T1, T2, and PD (based on Jernigan et al., 2011; Fennema-Notestine et al., 2013) measured global gray and white matter volumes; abnormal white matter lesions; ventricular and sulcal CSF; and true ICV due to the inclusion of CSF information from the T2. The path includes T1 alignment to a common orientation, registration of T2 and PD to T1 using a mutual information method (Maes et al., 1997), bias-correction using N3 (Sled et al., 1998), and a three-class tissue segmentation which utilizes Scott's L2E method (Scott, 2001) to determine robust tissue means and covariances for white matter, gray matter, and fluid. Each bias-corrected volume is then nonlinearly warped to the MNI atlas using the Advanced Normalization Tools (Avants et al., 2011) and intensity normalized using the robust white and gray matter means determined by L2E. Volumes were log transformed to stabilize the variance.

Second, FreeSurfer's automated T1-based segmentation approach (Dale et al., 1999; Desikan et al., 2006; Fischl et al., 1999; Fischl et al., 2002) (Version 4.5) provided primary measures of interest including the hippocampus and amygdala (as in our prior work Fennema-Notestine, 2009; Figure 1). Since we used 3T field strength and phased array head coils, we implemented modifications of the standard N3 (Sled et al., 1998) bias correction methods as recommended by Boyes et al., (2008), using our ICV mask. This approach relies on a probabilistic atlas and applies a Bayesian classification rule to assign a neuroanatomical label to each voxel. Third, we used FreeSurfer's automated cortical surface reconstruction and parcellation (Dale et al., 1999; Desikan et al., 2006; Fischl et al., 1999) to estimate thickness, surface area, and folding of the neocortex regionally as in prior work (Fennema-Notestine et al., 2009; Fennema-Notestine et al., 2001). Primary regions of interest were defined by common overlapping regions affected in the antisocial and maltreatment literature: inferior frontal regions of pars orbitalis, pars triangularis, pars opercularis; caudal and rostral middle frontal; and superior frontal cortices thickness, surface area, and folding index (Figure 1). The processing software provides measures for additional neuroanatomical regions that were not defined a priori. For the purposes of the present study we included the supramarginal and lingual gyri based on brief mention in prior literature (Kelly et al. 2013; Kelly et al. 2015); any reported effects in these two areas were considered exploratory.

2.4 Statistical Analyses

Independent samples t-tests and chi square tests were used for comparisons between LCPD and control boys. Neuroimaging analyses mainly employed multivariable linear regression. First, we compared LCPD boys to controls on neuroimaging measures, with and without controlling for the covariate of TBI; as LCPD boys had higher rates of mild TBI that may contribute to brain abnormalities (Perron and Howard, 2008) we felt it prudent to examine potential associations with mild TBI. Second, within the LCPD group, we explored neuroimaging correlates of Loss Events; Trauma Events; and C-G, C-TA and C-TAG symptoms, using multivariable linear regression. This can be viewed, after adjusting for controlling covariates, as a partial correlation analysis. Additional non-parametric Spearman's rho correlations were performed for the neuroimaging correlates of symptoms due to the small sample size to control for potential non-normal distributions. All analyses with volumetric measures (e.g., hippocampus, amygdala, gray matter, white matter, CSF volumes) included total ICV volume as a covariate to account for individual differences in head size. Reported values reflect the parameter estimates for the variable of interest.

3. Results

3.1 Background Characteristics

No significant group differences emerged on demographic indicators, psychopathy dimensions or age at first trauma or alcohol use (Table 1). LCPD boys had significantly more early disruptive behavior symptoms, higher mild TBI scores, and earlier substance use onset than controls.

3.2 Trauma and Loss Exposure and Symptoms (Table 1)

Significant differences were observed in earlier loss exposure; and higher levels of trauma-type events; stressor reactivity; trauma- and loss-related arousal symptoms; and trauma-risk factors. Despite similarities in SCI-TALS' Loss Events, only LCPD boys had family disruption placements (LEC; incarcerations, CPS removal, residential treatment placement, $m=7.26$, $S.D.=2.93$). LCPD boys experienced significantly more parental death and separations (82.6%, with 3 youth reporting parental death) than controls (32.1%, with none experiencing a parental death): $X^2(1, n=42) = 5.82, p=0.02$. Trends emerged with higher scores on re-experiencing ($p=0.052$), maladaptive coping ($p=0.063$), C-G ($p=0.072$), C-TA ($p=0.099$) and Combined C-TAG ($p=0.074$) Symptom-Indices for LCPD relative to control boys.

Although LCPD boys responded similarly on some maladaptive coping items, they more often endorsed engaging in high-risk behaviors (54.5% vs. 10.0%, respectively, $X^2(1, n=42)=9.36, p=0.003$) and self-medication (68.2% vs. 25.0%, $X^2(1, n=42)=7.83, p=0.006$) directly in response to loss and trauma. LCPD boys endorsed more items on the arousal (64%), re-experiencing (54%) and avoidance (42%) symptom domains, relative to controls' endorsement of 34% of items in each domain. Response rates to loss- and trauma-types are provided in Figure 2. The higher rate of "Other Trauma" endorsement among LCPD youths reflects drive-by shootings and intimate partner violence victimization.

3.3 Structural Abnormalities in LCPD Youth

We report statistics from the primary models and from models including TBI as a covariate (noted by *with TBI*) for comparisons. LCPD youth had less total gray matter ($t=2.11$, $p=0.04$; *with TBI* $t=2.45$, $p=0.02$) and smaller left hippocampal volumes ($t=2.57$, $p=0.01$; *with TBI* $t=2.09$, $p=0.04$) (Figure 3), even when controlling for TBI. Groups were not different on ICV volume ($t=1.4$, $p=0.17$; *with TBI* $t=1.1$, $p=0.28$). Groups did not differ significantly on volumes of white matter, CSF, abnormal white matter, right hippocampus, or amygdala ($p>0.05$).

LCPD youth had less frontal surface area within the left pars opercularis (posterior inferior frontal gyrus; $t=2.2$, $p=0.03$; but not significant *with TBI* $t=1.5$, $p=0.13$) and the left supramarginal gyrus ($t=2.3$, $p=0.03$; *with TBI* $t=2.0$, $p<0.05$) (Figure 3). Left caudal midfrontal cortex only tended to have less surface area ($t=1.7$, $p=0.10$; but not significant *with TBI* $t=1.0$). Left pars orbitalis surface area was less in the LCPD youth only when TBI was included as a covariate ($t=2.4$, $p=0.02$). Otherwise, groups did not differ on surface area within the right or left pars orbitalis, pars triangularis, superior frontal, or rostral midfrontal cortices (all $p>0.10$). None of these regions were different on cortical thickness between groups ($p>0.05$), nor were groups different on right hemisphere measures of these regions.

LCPD youth also had less cortical folding in regions including the left pars opercularis ($t=2.36$, $p=0.02$; *with TBI* $t=2.39$, $p=0.02$), left supramarginal gyrus ($t=2.54$, $p=0.01$; but not significant *with TBI* $t=1.87$, $p=0.07$), and left caudal midfrontal ($t=2.7$, $p=0.01$; but not significant *with TBI* $t=1.4$, $p>0.05$). Otherwise, groups did not differ on folding (all $p>0.10$).

3.4 Structural Associations with Loss Events, Trauma Events and Symptom Indices within LCPD Youth

LCPD youth showed numerous neuroanatomical associations with adversity-related symptoms, although limited associations with the number of loss- and trauma-type events which occurred exclusively within the left pars opercularis surface area (Table 2; Figure 4). Surface area of the left and right pars opercularis and the left lingual gyrus were consistently significantly associated with our symptom indices: C-G Symptom-Index ($\rho = -0.59$, -0.51 and -0.60 respectively), C-TA Symptom-Index ($\rho = -0.60$, -0.50 and -0.58 respectively), and the Combined C-TAG Symptom-Index ($\rho = -0.72$, -0.56 and -0.74 respectively); with higher symptom levels associated with less surface area. Less folding in the left and right pars opercularis tended to be associated with higher scores particularly for the Combined C-TAG Symptom-Index ($\rho = -0.48$ and -0.57 respectively). Higher C-TA Symptom-Index scores were also associated with less surface area in the right caudal midfrontal ($\rho = -0.43$). There were no significant associations with other regions, including the supramarginal and superior frontal gyri, for surface area, thickness, or folding measures or with total gray matter or left hippocampal volumes. The number of trauma-type events LCPD youth experienced was associated only with the left pars opercularis surface area, but loss-type events were only marginally associated.

4. Discussion

There is increasing recognition of the dose-dependent medical and mental health consequences of ACE-specific exposures in the general population, but the early-onset and extreme loss and trauma exposures experienced in high-risk populations suggest an altered developmental pathway that may be obscured by a narrow focus on disruptive (oppositional, aggressive) behaviors without the context of wide-ranging early-onset, chronic and cumulative adversity-related precipitants (Duke et al., 2010). Societal responses to trauma (CPS removal) and disruptive behavior (school expulsion, incarceration) are likely to amplify adversity-related negative outcomes (Peters P v. Compton Unified School District, 2015). In the present study, LCPD boys experienced, on average, over seven placements outside of their home (e.g., CPS removal, incarceration). LCPD youth demonstrated less overall gray matter alongside subtle neuroanatomical limbic and cortical differences relative to controls well-matched for risk factors (SES, neighborhood, head-of-household). Our findings of less overall gray matter and smaller left hippocampal volumes align well with non-delinquent maltreatment studies, while the lack of ICV volume group differences supports the similar background environments of controls (De Bellis, 2005; DeBrito et al., 2013; Edmiston et al., 2011; Hanson et al., 2015; Teicher et al., 2012). The predominance of effects in LCPD boys' prefrontal and limbic regions overlaps with findings reported among individuals characterized as psychopathic or Conduct Disordered, as well as maltreated but non-delinquent youth (e.g., Raine et al., 2000; Yang and Raine, 2009; Hart and Rubia, 2012; Kelly 2013; Kelly et al. 2015). Similar neuroanatomical findings across these supposedly distinct populations support further investigation, particularly because early cumulative adversity likely characterizes many of these individuals.

The impact of early-onset, cumulative adversity is particularly important given that emotional numbing and hyperarousal in response to stressors may appear as callous, unemotional and/or aggressive traits that are part of the diagnostic criteria for antisocial-spectrum disorders. This point is underscored by LCPD boys' significantly greater endorsement of adversity-related arousal symptoms and amplified by a profile of disruptive behavior symptoms emerging before age 10, against an even earlier onset of loss exposure, on average, by age four. Consistent with this concern, the inferior frontal gyrus pars opercularis, an area different between LCPD and control boys, was strikingly associated with grief-specific and trauma/adversity symptoms among LCPD youth, but very limited in associations with event-types, such as assessed by ACE studies. These findings support the impact of cumulative adversity-related symptoms on the well-being of these youth, and suggest the potential impact of stress on the developing brain (De Bellis, 2005; Gunnar and Quevedo, 2007). The observed effects in cortical surface area and folding, rather than cortical thickness, in these high-risk youth support the possibility of a delayed or altered neurodevelopmental course related to the more gradual surface area changes during this age range (Raznahan et al., 2011) rather than pruning that thins the cortex. Whether these differences are specific to myelination, pruning, or decreased growth factors (De Bellis, 2005; Kelly et al., 2013; Raznahan et al., 2011) should be further explored in longitudinal studies.

Our findings emphasize the relevance and association of these factors with the left hemisphere frontal cortex among LCPD boys. These regions share connections with, and are linked to, language- and executive-related functions providing an adversity-related bridge between the brain, cognitive deficits, behavioral symptoms and persistent offending styles (Anda et al., 2006; Lansing et al., 2014; Piquero, 2001; Raine et al., 2005). The left pars opercularis, supramarginal gyrus, and lingual gyrus have been associated with language-related functions (auditory processing, language comprehension and production, word identification, recognition, and naming), social communication/cognition, and executive functioning (Badre et al., 2010; Frey et al., 2008; Kozlovskiy et al., 2014; Klepousniotou et al., 2013; Mechelli et al., 2000; Piquero, 2001; Raine et al., 2005; Skipper et al., 2007). LCPD boys' neuroanatomical correlations with adversity-related symptoms, coupled with smaller left hippocampal volumes in LCPD boys compared to controls, provide support for both verbal and visual-spatial difficulties reported in delinquent and non-delinquent maltreated populations (Lansing et al., 2014; Mothes et al., 2015; Raine et al., 2005), and suggest that difficulties are most common when there is increased executive demand (e.g., verbal working memory).

Taken together, these results suggest that interventions targeting symptoms arising from early-onset cumulative adversity, and the cognitive deficits that share a common neuroanatomical basis, may be the most effective in improving outcomes and optimizing their neurodevelopmental trajectories. The impact of a range of stressors on neurodevelopment also suggests that adversity-exposed youth with early onset disruptive behavior and trauma-spectrum symptoms may fall within the developmental disorders continuum. The impact of adversity on the brain, including potential developmental delays and cognitive capacities should be a consideration when understanding school-readiness and academic failure in high-risk populations. These findings add to our understanding of the neurological impact of early-onset cumulative adversity, and may ultimately inform preventive measures, enhance diagnostic classification, and improve targeted treatment interventions for adversity-exposed high-risk youth.

4.1 Limitations and Future Directions

Although the LCPD youth had higher rates of mild TBI and substance use which could contribute to profile differences with controls (Perron and Howard, 2008), the use of a carefully calculated TBI score as a covariate in these models supports effects beyond physical brain injury. Due to power limitations and variability across participants, we were not able to additionally control for substance use, an important topic of future exploration. More serious substance use may also be consequence of higher levels of early-onset, cumulative adversity-exposure (Khoury et al., 2010), which is supported by the very early onset of loss among LCPD youth alongside their significantly greater endorsement of substance and alcohol use directly in response to their trauma and loss experiences.

The present study focuses on cumulative "lifetime" exposures, and symptomatic responses to specific loss and trauma events among adolescent boys. ACE studies find graded responses between number of ACE-specific exposures and negative health consequences. However, in our LCPD boys, adversity exposures exhibited only limited associations, while

adversity-related symptoms had strong neuroanatomical correlates, emphasizing the importance of exploring cumulative symptomatology during development.

Given co-occurring conditions and symptomatology (e.g., substance use) commonly noted among adversity-exposed youth, future studies involving LCPD or other high-risk youth must carefully address these factors using large samples. Future large scale studies should also address the frequency and severity, not just the presence, of adversity-related symptomatology, and include females, who are known to have extreme adversity exposure. Younger children followed longitudinally would also allow us to develop a more nuanced understanding of adversity-related symptoms relative to neuroanatomical correlates.

Additionally, while we have speculated about links between documented verbal deficits among LCPD youth in other studies and our neuroanatomical correlates of early-onset adversity exposure, longitudinal data are needed to delineate the cognitive effects associated with these brain abnormalities and to further explore right and left hemispheric dysfunction that may dominate at various periods of development. In particular, there is evidence that visual-spatial deficits are observed very early among children who later become LCPD (Raine et al., 2005) and that reported verbal deficits in the population may emerge only after adversity exposure (Aguilar, et al., 2000). These data provide intriguing hypotheses for the developmental trajectory of LCPD youth.

Finally, whether adversity exposure is a cause of, or a risk factor for, cognitive deficits and/or brain abnormalities is not yet clear. However, none of our current diagnostic terminology adequately aligns with the potential impact of cumulative adversities that occur early in the lifespan and may be chronic and/or co-occurring. The role of loss in symptom development and impairment is not captured by diagnoses such as PTSD, complex PTSD, or even Developmental Trauma Disorder which focuses on disrupted attachment in response to trauma but does not account for losses which may not qualify as “extreme” or traumatic. Similarly, Complicated/Prolonged Grief has not yet been accepted into the DSM, is formulated largely on loss in adult populations (death of a spouse) and fails to capture the developmental impact of attachment disruption. While our data strongly support the role of loss and a range of adversities in brain differences, no current diagnostic options convey the symptomatic range and/or developmental disruption that occurs in the context of early-onset, cumulative adversity-exposure. The present study, along with data indicating notable correlations between poverty and reduced cortical surface area with prominent differences in regions supporting language and decision-making skills (Holz et al., 2015; Noble et al., 2015), underscore the need to acknowledge the neurodevelopmental consequences of a range of exposures in our diagnostic nomenclature (D’Andrea et al., 2012).

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References

- [Accessed September 23, 2015] Cost adjusted for 2013 relative dollar value per Consumer Price Index. 2014. from <http://www.measuringworth.com/uscompare/>
- Abram KM, Teplin LA, Charles DR, Longworth SL, McClelland GM, Dulcan MK. Posttraumatic stress disorder and trauma in youth in juvenile detention. *Arch Gen Psychiatry*. 2004; 61(4):403–410. [PubMed: 15066899]
- Abram, KM.; Teplin, LA.; King, DC.; Longworth, SL.; Emanuel, KM.; Romero, EG.; McClelland, GM.; Dulcan, MK.; Washburn, JJ.; Welty, LJ.; Olson, ND. PTSD, Trauma, and Comorbid Psychiatric Disorders in Detained Youth. Office of Juvenile Justice and Delinquency Prevention; Washington, DC: 2013.
- Aguilar B, Sroufe LA, Egeland B, Carlson E. Distinguishing the early-onset/persistent and adolescence-onset antisocial behavior types: From birth to 16 years. *Dev Psychopathol*. 2000; 12(2): 109–132. [PubMed: 10847620]
- Diagnostic and statistical manual-text revision (DSM-IV-TR, 2000). American Psychiatric Association; 2000.
- Anda RF, Felitti VJ, Bremner JD, Walker JD, Whitfield C, Perry BD, Dube SR, Giles WH. The enduring effects of abuse and related adverse experiences in childhood. A convergence of evidence from neurobiology and epidemiology. *Eur Arch Psychiatry Clin Neurosci*. 2006; 256(3):174–186. 3232061. [PubMed: 16311898]
- Andershed, HA.; Kerr, M.; Stattin, H.; Levander, S. Psychopathic traits in non-referred youths: A new assessment tool. 2002.
- Ansell EB, Rando K, Tuit K, Guarnaccia J, Sinha R. Cumulative adversity and smaller gray matter volume in medial prefrontal, anterior cingulate, and insula regions. *Biological psychiatry*. 2012; 72(1):57–64. [PubMed: 22218286]
- Arroyo, W. PTSD and children and adolescents in the juvenile justice system. In: Eth, S., editor. *Review of Psychiatry Series*. Vol. Vol. 20. American Psychiatric Publishing; Washington DC: 2001. p. 59-86.
- Avants BB, Tustison NJ, Song G, Cook PA, Klein A, Gee JC. A reproducible evaluation of ANTs similarity metric performance in brain image registration. *Neuroimage*. 2011; 54(3):2033–2044. [PubMed: 20851191]
- Badre D, Kayser AS, D'Esposito M. Frontal cortex and the discovery of abstract action rules. *Neuron*. 2010; 66(2):315–326. doi:10.1016/j.neuron.2010.03.025. PMC 2990347. PMID 20435006. [PubMed: 20435006]
- Baglivio M, Epps N, Swartz K, Huq M, Sheer A, Hardt N. The prevalence of Adverse Childhood Experiences (ACE) in the lives of Juvenile Offenders. *OJJDP Journal of Juvenile Justice*. 2014; 3(2):1–23.
- Beers SR, De Bellis MD. Neuropsychological function in children with maltreatment-related posttraumatic stress disorder. *Am J Psychiatry*. 2002; 159(3):483–486. [PubMed: 11870018]
- Blair RJR. Neuroimaging of psychopathy and antisocial behavior: a targeted review. *Curr Psychiatry Rep*. 2010; 12(1):76–82. [PubMed: 20425314]
- Boyes RG, Gunter JL, Frost C, Janke AL, Yeatman T, Hill DL, Bernstein MA, Thompson PM, Weiner MW, Schuff N, Alexander GE, Killiany RJ, DeCarli C, Jack CR, Fox NC. Intensity non-uniformity correction using N3 on 3-T scanners with multichannel phased array coils. *Neuroimage*. 2008; 39(4):1752–1762. 2007/12/08. [PubMed: 18063391]
- Bremner JD. Traumatic stress: effects on the brain. *Dialogues Clin Neurosci*. 2006; 8(4):445–461. [PubMed: 17290802]
- Brown SA, Myers MG, Lippke L, Tapert SF, Stewart DG, Vik PW. Psychometric evaluation of the Customary Drinking and Drug Use Record (CDDR): a measure of adolescent alcohol and drug involvement. *J stud alcohol*. 1998; 59(4):427–438. [PubMed: 9647425]
- Cauffman E, Feldman SS, Waterman J, Steiner H. Posttraumatic stress disorder among female juvenile offenders. *J Am Acad Child Adolesc Psychiatry*. 1998; 37(11):1209–1216. [PubMed: 9808933]

- Centers for Disease Control and Prevention (CDC), National Center for Injury Prevention and Control. Report to Congress on mild traumatic brain injury in the United States: steps to prevent a serious public health problem. Centers for Disease Control and Prevention; Atlanta (GA): 2003.
- Cisler JM, Begle AM, Amstadter AB, Resnick HS, Danielson CK, Saunders BE, Kilpatrick DG. Exposure to interpersonal violence and risk for PTSD, depression, delinquency, and binge drinking among adolescents: data from the NSA-R. *J Trauma Stress*. 2012; 25(1):33–40. [PubMed: 22354506]
- Cohen MA. The monetary value of saving a high-risk youth. *J of Quant Criminol*. 1998; 14(1):5–33.
- Cook, A.; Blaustein, M.; Spinazzola, J.; van der Kolk, B. SAMHSA White Paper. 2003. Complex trauma in children and adolescents.
- D'Andrea W, Ford J, Stolbach B, Spinazzola J, van der Kolk BA. Understanding interpersonal trauma in children: why we need a developmentally appropriate trauma diagnosis. *Am J Orthopsychiatry*. 2012; 82(2):187–200. [PubMed: 22506521]
- Dale AM, Fischl B, Sereno MI. Cortical surface-based analysis. I. Segmentation and surface reconstruction. *Neuroimage*. 1999; 9(2):179–194. [PubMed: 9931268]
- De Bellis MD, Keshavan MS, Shifflett H, Iyengar S, Beers SR, Hall J, Moritz G. Brain structures in pediatric maltreatment-related posttraumatic stress disorder: a sociodemographically matched study. *Biol Psychiatry*. 2002; 52(11):1066–1078. [PubMed: 12460690]
- De Bellis MD. The psychobiology of neglect. *Child maltreat*. 2005; 10(2):150–172. [PubMed: 15798010]
- De Brito SA, Viding E, Sebastian CL, Kelly PA, Mechelli A, Maris H, McCrory EJ. Reduced orbitofrontal and temporal grey matter in a community sample of maltreated children. *J Child Psychol Psychiatry*. 2013; 54(1):105–112. [PubMed: 22880630]
- Dell'Osso L, Shear MK, Carmassi C, Rucci P, Maser JD, Frank E, Cassano GB. Validity and reliability of the Structured Clinical Interview for the Trauma and Loss Spectrum (SCI-TALS). *Clin Pract Epidemiol Ment Health*. 2008; 4(1):2. [PubMed: 18226228]
- Dembo R, Jainchill N, Turner C, Fong C, Farkas S, Childs K. Levels of psychopathy and its correlates: a study of incarcerated youths in three states. *Behav Sci Law*. 2007; 25(5):717–738. [PubMed: 17899531]
- Desikan RS, Segonne F, Fischl B, Quinn BT, Dickerson BC, Blacker D, Buckner RL, Dale AM, Maguire RP, Hyman BT, Albert MS, Killiany RJ. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. *Neuroimage*. 2006; 31(3):968–980. [PubMed: 16530430]
- Donnellan MB, Ge X, Wenk E. Cognitive abilities in adolescent-limited and life-course-persistent criminal offenders. *J Abnorm Psychol*. 2000; 109(3):396–402. [PubMed: 11016109]
- Duke NN, Pettingell SL, McMorris BJ, Borowsky IW. Adolescent violence perpetration: associations with multiple types of adverse childhood experiences. *Pediatrics*. 2010; 125(4):e778–e786. [PubMed: 20231180]
- Dunst CJ, Leet HE. Measuring the adequacy of resources in households with young children. *Child Care Health Dev*. 1987; 13(2):111–125. [PubMed: 3581439]
- Edmiston EE, Wang F, Mazure CM, Guiney J, Sinha R, Mayes LC, Blumberg HP. Corticostriatal- limbic gray matter morphology in adolescents with self-reported exposure to childhood maltreatment. *Arch Pediatr Adolesc Med*. 2011; 165(12):1069–1077. [PubMed: 22147775]
- Ermer E, Cope LM, Nyalakanti PK, Calhoun VD, Kiehl KA. Aberrant paralimbic gray matter in criminal psychopathy. *J Abnorm Psychol*. 2012; 121(3):649–658. [PubMed: 22149911]
- Faul, M.; Xu, L.; Wald, MM.; Coronado, VG. Traumatic brain injury in the United States: Emergency department visits, hospitalizations and deaths 2002–2006. Centers for Disease Control and Prevention, National Center for Injury Prevention and Control; Atlanta, GA: 2010.
- Fennema-Notestine C, Ellis RJ, Archibald SL, Jernigan TL, Letendre SL, Notestine RJ, Taylor MJ, Theilmann RJ, Julaton MD, Croteau DJ, Wolfson T, Heaton RK, Gamst AC, Franklin DR Jr, Clifford DB, Collier AC, Gelman BB, Marra C, McArthur JC, McCutchan JA, Morgello S, Simpson DM, Grant I, the CHARTER Group. Increases in brain white matter abnormalities and subcortical gray matter are linked to CD4 recovery in HIV infection. *J Neurovirol*. 2013; 19(4):393–401. NIHMSID: 504069. [PubMed: 23838849]

- Fennema-Notestine C, Hagler DJ Jr, McEvoy LK, Fleisher AS, Wu EH, Karow DS, Dale AM, the Alzheimer's Disease Neuroimaging Initiative. Structural MRI biomarkers for preclinical and mild Alzheimer's disease. *Hum Brain Mapp.* 2009; 30(10):3238–3253. PMID: 2951116. [PubMed: 19277975]
- Fennema-Notestine C, Panizzon MS, Thompson WR, Chen CH, Eyler LT, Fischl B, Franz CE, Grant MD, Jak AJ, Jernigan TL, Lyons MJ, Neale MC, Seidman LJ, Tsuang MT, Xian H, Dale AM, Kremen WS. Presence of ApoE epsilon4 allele associated with thinner frontal cortex in middle age. *J Alzheimers Dis.* 2011; 26(Suppl 3):49–60. NIHMSID: 350682. [PubMed: 21971450]
- Fennema-Notestine C, Stein MB, Kennedy CM, Archibald SL, Jernigan TL. Brain morphometry in female victims of intimate partner violence with and without posttraumatic stress disorder. *Biol Psychiatry.* 2002; 52(11):1089–1101. [PubMed: 12460692]
- Fischl B, Salat DH, Busa E, Albert M, Dieterich M, Haselgrove C, van der Kouwe A, Killiany R, Kennedy D, Klaveness S, Montillo A, Makris N, Rosen B, Dale AM. Whole brain segmentation: automated labeling of neuroanatomical structures in the human brain. *Neuron.* 2002; 33(3):341–355. [PubMed: 11832223]
- Fischl B, Sereno MI, Dale AM. Cortical surface-based analysis. II: Inflation, flattening, and a surface-based coordinate system. *Neuroimage.* 1999; 9(2):195–207. [PubMed: 9931269]
- Ford, JD.; Courtois, CA., editors. Treating complex traumatic stress disorders in children and adolescents: Scientific foundations and therapeutic models. Guilford Press; 2013.
- Frey S, Campbell JS, Pike GB, Petrides M. Dissociating the human language pathways with high angular resolution diffusion fiber tractography. *J Neurosci.* 2008; 28(45):11435–11444. [PubMed: 18987180]
- Giedd JN, Stockman M, Weddle C, Liverpool M, Alexander-Bloch A, Wallace GL, Lee NR, Lalonde F, Lenroot RK. Anatomic magnetic resonance imaging of the developing child and adolescent brain and effects of genetic variation. *Neuropsychol Rev.* 2010; 20(4):349–361. 3268519. [PubMed: 21069466]
- Giedd JN, Raznahan A, Alexander-Bloch A, Schmitt E, Gogtay N, Rapoport JL. Child psychiatry branch of the National Institute of Mental Health longitudinal structural magnetic resonance imaging study of human brain development. *Neuropsychopharmacology.* 2015; 40:43–49. [PubMed: 25195638]
- Gray MJ, Litz BT, Hsu JL, Lombardo TW. Psychometric properties of the life events checklist. *Assessment.* 2004; 11(4):330–341. [PubMed: 15486169]
- Gunnar M, Quevedo K. The neurobiology of stress and development. *Annu. Rev. Psychol.* 2007; 58:145–173. [PubMed: 16903808]
- Hanson JL, Nacewicz BM, Sutterer MJ, Cayo AA, Schaefer SM, Rudolph KD, Davidson RJ. Behavioral problems after early life stress: contributions of the hippocampus and amygdala. *Biol Psychiatry.* 2015; 77(4):314–323. [PubMed: 24993057]
- Hart H, Rubia K. Neuroimaging of child abuse: a critical review. *Front Hum Neurosci.* 2012; 6:52. 3307045. [PubMed: 22457645]
- Hennessey, M.; Ford, JD.; Mahoney, K.; Ko, SJ.; Siegfried, CB. Trauma among Girls in the Juvenile Justice System. National Child Traumatic Stress Network Juvenile Justice Working Group; Los Angeles, CA: 2004.
- Holman, B.; Ziedenberg, J. The Dangers of Detention: The Impact of Incarcerating Youth in Detention and Other Secure Facilities. Justice Policy Institute; Washington DC: 2006.
- Holz NE, Boecker R, Hohm E, Zohsel K, Buchmann AF, Blomeyer D, Laucht M. The Long-Term Impact of Early Life Poverty on Orbitofrontal Cortex Volume in Adulthood: Results from a Prospective Study Over 25 Years. *Neuropsychopharmacology.* 2015; 40(4):996–1004. [PubMed: 25315195]
- Horowitz MJ, Siegel B, Holen A, Bonanno GA, Milbrath C, Stinson CH. Diagnostic criteria for complicated grief disorder. *Focus.* 2003; 1(3):290–298.
- Jennings WG, Reingle JM. On the number and shape of developmental/life-course violence, aggression, and delinquency trajectories: A state-of-the-art review. *J Crim Justice.* 2012; 40(6): 472–489.

- Jernigan TL, Archibald SL, Fennema-Notestine C, Taylor MJ, Theilmann RJ, Julaton MD, Notestine RJ, Wolfson T, Letendre SL, Ellis RJ, Heaton RK, Gamst AC, Franklin DR Jr, Clifford DB, Collier AC, Gelman BB, Marra C, McArthur JC, McCutchan JA, Morgello S, Simpson DM, Grant I, the CHARTER Group. Clinical factors related to brain structure in HIV: the CHARTER study. *J Neurovirol.* 2011; 17(3):248–257. PMID: 3702821. [PubMed: 21544705]
- Keaton, S.; Burke, C.; Rohanna, K.; Sievers, S.; Schafer, E. SANDAG Executive Summary. 2008. San Diego County's Disproportionate Minority Contact (DMC): Identification and Assessment.
- Kelly PA, Viding E, Wallace GL, Schaer M, De Brito SA, Robustelli B, McCrory EJ. Cortical thickness, surface area, and gyrification abnormalities in children exposed to maltreatment: neural markers of vulnerability? *Biological psychiatry.* 2013; 74(11):845–852. [PubMed: 23954109]
- Kelly PA, Viding E, Puetz VB, Palmer AL, Mechelli A, Pingault JB, Samuel S, McCrory EJ. Sex differences in socioemotional functioning, attentional bias, and gray matter volume in maltreated children: A multilevel investigation. *Development and psychopathology.* 2015; 27:1591–1609. [PubMed: 26535946]
- Khoury L, Tang YL, Bradley B, Cubells JF, Ressler KJ. Substance use, childhood traumatic experience, and Posttraumatic Stress Disorder in an urban civilian population. *Depress Anxiety.* 2010; 27(12):1077–1086. [PubMed: 21049532]
- Klepousniotou E, Gracco VL, Pike GB. Pathways to lexical ambiguity: fMRI evidence for bilateral fronto-parietal involvement in language processing. *Brain Lang.* 2013; 131:56–64. [PubMed: 24183467]
- Koenen KC, Moffitt TE, Poulton R, Martin J, Caspi A. Early childhood factors associated with the development of post-traumatic stress disorder: results from a longitudinal birth cohort. *Psychological medicine.* 2007; 37(02):181–192. [PubMed: 17052377]
- Kozlovskiy SA, Pyasik MM, Korotkova AV, Vartanov AV, Kiselnikov AA, Glozman JM. Selective Involvement of Lingual Gyrus in Working Memory and Perception of Different Types of Visual Stimuli. *J Int Neuropsychol Soc.* 2014; 20(S2):43. doi:10.1017/S1355617714000915.
- Kruesi MJ, Casanova MF, Mannheim G, Johnson-Bilder A. Reduced temporal lobe volume in early onset conduct disorder. *Psychiatry Res.* 2004; 132(1):1–11. [PubMed: 15546698]
- Lansing AE, Max JE, Delis DC, Fox PT, Lancaster J, Manes FF, Schatz A. Verbal learning and memory after childhood stroke. *J Int Neuropsychol Soc.* 2004; 10(5):742–752. [PubMed: 15327721]
- Lansing AE, Washburn JJ, Abram KM, Thomas UC, Welty LJ, Teplin LA. Cognitive and Academic Functioning of Juvenile Detainees Implications for Correctional Populations and Public Health. *J Correct Health Care.* 2014; 20(1):18–30. [PubMed: 24352405]
- Lebel C, Beaulieu C. Longitudinal development of human brain wiring continues from childhood into adulthood. *J Neurosci.* 2011; 31(30):10937–10947. [PubMed: 21795544]
- Lenroot RK, Giedd JN. Brain development in children and adolescents: insights from anatomical magnetic resonance imaging. *Neurosci Biobehav Rev.* 2006; 30(6):718–729. [PubMed: 16887188]
- Liebenberg L, Ungar M. A comparison of service use among youth involved with juvenile justice and mental health. *Children and Youth Services Review.* 2014; 39:117–122. services. *American Journal of Public Health,* 95(10), 1773-1780.
- Lloyd DA, Turner RJ. Cumulative adversity and posttraumatic stress disorder: evidence from a diverse community sample of young adults. *American Journal of Orthopsychiatry.* 2003; 73(4):381. [PubMed: 14609400]
- Lupien SJ, McEwen BS, Gunnar MR, Heim C. Effects of stress throughout the lifespan on the brain, behaviour and cognition. *Nat Rev Neurosci.* 2009; 10(6):434–445. [PubMed: 19401723]
- Ly M, Motzkin JC, Philippi CL, Kirk GR, Newman JP, Kiehl KA, Koenigs M. Cortical thinning in psychopathy. *Am J Psychiatry.* 2012; 169(7):743–749. 3815681. [PubMed: 22581200]
- Maes F, Collignon A, Vandermeulen D, Marchal G, Suetens P. Multimodality image registration by maximization of mutual information. *IEEE Trans Med Imaging.* 1997; 16(2):187–198. [PubMed: 9101328]
- Max JE, Lansing AE, Koele SL, Castillo CS, Bokura H, Schachar R, Collings N, Williams KE. Attention deficit hyperactivity disorder in children and adolescents following traumatic brain injury. *Dev Neuropsychol.* 2004; 25(1–2):159–177. [PubMed: 14984333]

- Max JE, Robertson BAM, Lansing AE. The phenomenology of personality change due to traumatic brain injury in children and adolescents. *J Neuropsychiatry Clin Neurosci*. 2001; 13(2):161–170. [PubMed: 11449023]
- McCrary E, De Brito SA, Viding E. Research review: the neurobiology and genetics of maltreatment and adversity. *J Child Psychol Psychiatry*. 2010; 51(10):1079–1095. [PubMed: 20546078]
- Mechelli A, Humphreys GW, Mayall K, Olson A, Price CJ. Differential effects of word length and visual contrast in the fusiform and lingual gyri during reading. *Proc Biol Sci*. 2000; 267(1455): 1909–1913. 8. [PubMed: 11052544]
- Moffitt TE. Adolescence-limited and life-course-persistent antisocial behavior: a developmental taxonomy. *Psychological review*. 1993; 100(4):674. [PubMed: 8255953]
- Moffitt TE. Adolescence-limited and life-course-persistent antisocial behavior: a developmental taxonomy. *Psychological review*. 1993; 100(4):674. [PubMed: 8255953]
- Moffitt TE, Caspi A. Childhood predictors differentiate life-course persistent and adolescence-limited antisocial pathways among males and females. *Development and psychopathology*. 2001; 13(02): 355–375. [PubMed: 11393651]
- Moffitt, TE. Life-course-persistent versus adolescence-limited antisocial behavior. In: Cicchetti, D.; Cohen, D., editors. *Developmental Psychopathology*. 2nd ed. Vol. Volume 3. Wiley; New York: 2006. 2006
- Morgan AB, Lilienfeld SO. A meta-analytic review of the relation between antisocial behavior and neuropsychological measures of executive function. *Clinical psychology review*. 2000; 20(1):113–136. [PubMed: 10660831]
- Mothes L, Kristensen CH, Grassi-Oliveira R, Fonseca RP, Lima Argimon II, Irigaray TQ. Childhood maltreatment and executive functions in adolescents. *Child Adolesc Ment Health*. 2015; 20(1):56–62.
- Noble KG, Houston SM, Brito NH, Bartsch H, Kan E, Kuperman JM, Sowell ER. Family income, parental education and brain structure in children and adolescents. *Nat Neurosci*. 2015; 18(5):773–778. [PubMed: 25821911]
- Panizzon MS, Fennema-Notestine C, Eyler LT, Jernigan TL, Prom-Wormley E, Neale M, Xian H. Distinct genetic influences on cortical surface area and cortical thickness. *Cerebral Cortex*. 2009; 19:2728–2735. [PubMed: 19299253]
- Perron BE, Howard MO. Prevalence and correlates of traumatic brain injury among delinquent youths. *Crim Behav Ment Health: CBMH*. 2008; 18(4):243–255. [PubMed: 18803295]
- Perry BD, Beauchaine T, Hinshaw S. Child maltreatment: A neurodevelopmental perspective on the role of trauma and neglect in psychopathology. *Child and adolescent psychopathology*. 2008:93–128.
- [Accessed October 28, 2015] 2015. <http://www.publiccounsel.org/tools/assets/files/0644.pdf>
- Piquero AR, Daigle LE, Gibson C, Piquero NL, Tibbetts SG. Are life-course-persistent offenders at risk for adverse health outcomes? *J Res Crime Delinq*. 2007; 44:185–207.
- Piquero A. Testing Moffitt's neuropsychological variation hypothesis for the prediction of life-course persistent offending. *Psychology, Crime and Law*. 2001; 7(1–4):193–215.
- Prigerson HG, Shear MK, Jacobs SC, Reynolds CF, Maciejewski PK, Rosenheck R, Davidson JR, Pilkonis PA, Wortman CB, Williams JB, Widiger TA, Weiss R, Beery LC, Rynearson EK, Frank E, Kupfer DJ, Zisook S. Consensus criteria for traumatic grief: A rationale and preliminary empirical test. *Br J Psychiatry*. 1999; 174:67–73. [PubMed: 10211154]
- Puzzanchera, C. Juvenile arrests 2012. US Department of Justice, Office of Justice Programs, Office of Juvenile Justice and Delinquency Prevention; Washington, DC: 2014. p. 3
- Raine A, Lencz T, Bihlre S, LaCasse L, Colletti P. Reduced prefrontal gray matter volume and reduced autonomic activity in antisocial personality disorder. *Arch Gen Psychiatry*. 2000; 57(2):119–127. discussion 128–119. [PubMed: 10665614]
- Raine A, Moffitt TE, Caspi A, Loeber R, Stouthamer-Loeber M, Lynam D. Neurocognitive impairments in boys on the life-course persistent antisocial path. *J abnorm psychol*. 2005; 114(1): 38. [PubMed: 15709810]
- Raznahan A, Shaw P, Lalonde F, Stockman M, Wallace GL, Greenstein D, Giedd JN. How does your cortex grow? *J Neurosci*. 2011; 31:7174–7177. [PubMed: 21562281]

- Robinson BL, Shergill SS. Imaging in posttraumatic stress disorder. *Curr Opin Psychiatry*. 2011; 24(1):29–33. [PubMed: 21088585]
- Schilling EA, Aseltine RH, Gore S. The impact of cumulative childhood adversity on young adult mental health: measures, models, and interpretations. *Social science & medicine*. 2008; 66(5): 1140–1151. [PubMed: 18177989]
- Scott D. Parametric statistical modeling by minimum integrated square error. *Technometrics*. 2001; 43(3)
- Sheridan MA, Fox NA, Zeanah CH, McLaughlin KA, Nelson CA 3rd. Variation in neural development as a result of exposure to institutionalization early in childhood. *Proc Natl Acad Sci U S A*. 2012; 109(32):12927–12932. 3420193. [PubMed: 22826224]
- Sickmund, M.; Puzzanchera, C. Juvenile Offenders and Victims: 2014 National Report. US Department of Justice, Office of Justice Programs, Office of Juvenile Justice and Delinquency Prevention; Washington, DC: 2014.
- Silver, JM.; McAllister, TW.; Yodofsky, SC., editors. Textbook of Traumatic Brain Injury. American Psychiatric Publishing; Arlington, Va: 2005. p. 27-39. Arlington, VA
- Skipper JI, Goldin-Meadow S, Nusbaum H, Smal S.L.I. Speech-associated gestures, Broca's area, and the human mirror system. *Brain Lang*. 2007; 101(3):260–277. doi:10.1016/j.bandl.2007.02.008.PMC 2703472. PMID 17533001. [PubMed: 17533001]
- Sled JG, Zijdenbos AP, Evans AC. A nonparametric method for automatic correction of intensity nonuniformity in MRI data. *IEEE Trans Med Imaging*. 1998; 17(1):87–97. [PubMed: 9617910]
- Teicher MH, Andersen SL, Polcari A, Anderson CM, Navalta CP, Kim DM. The neurobiological consequences of early stress and childhood maltreatment. *Neuroscience & Biobehavioral Reviews*. 2003; 27(1):33–44. [PubMed: 12732221]
- Teicher MH, Anderson CM, Polcari A. Childhood maltreatment is associated with reduced volume in the hippocampal subfields CA3, dentate gyrus, and subiculum. *Proc Natl Acad Sci*. 2012; 109(9):E563–E572. [PubMed: 22331913]
- Teplin LA, Abram KM, McClelland GM, Dulcan MK, Mericle AA. Psychiatric disorders in youth in juvenile detention. *Archives of general psychiatry*. 2002; 59(12):1133–1143. [PubMed: 12470130]
- Teplin LA, Abram KM, McClelland GM, Washburn JJ, Pikus AK. Detecting mental disorder in juvenile detainees: who receives services. *American Journal of Public Health*. 2005; 95(10): 1773–1780. [PubMed: 16186454]
- Van der Kolk BA, Hopper J, Crozier J. Child abuse in America: Prevalence and consequences. *Journal of Aggression, Maltreatment, and Trauma*. 2001
- Wechsler D. Wechsler abbreviated scale of intelligence. Psychological Corporation. 1999
- Widom, CS. Handbook of child maltreatment. Springer Netherlands; 2014. Longterm consequences of child maltreatment; p. 225-247.
- Wilson KR, Hansen DJ, Li M. The traumatic stress response in child maltreatment and resultant neuropsychological effects. *Aggression and Violent Behavior*. 2011; 16(2):87–97.
- Wolpaw, JW.; Ford, JD. Assessing exposure to psychological trauma and post-traumatic stress in the juvenile justice population. National Child and Traumatic Stress Network; 2004.
- Yang Y, Raine A. Prefrontal structural and functional brain imaging findings in antisocial, violent, and psychopathic individuals: a meta-analysis. *Psychiatry Research: Neuroimaging*. 2009; 174(2):81–88. [PubMed: 19833485]

Highlights

- Less gray matter and smaller left hippocampal volumes in LCPD boys than controls
- LCPD had less cortical surface area in pars opercularis and supramarginal cortices
- Traumatized, conduct disordered and LCPD youths' neuroanatomical profiles overlap
- Among LCPD boys, cumulative adversity-related symptoms are linked to pars opercularis
- Concurrent treatment of adversity symptoms and cognitive deficits may be optimal

Figure 1.

MRI regions of interest from FreeSurfer: A) coronal section of the probabilistic segmentation: hippocampus (gold) and amygdala (light blue); and B) lateral sagittal view of cortical parcellations: superior (aquamarine); mid frontal caudal (brown) and rostral (purple); inferior frontal including pars opercularis (tan), pars triangularis (orange), pars orbitalis (dark green, left of pars triangularis); supramarginal gyrus (light green); and lingual gyrus (mesial surface, not seen).

Figure 2.
SCI-TALS Event Profile: Percent of Sample Endorsing Loss and Trauma Types

Figure 3.

Group differences in left hippocampal volume (A), left pars opercularis surface area (B), and left supramarginal gyrus surface area (C). Data presented reflect estimated marginal means from regression models using standard error bars; the model for left hippocampal volume included ICV.

Figure 4.

Associations between left pars opercularis surface area and levels of loss events, trauma events, Cumulative Grief (C-G) Symptom-Index, Cumulative Trauma and Adversity (C-TA) Symptom-Index and combined Cumulative Trauma, Adversity and Grief (C-TAG) Symptom-Index in LCPD boys. Full statistics reported in Table 2 include the t values of parameter estimates from the primary model (effects remained significant with TBI as a covariate in secondary models). For visualization, simple linear fits are modeled here with Spearman's rho (ρ) presented. significance[†] $p < 0.10$, *** $p < 0.005$.

Table 1

Demographic and clinical characteristics.

Demographic Background	Control Boys (n = 20)			LCPD Boys (n = 23)		
	Mean	SD	Range	Mean	SD	Range
Age at Assessment ^{ns}	17.25	0.91	(16–19)	17.14	0.83	(16–18)
Family Resources Scale (Raw Score) ^{ns}	20.18	3.66	(15–25)	21.66	3.17	(15–25)
Early Disruptive Behavior Symptoms ^{***}	2.30	2.74	(0–10)	12.32	3.98	(6–19)
Mild TBI Severity Score ^{***}	0.45	0.76	(0–2)	2.64	1.40	(0–6)
Age of Earliest Loss Exposure (LEC) [*]	9.17	6.00	(0–18)	5.07	6.16	(0–17)
Age of Earliest Trauma Exposure (LEC) ^{ns}	10.84	4.07	(4–17)	10.57	3.75	(4–17)
Age of Alcohol Use Onset ^{ns}	14.00	2.72	(9–18)	13.18	2.75	(6–17)
Age of Any Substance Use Onset ^{**}	15.09	1.51	(13–18)	12.50	2.48	(6–16)
YPI Total (Number of Items)	116.94	17.71	(84–149)	120.68	25.09	(77–174)
Interpersonal Domain: Grandiosity and Manipulation (20) ^{ns}	47.65	9.26	(34–62)	44.82	11.44	(24–65)
Affective Domain: Callous and Unemotional(15) ^{ns}	33.41	4.26	(28–41)	35.41	6.98	(22–51)
Behavioral Domain: Impulse and Irresponsibility (15) ^{ns}	35.88	7.02	(21–46)	40.45	9.32	(24–60)
Full Scale IQ (4 subtest) ^{***}	102.30	10.93	(79–118)	90.09	9.02	(76–107)
Verbal IQ ^{***}	101.85	8.99	(87–112)	88.52	11.33	(70–109)
Performance IQ [*]	101.95	11.83	(77–120)	93.83	7.18	(82–109)
SCI-TALS (Number of Items)						
Domain I Loss Events (10) ^{ns}	3.60	2.09	(0–7)	4.09	2.18	(1–9)
Domain II Grief Reactions (27) [†]	8.70	6.71	(1–22)	12.23	6.70	(2–23)
Domain II-A C-G Symptom-Index (20) ^{†p=.072}	5.65	5.94	(0–18)	8.82	5.16	(0–16)
Domain II-B Grief Personality Characteristics (7) ^{ns}	3.05	1.54	(1–5)	3.41	1.87	(0–7)
Domain III Trauma Events (21) ^{***}	4.05	3.22	(0–13)	8.68	3.83	(2–16)
Domain IV Physical, Emotional and Cognitive Reactions to Loss/Trauma (18) [*]	5.30	4.57	(0–18)	8.68	4.94	(0–17)
Domain V Re-experiencing/Intrusions (9) ^{†p=.052}	3.05	3.00	(0–9)	4.86	2.87	(0–9)
Domain VI Avoidance/Numbing (12) ^{ns}	4.10	3.57	(0–12)	5.05	3.91	(0–12)
Domain VI-A Avoidance (4) ^{ns}	1.40	1.19	(0–4)	1.59	1.37	(0–4)
Domain VI-B Numbing (7) ^{ns}	2.25	2.17	(0–7)	2.86	2.40	(0–7)
Domain VII Maladaptive Coping (8) ^{†p=.063}	1.10	1.71	(0–6)	2.05	1.50	(0–4)
Domain VIII Arousal/Reactivity (5) [*]	1.70	1.98	(0–5)	3.00	1.72	(0–5)
Domain IX Personal Risk Factors (6) ^{***}	1.45	1.43	(0–4)	3.59	1.79	(0–6)
C-TA Symptom-Index (26) ^{ns}	8.85	7.83	(0–24)	12.91	7.75	(0–26)
Combined C-TAG Symptom-Index (46) ^{†p=.074}	14.50	13.34	(0–42)	21.73	12.15	(0–42)
Race	n		%	n		%
Latino	7		35.0	7		30.4

	Control Boys (n = 20)			LCPD Boys (n = 23)		
Demographic Background	Mean	SD	Range	Mean	SD	Range
African American	5		25.0	8		34.8
Caucasian	8		40.0	8		34.8

ns=not significant;

[†]
 $p<0.10$,

^{*}
 $p<0.05$;

^{**}
 $p<0.01$;

^{***}
 $p<0.001$.

Table 2

Structural associations with loss events, trauma events, and symptoms in LCPD boys.

Region by MRI Measure	Loss Events (Domain I)	Trauma Events (Domain III)	C-G Symptom-Index (Domain II-A)	C-TA Symptom-Index (Domains V, VI, VIII)	Combined C-TAG Symptom-Index (Domains II-A, V, VI, VIII)
Surface Area	<i>t</i>	<i>t</i>	<i>t</i>	<i>t</i>	<i>t</i>
Left Pars Opercularis	-1.9 [†]	-2.2 [*]	-0.38 [†]	-3.1 ^{***}	-3.7 ^{***}
Right Pars Opercularis	-0.2 ^{ns}	-0.9 ^{ns}	-0.12 ^{ns}	-2.5 [*]	-3.0 ^{**}
Left Lingual Gyrus	-1.0 ^{ns}	-1.0 ^{ns}	-0.24 ^{ns}	-3.3 ^{***}	-3.9 ^{***}
Right Caudal MidFrontal Folding	-0.9 ^{ns}	-0.2 ^{ns}	-0.60 ^{ns}	-2.2 [*]	-1.5 ^{ns}
Left Pars Opercularis	-1.1 ^{ns}	0.2 ^{ns}	-0.18 ^{ns}	-0.8 ^{ns}	-1.1 ^{ns}
Right Pars Opercularis	0.0 ^{ns}	-0.4 ^{ns}	-0.19 ^{ns}	-1.7 [†]	-2.2 [*]
Right Pars Orbitals	1.3 ^{ns}	0.8 ^{ns}	-0.6 ^{ns}	-0.3 ^{ns}	-0.4 ^{ns}

Statistics reported include the *t* values of parameter estimates from the primary model (effects remained significant with TBI as a covariate in secondary models) and Spearman's rho (ρ). Significance of *t* value:

ns=not significant;

[†] *p* 0.10,

^{*} *p*<0.05;

^{**} *p*<0.01;

^{***} *p*<0.005