CHAPTER FOUR

The impact of childhood poverty on brain health: Emerging evidence from neuroimaging across the lifespan

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Abstract

Experiencing poverty in childhood has been associated with increased risk for physical and mental health difficulties later in life. An emerging body of evidence suggests that brain development may be one mediator of this relation. In this chapter, we discuss evidence for an association between childhood poverty and brain structure/function. First, we examine the association from a lifespan perspective discussing studies at multiple developmental stages from the prenatal period to late adulthood. Second, we

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examine existing studies that link childhood poverty, brain development, and physical and mental health outcomes. Third, we discuss studies linking childhood poverty and environmental risks and protective factors. Lastly, we discuss suggestions for future studies including advances in network neuroscience, population neuroscience, using multiple imaging modalities, and the use of longitudinal neuroimaging studies. Overall, associations between childhood poverty, brain development, and development over the life course may help to both better understand and eventually reveal salient intervention strategies to mitigate social disparities in health.

Abbreviations

BOLD	blood oxygenation level dependent
DTI	diffusion tensor imaging
EEG	electroencephalography
ERP	event related potentials
fMRI	functional magnetic resonance image
MRI	magnetic resonance imaging
MT	magnetization transfer
SE	socioeconomic status

1. Introduction

There is an extensive literature linking childhood socioeconomic status (SES) to behavioral outcomes across several domains including physical health and mental health (Adler & Rehkopf, 2008; Kim, Evans, Chen, Miller, & Seeman, 2018; Wadsworth, Evans, Grant, Carter, & Duffy, 2016). SES refers to an individual or family's level of occupation, income, education or a combination of these indicators (McLoyd, 1998). Low SES is referred to as "poverty" when an individual or family's SES is below a certain threshold, typically the poverty threshold in which a country deems adequate based upon the family's income and number of people living in the home. For the chapter, SES will refer to when a combination of SES indicators is used (family income, education, occupation). When an indicator of SES is used in isolation, it will be specified such as the study used "family income" as a measure of SES.

A growing body of literature suggests potential mechanisms in which childhood poverty "gets under the skin" (Hackman, Farah, & Meaney, 2010; Kim et al., 2018; McEwen, 2012). The relations between childhood poverty and brain health has emerged as a potential pathway wherein childhood poverty may impact neural development, which in turn is associated

with alterations in physical and mental outcomes (Farah, 2018; Hackman et al., 2010). Studies are beginning to expand to include examinations of the relations between childhood poverty and brain health in multiple periods of development (Farah, 2018; Johnson, Riis, & Noble, 2016). Further, studies are emerging that expand beyond the relation between childhood poverty and brain structure as variations of brain structure provide limited insight into brain function. Several reviews of the literature of the association between childhood poverty and brain exist but focus on specific developmental periods (Buckley, Broadley, & Cascio, 2019; Hackman et al., 2010).

Thus, this chapter adopts a lifespan perspective to examine the evidence about childhood poverty and brain development by focusing on the prenatal period and infancy, childhood, adolescence, and adulthood/late adulthood. Second, we discuss studies that have linked childhood poverty and brain development to physical health, behavioral outcomes, and mental health. Third, we discuss studies of both risk and protective factors related to childhood poverty and brain development. Lastly, we provide some ideas to enrich our understanding of childhood poverty and brain development using network neuroscience, population neuroscience, utilization of multiple neuroimaging modality, longitudinal, and mediation analysis studies. Studies included in the chapter were identified using keywords such as "poverty," "childhood poverty," "brain development," "brain structure," "brain function." The chapter is not a comprehensive review, rather a few studies we chosen for each section to illustrate a concept. Studies were not included that did not measure childhood SES or poverty or if brain development (structure/function) were not measured using a neuroimaging method such as structural MRI, fMRI, DTI, or EEG (see "Abbreviations" section for abbreviations used in the chapter).

2. Lifespan perspective

The early studies of the association between childhood poverty and brain development, borrowing from animal studies, focused on brain structure, specifically the hippocampus and amygdala. Evidence from animal models suggests that exposure to early adversity, such as high levels of stress, has causal effects on brain development (McEwen, 2008, 2012; Palma-Gudiel, Córdova-Palomera, Leza, & Fananás, 2015). However, there is extensive evidence that certain brain regions have heightened susceptibility to the effects of early adversity. Early life stress negatively affects

neurogenesis in the hippocampus (Lajud & Torner, 2015), a brain region involved in learning and memory (Oomen et al., 2010). Further, early life stress is associated with increased dendritic arborization in the amygdala (Vyas, Mitra, Rao, & Chattarji, 2002), a region involved in salience processing, social behaviors, and fear learning (Santos, Mier, Kirsch, & Meyer-Lindenberg, 2011; van Marle, Hermans, Qin, & Fernández, 2009). This evidence suggests that similar processes may be operating in human children experiencing highly stressful situations such as poverty.

Advances in neuroimaging techniques, such as structural MRI, made it possible to examine gray matter volume of certain brain regions noninvasively in humans. While operational definitions of poverty varied (family income, parental education, income-to-needs ratio), studies consistently found a positive association between childhood SES and hippocampal volume in humans (Dufford, Bianco, & Kim, 2019; Hanson, Chandra, Wolfe, & Pollak, 2011; Jednoróg et al., 2012; Luby et al., 2013; Noble et al., 2015; Noble, Houston, Kan, & Sowell, 2012). There is less consistent evidence concerning amygdala structure in which some studies found a positive associations (Luby et al., 2013) and some studies found a negative association (Dufford et al., 2019). These early studies provided a critical foundation for the study of the relations between childhood poverty and brain development. However, these foundational findings do not reflect the enormous complexity of brain development over the life course, in particular different maturational periods of brain plasticity to environmental influences (Blair & Raver, 2012; Boyce, 2016; Tomalski & Johnson, 2010). This suggests that as the brain is changing across the lifespan, its relations with childhood poverty may also vary depending on developmental periods (Brito & Noble, 2014; Tottenham & Sheridan, 2010).

3. Prenatal period and infancy

The fetal brain undergoes rapid and unparalleled development and organization in utero (Stiles & Jernigan, 2010). As developmental periods of rapid development are accompanied with increased vulnerability for the brain (Johnson, 2005; Rodier, 1994; Westermann et al., 2007), it is critical to examine the potential relations between prenatal poverty and brain development. Infancy (particularly the first 2 years of life) is also a developmental period that is a critical foundation for brain maturation and subsequent cognitive and socioemotional development

(Knickmeyer et al., 2008; Uzgiris, 1973). However, the prenatal period and infancy is perhaps the least well understood time period concerning the relation between poverty and brain development. This could be due to the difficulty inherent in examining brain development during early life. While neuroimaging of children in this time period is becoming more accessible and feasible (Graham et al., 2015; Li et al., 2019), studies of the relation between prenatal experiences of poverty and brain development are still extremely limited. For example, studies using fetal MRI are quite limited and have not yet examined prenatal experiences of poverty with concurrent brain structure/function.

Studies of prenatal experiences typically involve assessments of brain development shortly after birth, to mitigate possible postnatal influences. Although not without difficulty, neonatal brain structure and function can be measured in vivo using MRI, typically during the neonate's natural sleep. One study found that low SES neonates have greater local brain volumes in the inferior frontal, cingulate, middle frontal and temporal pole, superior and middle occipital gyri (Spann, Bansal, Hao, Rosen, & Peterson, 2019). These findings contrast with the typical finding of a positive association between SES and brain volume. For example, using structural MRI, a study of 1-month-old infants found that lower SES was associated with lower cortical gray and deep gray matter volumes (Betancourt et al., 2016). Another study in infancy, using longitudinal neuroimaging, found that infants from lower income households had smaller or less gray matter volume in both the frontal and parietal lobes (Hanson et al., 2013). Infants from lower income families also had slower trajectories of growth in infancy and childhood. Using structural MRI and a large sample of infants, maternal education was positively associated with infant total white matter and gray matter volume (Knickmeyer et al., 2016). Whether SES is positively or negatively associated with infant brain structure require further examinations. Spann et al. (2019) suggest that early brain development involves both progressive and regressive processes. The first year of life is associated with dendritic arborization and glial cell multiplication to support synaptogenesis (Huttenlocher, De, Garey, & der Loos Van, 1982) while later in infancy and into middle childhood, growth is slowed by apoptosis and synaptic pruning (Huttenlocher, 1984). Due to the cross-sectional nature of existing studies, further longitudinal studies will be needed to determine how the direction of the association between SES and brain structure may change depending on which period of development is being examined. These findings

highlight the complexity of this relation as well as how considering developmental trajectories is critical.

The association between childhood poverty and brain function has also been examined in infancy using EEG. EEG is a measure of brain function that measures electric brain activity through the scalp (Blinowska & Durka, 2006) and is widely used in infant studies. EEG can measure brain responses to specific time-epochs (ERP) or when individuals are engaged in observations of general stimuli known as resting baseline EEG (Marshall & Fox, 2007). In a study of 6–9 month olds, using resting baseline EEG, infants from low income households had lower frontal gamma power, resting brain oscillations association with language and cognitive skills in toddlers as well as an indicator of selective attention (Tomalski et al., 2013). Family SES was also associated with EEG activity during an error-detection task among older infants (aged 16–18 months). Infants from families with lower SES had lower activation of error-detection related EEG signal in the executive attention network (Conejero, Guerra, Abundis-Gutiérrez, & Rueda, 2018). Brain function in infancy can also be measured using resting-state fMRI which measures the intrinsic functional architecture of the brain by examining correlations in BOLD signal. Functional brain network development was associated with SES in a sample of infants at 6 months of age (Gao et al., 2014). SES had a significant positive association with measures of functional network maturation in the sensorimotor network and default mode network. These studies suggest that associations between childhood SES and brain structure/function can be detected early in development.

4. Childhood

In childhood, a study found a positive association between income-to-needs ratio and left hippocampus volumes and right amygdala volumes in children ages 6–12 (Luby et al., 2013). The associations between income-to-needs ratio and brain volumes were mediated by caregiving quality as well as stressful life events exposure (Luby et al., 2013). Studies have found positive associations between childhood poverty and cortical thickness and surface area in childhood (Lawson, Duda, Avants, Wu, & Farah, 2013; Noble et al., 2015). The most robust associations with brain

surface morphometry appear to occur in prefrontal, anterior cingulate cortex, and medial temporal lobe regions.

While the findings for a relation between childhood poverty and brain structure are quite robust, the associations between childhood poverty and brain function are more limited. Prefrontal cortex activation was decreased in children (8–12 years old) experiencing lower SES during a stimulus-response mapping task (Sheridan, Sarsour, Jutte, D'Esposito, & Boyce, 2012). Another study in children (8–12 years old) found that children experiencing lower SES had lower hippocampal activation during a declarative memory task (Sheridan, How, Araujo, Schamberg, & Nelson, 2013). Two studies have found links between childhood SES, task-related functional activity, and reading deficits in childhood (ages 5–9) (Noble, Wolmetz, Ochs, Farah, & McCandliss, 2006; Raizada, Richards, Meltzoff, & Kuhl, 2008).

5. Adolescence

There is also emerging evidence of the association between childhood poverty and brain development in adolescence. Adolescence is also a time period in which the brain is developing rapidly, and prefrontal regions are developing at a slower rate than subcortical affective systems. Ziegler et al. used an innovative imaging technique known as MT, a marker of myelination and found that childhood disadvantage was associated with lower global MT and lower intra-cortical MT increases in sensory-motor, cingulate, insular, prefrontal, and subcortical areas (Ziegler et al., 2019). This suggests that childhood poverty may impact the myelination of white matter tracts that is occurring during adolescence. Weissman et al. also focused on adolescence; however, this study used resting-state fMRI to examine how changes in family income across adolescence were associated with connectivity of the default mode network (Weissman, Conger, Robins, Hastings, & Guyer, 2018). The connectivity of the default mode network depended on the slope of change in their family income with increases in family income across adolescence associated with greater prefrontal connectivity. Overall, studies from childhood and adolescent yield evidence suggesting relations between childhood poverty and subcortical gray matter structure (particularly the hippocampus), associations with cortical thickness and surface area (primarily prefrontal regions), as well as indications of an association with both structural and functional connectivity.

6. Adulthood and late adulthood

A series of studies have examined the prospective association between childhood poverty and brain structure/function in early adulthood (age 24). These longitudinal studies used measurements of family income-to-needs ratio measured at ages 9, 13, 17, and 24, finding a prospective relation between childhood poverty and prefrontal activation during an emotion regulation task (Kim et al., 2013), hippocampal function and visuospatial memory (Duval et al., 2017), and default mode network functional connectivity (Sripada, Swain, Evans, Welsh, & Liberzon, 2014). Using a multimodal approach, a study suggests a prospective association between childhood poverty (family income-to-needs ratio) and brain response to emotional faces in adulthood (Javanbakht et al., 2015). Specifically, lower family income-to-needs-ratio was associated with greater amygdala activation to threatening faces as well as lower prefrontal cortex activation to threatening faces. This suggests that childhood poverty may play a role in socioemotional development, specifically in the processing of social threats (Javanbakht et al., 2015).

There is also evidence that childhood SES is associated with brain structure/function in middle and late adulthood. In a sample of 42 middle aged, neurologically healthy men, a study reported differences in structural brain networks in men from neighborhoods varying in socioeconomic deprivation (Krishnadas et al., 2013). Men from the most socioeconomically deprived neighborhoods had structural brain networks that were less modular (a measure of the extent to which brain subnetwork organize into modules or units that are discrete entities with functions that are separable from other modules). Typically, higher modularity is a measure associated with more efficient information processing. These findings suggest that experiencing a neighborhood with high socioeconomic deprivation is associated with brain network efficiency (Rubinov & Sporns, 2010). Using a multimodal approach, for middle early (35–49) and middle late (50–64) adulthood, lower SES individuals had lower resting-state network segregation (a measure of how efficiently a brain network is organized) and diminished mean cortical thickness (Chan et al., 2018). These differences were not observed in the older age group (65–89). These findings suggest that high SES may be a protective factor for age-related decline in the brain. A study of participants in late adulthood (age 64) found that their recollections of their SES (home conditions and parental occupation) at age 11 was

negatively associated with their hippocampal volume in late adulthood (Staff et al., 2012). Overall, these studies suggest that associations with childhood poverty can persist into adulthood and potentially have prospective relations into late adulthood. As demonstrated by the Chan et al. study, it will be important to examine how SES may impact brain aging and cognitive decline.

The current studies have provided evidence for associations between childhood poverty and brain development at multiple developmental stages. However, future studies will be needed to identify age sensitive periods for exposure to poverty. This has posed an analytic challenge as it is difficult to disentangle periods of development that have greater "sensitivity" to poverty exposure versus the duration of poverty exposure from the prenatal period until the development period in which brain development is being examined. To address this issue, future studies may benefit from utilizing human and animal model comparison studies (Perry et al., 2019), advanced statistical methods borrowing from structural equation modeling (Kievit et al., 2018), examining the efficacy of interventions at different developmental periods (Brody et al., 2017). For the remainder of the chapter, we discuss suggestions for study designs and methodologies that may facilitate understanding of this complex relation.

7. Links to physical health, behavioral outcomes, and mental health

An extensive literature documents that childhood poverty is associated with less positive physical and mental health outcomes (Adler & Rehkopf, 2008; Bradley & Corwyn, 2002; Kim et al., 2018; Wadsworth et al., 2016). Childhood poverty is associated with health outcomes later in life such as heart disease, obesity, and various infectious diseases (Haan, Kaplan, & Camacho, 1987; Lee, Andrew, Gebremariam, Lumeng, & Lee, 2014; Tomatis, 1997). The chronic stress associated with childhood poverty may underlie physical health and brain development sequelae of early poverty. Greater community socioeconomic disadvantage was associated with reduced cortical tissue volume, cortical surface area, and cortical thickness (Gianaros et al., 2017). Cardiometabolic risk (measures of adiposity, blood pressure, glucose, insulin, and lipids) mediated this association. Further, flatter diurnal cortisol decline (a measure of dysregulation) also mediated this association. These findings suggest a critical role of physical health and stress

physiology in the link between poverty and brain development. Further supporting the role of physical health as a potential mediator, adiposity, cigarette smoking, and levels of C-reactive protein mediated the association between SES and white matter fractional anisotropy in adults (Gianaros, Marsland, Sheu, Erickson, & Verstynen, 2012). These findings suggest that future studies should focus on both inflammatory pathways as well as the association between childhood poverty, brain development, and dysregulation of stress response systems (Miller et al., 2009).

While early studies primarily established links between childhood poverty and the brain, recent studies have endeavored to extend these pathways to include how childhood poverty may be associated with behavioral outcomes and how measures of brain development may be also associated with these outcomes. It is critical to examine how structural and functional variations associated with childhood poverty are related to behaviors to avoid engaging in reverse inference (Ellwood-Lowe, Sacchet, & Gotlib, 2016). The association between childhood poverty and brain development could be a potential mechanistic pathway underlying the relations between childhood poverty and neurocognitive development (Farah, 2018; Johnson et al., 2016). The neurocognitive domains most robustly associated with SES appear to be executive functioning and language (Farah et al., 2006; Noble, Norman, & Farah, 2005). Lower family income was associated with lower performance on four cognitive assessments: a flanker task (inhibition), working memory, vocabulary, and reading (Noble et al., 2015). Cortical surface area was also positive associated with performance on these assessments. Of interest, surface area mediated the association between family income and cognitive performance on the flanker task and working memory task. Thus, lower cortical surface area may play an important role in the link between family income and executive functioning.

Language is another domain in which children that have experienced childhood poverty have difficulties (Farah et al., 2006). Cortical thickness mediated the link between SES and language abilities in children ages 3–21 (Khundrakpam et al., 2019). Cognitive abilities (such as executive functioning) and language play an important role in academic achievement. Hair et al. found that regional gray matter volumes from children 1.5 times below the federal poverty line were 3–4% points lower than the developmental norm (Hair, Hanson, Wolfe, & Pollak, 2015). Low-income children scored 4–7 points lower on standardized tests which was mediated by diminished gray matter volumes (Hair et al., 2015). This group of studies suggest

that income inequalities in cognitive development may be mediated, at least in part, by underlying brain impacts of disadvantage.

In addition to relations between childhood poverty and behavioral outcomes such as cognition, it is also important to investigate the role of brain structure and function in mental health sequelae of early disadvantage. Children that have experienced poverty have an increased risk of developing mental disorders, such as anxiety and depression, later in life (Bradley & Corwyn, 2002; Gilman, Kawachi, Fitzmaurice, & Buka, 2002; Wadsworth et al., 2016). Using data from the PING study ($n = 1196$), lower family income and parental education was associated with lower amygdala volumes in adolescents (13–21) but not at younger ages (3–12). For a subsample ($n = 327$), lower parental education (not family income) was associated with greater internalizing symptoms (Merz, Tottenham, & Noble, 2018). Interestingly, smaller amygdala volumes were associated with greater levels of internalizing symptoms. These findings highlight the potential roles of childhood poverty and amygdala volume in the development of symptoms of anxiety and depression. Using task-based fMRI, gene methylation that was associated with SES in participants age 11–19 years old was associated with greater activation of the amygdala during a task in which participants viewed threatening stimuli (Swartz, Hariri, & Williamson, 2017). Further, this study found that the increases in amygdala reactivity moderated the relation between a positive family history of depression and later depressive symptoms. These studies suggest that variations in brain structure/function related to childhood SES have further associations with mental health symptoms.

8. Risks and protective factors

8.1 Cumulative risk

Future studies of the association between childhood poverty and brain development will benefit from being driven by theoretical models. Recent neuroimaging studies have adopted models of early adversity from developmental psychology. Compared to other forms of early adversity, childhood poverty is associated with a multitude of risk factors which portend deleterious development above and beyond singular risks (Evans, Li, & Whipple, 2013; Sameroff, Seifer, Zax, & Barocas, 1987). Cumulative risk typically includes both physical and psychosocial stressors, both of which commonly occur for individuals experiencing childhood poverty.

For example, one conceptualization of cumulative risk includes physical risks (noise, crowding, suboptimal housing) and psychosocial risks (family turmoil, child separation from family, violence) which are factors that children experiencing childhood poverty are more likely to be exposed to (Evans, 2004; Evans et al., 2013).

Recent studies of childhood poverty have included cumulative risk as a potential mediator of the relation between childhood poverty and the brain. As discussed, one study found that cumulative risk exposure (averaged between ages 13 and 17) mediated the association between childhood income-to-needs ratio and prefrontal cortex activity during an emotion regulation task (Kim et al., 2013). Greater cumulative risk exposure in childhood has also been associated with lower white matter fractional anisotropy in white matter tracts that were also associated with family income such as the cingulum bundle and superior longitudinal fasciculus (Dufford & Kim, 2017). These studies provide converging evidence that for childhood poverty, the exposure to multiple risks may be a potential pathway in which the stress associated with cumulative risk is associated with variations in brain development.

More typically studies of childhood poverty and brain development focus on a singular risk factors such as maltreatment or neglect. One dimension of early adversity, deprivation, is the absence of expected inputs that may impact neural proliferation and pruning (McLaughlin, Sheridan, & Lambert, 2014). The other dimension for early adversity, threat, is associated with alterations in fear learning processes (McLaughlin et al., 2014). The model suggests that different early adversities can be placed upon an axis based upon high versus low threat and high versus low deprivation. For example, neglect typically involves high deprivation but low threat whereas physical abuse typically involves high threat and low deprivation. However, childhood poverty is more difficult to describe accurately in terms of these dimensions as it involves both deprivation and threat.

8.2 Parenting interventions

It is critical for the understanding of the association between childhood poverty and brain development to examine potential protective effects that ameliorate this relation as well as potential interventions to mitigate the potential impacts of poverty on brain development. While protective factors and behavioral interventions for poverty exposure are abundant in the developmental psychology literature, there are a dearth of studies examining

potential protective factors and interventions for the relation between childhood poverty and brain development. A longitudinal study of African American youth experiencing rural poverty has tested supportive parenting as a potential protective factor for the association between poverty and brain development (Brody et al., 2017). This study found that the amount of years living in poverty from ages 11 to 18 were associated with lower hippocampal (also dentate gyrus and CA3 subfields) and amygdala volumes. Participants in this study were a part of randomized, controlled trial design in which children and their parents were randomly assigned to a supportive parenting intervention or a control condition. Participants of parents that had participated in the supportive parenting intervention did not have the association between number of years living in poverty and hippocampal/amygdalar gray matter volume at age 25. These findings provide neural evidence for supportive parenting as a potential protective factor for children experiencing poverty. It also supports the potential utility of psychosocial interventions for ameliorating the association between childhood poverty and gray matter structure (Brody et al., 2017).

Using data collected from this study, there was evidence for the supportive parenting intervention having protective effects for resting-state functional connectivity (Brody, Yu, Nusslock et al., 2019). The number of years spent living in poverty from ages 11 to 18 had a prospective negative association with resting-state functional connectivity in the central executive and emotion regulation networks. The central executive network is involved in cognitive control, working memory, and is comprised of the dorsolateral prefrontal cortex and posterior parietal cortex. The emotion regulation network is involved in top-down control of limbic circuitry and is comprised of the inferior gyrus, middle temporal gyrus, and precentral gyrus. At the age of 25, participants whose parents had participated in the supportive parenting intervention did not have the association between years lived in poverty and central executive and emotion regulation network functional connectivity. Both studies highlight supportive parenting as a potential protective factors and intervention target for future studies examining childhood poverty and brain development.

Currently, in the developmental psychology and the developmental neuroscience literature, parenting has been highlighted as a protective factors and intervention target for the associations between childhood poverty and developmental outcomes (Brody, Yu, Miller, Ehrlich, & Chen, 2019). However, parents experiencing poverty are often under an enormous amount of stress and working multiple jobs. While there is

evidence for intervening on positive parenting, this should not be the only protective factor that is examined using a developmental neuroscience framework. Potential protective factors for neuroimaging studies to focus on in the future could be individual-level factors such as coping or self-esteem (Harrison, Loxton, & Somhlaba, 2019), family emotional climate (Miller & Chen, 2013), school-level factors such as school-based interventions, or neighborhood-level factors such investments in after-school activities (Sharma, Mustanski, Dick, Bolland, & Kertes, 2019). Overall, the extant studies of the association between childhood poverty and brain development suggest that this relation is not fixed or immutable. Therefore, investments in studies that examine the mechanisms as well as the protective factors/targets for intervention are critical moving forward. In this section, we reviewed the latest developments in neuroimaging research examining the role of childhood SES in brain develop. We also discussed important future directions for the field to further the understanding of the neural embedding of childhood SES for psychological and physical health.

9. Future directions

9.1 Network neuroscience

As we have discussed, it is critical for the study of childhood poverty and brain development to study the brain beyond singular regions. It is also critical to combine multiple modalities and eventually combine multiple levels of analysis. Adopted from basic neuroscience studies, developmental neuroimaging has begun to examine the brain as a complex network of interconnected regions (Cao, Huang, Peng, Dong, & He, 2016; Zuo et al., 2017). Borrowing methods from graph theory (Rubinov & Sporns, 2010), this field of research is beginning to understand the complex interactions between brain regions as well as how they develop over time (Cao et al., 2016). Network neuroscience has intersected with an approach to studying the brain known as "connectomics." Connectomics attempts to provide a description of the connections between all regions of the brain (Behrens & Sporns, 2012). Connectomes at the macroscale can be measured using neuroimaging techniques in which each brain region is conceptualized as a node and each connection between nodes is an edge (Rubinov & Sporns, 2010). These analyses typically result in an adjacency or "connectivity" matrix representing the "connections" between all the

nodes. This is typically measured by "structural connections" in the form of the connectivity strength between regions measured with diffusion weighted MRI (Hagmann et al., 2010). For functional connectomes, connectivity matrices typically are comprised of the correlation in BOLD timeseries among nodes calculated from resting-state fMRI or task-based fMRI. While connectomic approaches are becoming quite popular, the field of developmental connectomics is quite new and has only recently been used to examine the association between childhood poverty and brain development (Cao et al., 2016).

Studies that we have discussed have used structural connectomics approaches as well as combinations of structural and functional connectomic approaches. In addition to structural connectomes calculated based upon diffusion MRI, they can be calculate based upon correlations in structural measures such as cortical thickness (Alexander-Bloch, Raznahan, Bullmore, & Giedd, 2013). Further global metrics of the organization of brain networks can provide insight into how brain networks are organized. These graph theoretic measures can quantify the degree to which networks are integrated or segregated. Brain network segregation measures the brain's ability for specialized processing to occur in densely interconnected brain regions (Rubinov & Sporns, 2010). Graph theoretic measures can also measure brain integration which quantifies the brain's ability to combine specialized information from distributed brain regions (Rubinov & Sporns, 2010). Network segregation was examined based upon resting-state networks and a study found that individuals experiencing lower SES had reduced network segregation in middle aged individuals (Chan et al., 2018). This evidence suggests that SES is associated with the brain's ability to organize into units for specialized processing. Another measures of network segregation, modularity, measures the degree to which a network can be subdivided into clearly delineated and nonoverlapping groups (Chan et al., 2018). Comparing structural connectome modularity in individuals from areas experiencing low versus high socioeconomic deprivation, individuals from areas of high socioeconomic deprivation had lower network modularity (Krishnadas et al., 2013). Further evidence of an association between SES and network segregation was found using a large sample of 1012 youth ages 8–22. Using resting-state functional connectomes, youth experiencing high neighborhood SES had lower levels of initial local segregation and had the largest increases over time in local segregation (Tooley et al., 2019). Further, neighborhood SES moderated the relation between age and local segregation such that youth experiencing higher neighborhood SES had faster increases local

segregation over time. This study suggests that SES may be an important factor that may influence how brain networks organize across development.

Evidence from these early studies utilizing network neuroscience suggests an association between poverty and brain network segregation. Future studies are needed to expand our understanding of the intersection of poverty and connectomics. As demonstrated by the studies discussed, network neuroscience is an advantageous approach to study this link. First, network neuroscience is a useful framework for multimodal studies as similar analysis can be conducted independent of modality (Scholtens & van den Heuvel, 2018). This facilitates comparison of structural networks to functional networks or can combine them (Wang, Dai, Gong, Zhou, & He, 2015). Network neuroscience can provide mathematical descriptions of how brain regions relate to one another and therefore are useful for studying brain network development over time (Rubinov & Sporns, 2010). Lastly, network neuroscience provides the ability to measure brain networks at multiple levels of analysis. For example, network neuroscience can unify descriptions of connections at the level of synapses, the level of individual neuronal connections, up to descriptions of the connectivity between populations of neurons and brain regions (Scholtens & van den Heuvel, 2018). As neuroimaging techniques improve in their resolution, studies will begin to have the ability to examine these multiple levels of analyses and network neuroscience can combine data across these levels; this will be critical for understanding potential biological processes underlying the association between childhood poverty and brain development.

9.2 Population neuroscience

Along with the emerging interest in connectomics, neuroscience has also become interested in population neuroscience. Concerns related to adequate statistical power for neuroimaging studies (Cremers, Wager, & Yarkoni, 2017), have motivated larger sample sizes. Population neuroscience typically involves data from large-scale repositories from many sites. By combining data from many different participants and research sites, the hope is to be able to have the statistical power and amount of data to be able to examine research questions not obtainable by smaller scale studies (Paus, 2010). One of the first example of population neuroscience studies has been influential in the study of the association between childhood poverty and brain development. A study used structural MRI data from the Pediatric Imaging, Neurocognition, and Genetics study (PING) (Jernigan et al., 2016).

The PING dataset is comprised of 1493 children aged from 3 to 20 years old. In addition to neuroimaging data, the PING data included genetic and cognitive data. The large sample size of the PING dataset afforded the ability to examine nonlinear associations between family income and surface morphometry. As discussed, this study found a logarithmic association between family and surface area. However, this dataset includes only bins of family income data and is cross-sectional. Therefore, future population neuroscience studies of childhood poverty should collect SES information (maternal education and family income-to-needs ratio) across multiple timepoints of development as well as have multiple neuroimaging measures across time.

Recently, more datasets of large samples are becoming available. The Philadelphia Neurodevelopmental Cohort (PNC) is another large-scale neuroimaging study (9498 children from 8 to 21 years old) in which the association between poverty and brain development can be studied (Satterthwaite et al., 2014). Although it is primarily focused on substance abuse, the Adolescent Brain Cognitive Development (ABCD) study has the potential to be leveraged to study the relation between childhood poverty and brain development using longitudinal data (Casey et al., 2018). The ABCD study is collecting data from over 10,000 youth aged 8–10 with additional data collected through adolescence.

Overall, data from population neuroscience studies provide large amounts of data to examine associations that may not be able to be properly studies in smaller samples. For the study of the relation between childhood poverty and brain development, population neuroscience may be critical to support analyses that typically require large amounts of data such as network analyses. Also, it is difficult to conduct longitudinal studies, despite these being critical to understand brain development. Therefore, large-scale multi-site studies may be able to achieve large longitudinal samples by combining data across sites. However, with large-scale neuroimaging studies such as PING, PNC, and ABCD it may be difficult to obtain detailed information about SES from each participant. We suggest that future studies of the association between childhood poverty and brain development will benefit from a combination of data from large-scale population neuroscience studies that may have limited detail in the collection of SES and smaller scale studies that can provide more detailed assessments of SES. Further, prior large samples (Gianaros et al., 2008; Staff et al., 2012) have relied on retrospective reports of childhood poverty which may be difficult to recall accurately. Therefore, future population neuroscience studies should collect

information regarding childhood SES during childhood and at multiple timepoints across development.

9.3 Utilizing multiple neuroimaging modalities

While most of the early studies of the association between childhood poverty and brain development focused on gray matter volume, recent studies have expanded to other and complimentary neuroimaging modalities (Uludağ & Roebroeck, 2014). Use of multiple modalities can provide comprehensive measurements of multiple aspects of brain development (Biessmann, Plis, Meinecke, Eichele, & Muller, 2011). Ultimately, the goal is to provide converging and complimentary information about SES and brain development in order to have a deeper understanding. Beyond gray matter volume, as obtained from structural MRI, complimentary measures of gray matter structure called cortical thickness and surface area can be obtained (Brito & Noble, 2014). While cortical thickness and surface area contribute to cortical volume, they can provide unique information potential underlying processes. Cortical thickness and surface area have distinct genetic and development patterns (Panizzon et al., 2009; Wierenga, Langen, Oranje, & Durston, 2014). Often studies will measure cortical thickness and surface area together (Noble et al., 2015). While measuring these aspects of brain structure is important, it is still unclear what specific biological processes they capture. For example, cortical thinning observed across childhood was thought to reflect synaptic pruning (Gogtay et al., 2004; Nie, Li, & Shen, 2013); however, a recent study provided evidence that this thinning may be due to myelination of white matter (Natu et al., 2019). Therefore, studies of the relation between childhood poverty and brain structure may benefit from examining gray matter and white matter structure.

Recent studies have examined brain structure beyond gray matter volume to include white matter structure. White matter undergoes a protracted developmental trajectory which does not reach its peak until early adulthood (Lebel et al., 2012; Lebel, Treit, & Beaulieu, 2019). This may make it particularly susceptible to the influences of childhood poverty. As white matter development is linked with variations cognitive (Nagy, Westerberg, & Klingberg, 2004), language (Wong, Chandrasekaran, Garibaldi, & Wong, 2011), and socioemotional development (Versace et al., 2015), it is another important brain pathway to examine. Using data from the PING study, Ursache et al. found that SES had a positive association with white matter

structure in a large sample of children ages 3–21. White matter structure can be measured in terms of its organization (known as fractional anisotropy). Higher SES was association with higher fractional anisotropy in the right parahippocampal cingulum and right superior corticostriate tract (Ursache, Noble, Pediatric Imaging, Neurocognition and Genetics Study, 2016). Another study found converging evidence of a link between family income-to-needs ratio and fractional anisotropy in the cingulum bundle in children ages 8–10. This study also found this association in the uncinate fasciculus, superior longitudinal fasciculus, inferior longitudinal fasciculus, and corticospinal tracts (Dufford & Kim, 2017). These studies provide evidence that the association between childhood poverty and brain development may not be unique to gray matter (regions involved in the computational processes of the brain) but also evident in white matter (tracts involved in transmission of information among regions).

Regarding multimodal neuroimaging, we also suggest that our understanding can be advanced by combining studies of structure and function. While we have a general idea of the functional roles of regions of the brain that are associated with childhood poverty, such as the hippocampus, it is often unclear what specific functional processed may be involved. Therefore, studies that combine structural and functional measures may give critical insight into how structural-functional relations may be associated with childhood poverty. Unfortunately, many studies of childhood poverty examine these associations separately. A study utilized both measures of cortical thickness and resting-state functional networks to examine differences in network organization based upon SES in adulthood (Chan et al., 2018). This study demonstrates that examining multiple modalities in concert may provide a deeper understanding of SES-brain relations. As each neuroimaging modality has its own strengths and weakness, combining them can enhance future studies. For example, EEG has exceptional temporal resolution but poor spatial resolution, while fMRI may not be able to examine rapid processes in the brain but has exceptional spatial resolution. Therefore, combining modalities may provide unique insight into the biological processes underlying the association between childhood poverty and brain development.

9.4 Longitudinal studies and mediation analysis

As we have discussed, the relation between childhood poverty and brain structure may depend on which developmental period is being examined.

Therefore, our understanding of this association will be enhanced using longitudinal data. Cross-sectional studies are limited in their ability to provide context related to the possible neurobiological underpinnings of the association. For example, several studies have reported a positive association between family income and hippocampal volume (Dufford et al., 2019; Hanson et al., 2011; Jednoróg et al., 2012; Luby et al., 2013; Noble et al., 2015, 2012). However, it is critical for these studies to consider the developmental stage of the participant in the study (Tottenham & Sheridan, 2010), while some studies would interpret this findings as a reduction in volume due to "damage" or stress altering the neural structure of the hippocampus, an alternative hypothesis is that at this developmental stage (middle childhood) the hippocampus is undergoing synaptic pruning which would also result in a decreased hippocampal volume (Callaghan & Tottenham, 2016; Tottenham & Sheridan, 2010). The experience of poverty may impact brain developmental by accelerating maturation, i.e., the lower hippocampal volume may be an indication of accelerated maturation, a response of the brain to adapt to environmental adversity (Callaghan & Tottenham, 2016; VanTieghem & Tottenham, 2017). As brain development is complex, it is critical for studies to have multiple timepoints of neuroimaging data. Longitudinal neuroimaging data allows for brain developmental trajectories to be examined; as discussed, these brain developmental trajectories can not only help inform interpretations regarding underlying neural processes but also the trajectories can be predictive of behavioral outcomes (Hanson et al., 2013). The brain trajectory approach from longitudinal data can also be informative regarding when trajectories diverge between children experiencing poverty and those not. These divergences may indicate development periods that are critical for intervention.

Longitudinal data also affords the ability to examine prospective relations between childhood poverty and brain development. As a large body of research has indicated that experiencing poverty in childhood has long-lasting associations with mental and physical health in adulthood, it is critical to examine prospective associations between childhood poverty and brain development. While identifying prospective relations between childhood poverty and brain development can demonstrate the potential long-lasting effect associations, this can also advance our understanding of potential protective factors that can ameliorate the association. We may be able to harness longitudinal studies to identify factors for those individuals that experienced poverty in childhood but have not experienced mental and

physical health issues in adulthood. However, as discussed, it is critical for longitudinal studies to have accurate measures of childhood SES as retrospective recall of childhood indicators of SES may have limited accuracy (Jivraj, Goodman, Ploubidis, & de Oliveira, 2017).

Longitudinal studies also afford the ability to test potential mediators of the associations between childhood SES and brain development. Testing mediation in cross-sectional data has been shown to be biased (Maxwell & Cole, 2007), therefore it is critical for studies testing potential mediators of the relations between childhood poverty and brain development to utilize longitudinal data. The identification of mediators has the potential to inform potential mechanisms underlying the associations between childhood poverty and brain development as well as provide targets for interventions that may be particularly efficacious. However, to date, studies of the mediators of the relation between childhood poverty and brain development are rare. Caregiver support was found to mediate the association between income-to-needs ratio and hippocampal volume in children ages 6–12 (Luby et al., 2013). These findings suggest that the quality of caregiver support may play an important role in the associations between childhood SES and brain structure. Further, this may suggest that an intervention on parenting quality could potentially mitigate this relation; evidence for this has recently been found (Brody et al., 2017). The identification of potential mediators of the relation between childhood poverty and brain development can also test potential underlying mechanisms. Although it is problematic to conclude that a mediator identifies a "mechanism," evidence of statistical mediation is necessary but not sufficient to conclude a pathway is mechanistic (Tryon, 2018). Therefore, identifying mediators can be an important first step toward understanding the underlying mechanism of the associations between childhood poverty and brain structure. Subsequent analyses of the mediators that are identified are needed to establish causality and why a statistical mediation is observed in terms of in terms of a series of causal steps (Tryon, 2018).

Ultimately, a critical goal for future studies will be to build predictive models (Stringer & Tommerdahl, 2015) to identify individuals that have experienced childhood poverty and are at the highest risk for mental or physical health issues later in life. Identifying prospective relations is a critical first step in building predictive models; however, to improve the accuracy and generalizability of predictive models it is critical to test the model in a set of data that was not used to train the model (Picard & Cook, 1984). Using

methods adopted from machine learning, cross-validation techniques can be used to test the accuracy of predictive models in an unbiased manner (Taylor, Ankerst, & Andridge, 2008; Woo, Chang, Lindquist, & Wager, 2017). Longitudinal studies are labor-intensive and expensive (especially the cost of multiple neuroimaging sessions); however, they are critical to provide a deeper understanding of the association between childhood poverty and brain development as well as provide the opportunity to examine mediators of the association.

10. Conclusions

Childhood poverty and brain development is a dynamic and complex process. First, the associations between childhood poverty and brain development have been identified across the life span from the prenatal period to aging populations. However, as discussed, we suggest that the directionality between childhood poverty and brain structure/function often depends on the developmental period being examined. While there is evidence of long-lasting prospective relations between childhood poverty and brain structure/function, in certain developmental periods this coupling may be stronger or weaker during other developmental periods. We also conclude that the association between childhood poverty and brain development is a complex process. Studies have begun to address this complexity by utilizing longitudinal studies, multimodal neuroimaging, network neuroscience, population neuroscience, theoretical models, plus examining health/behavioral outcomes, as well as protective factors. Further, we suggest that future studies of the association between childhood poverty and brain development may benefit from some of or a combination of these methods. Studies of the association between childhood poverty and brain health have and will continue to provide critical information about potential mechanisms underlying the association between childhood poverty and physical and mental health issues later in life.

References

Adler, N. E., & Rehkopf, D. H. (2008). US disparities in health: Descriptions, causes, and mechanisms. *Annual Review of Public Health*, *29*, 235–252.

Alexander-Bloch, A., Raznahan, A., Bullmore, E., & Giedd, J. (2013). The convergence of maturational change and structural covariance in human cortical networks. *Journal of Neuroscience*, *33*(7), 2889–2899.

Behrens, T. E., & Sporns, O. (2012). Human connectomics. *Current Opinion in Neurobiology*, *22*(1), 144–153.

Betancourt, L. M., Avants, B., Farah, M. J., Brodsky, N. L., Wu, J., Ashtari, M., et al. (2016). Effect of socioeconomic status (SES) disparity on neural development in female African-American infants at age 1 month. *Developmental Science*, *19*(6), 947–956.

Biessmann, F., Plis, S., Meinecke, F. C., Eichele, T., & Muller, K.-R. (2011). Analysis of multimodal neuroimaging data. *IEEE Reviews in Biomedical Engineering*, *4*, 26–58.
Blair, C., & Raver, C. C. (2012). Child development in the context of adversity: Experiential canalization of brain and behavior. *American Psychologist*, *67*(4), 309.
Blinowska, K., & Durka, P. (2006). Electroencephalography (EEG). In *Wiley encyclopedia of biomedical engineering*. Wiley.
Boyce, W. T. (2016). Differential susceptibility of the developing brain to contextual adversity and stress. *Neuropsychopharmacology*, *41*(1), 142.
Bradley, R. H., & Corwyn, R. F. (2002). Socioeconomic status and child development. *Annual Review of Psychology*, *53*(1), 371–399.
Brito, N. H., & Noble, K. G. (2014). Socioeconomic status and structural brain development. *Frontiers in Neuroscience*, *8*, 276.
Brody, G. H., Gray, J. C., Yu, T., Barton, A. W., Beach, S. R., Galván, A., et al. (2017). Protective prevention effects on the association of poverty with brain development. *JAMA Pediatrics*, *171*(1), 46–52.
Brody, G. H., Yu, T., Miller, G. E., Ehrlich, K. B., & Chen, E. (2019). Preventive parenting intervention during childhood and young black adults' unhealthful behaviors: A randomized controlled trial. *Journal of Child Psychology and Psychiatry*, *60*(1), 63–71.
Brody, G. H., Yu, T., Nusslock, R., Barton, A. W., Miller, G. E., Chen, E., et al. (2019). The protective effects of supportive parenting on the relationship between adolescent poverty and resting-state functional brain connectivity during adulthood. *Psychological Science*, *30*, 1040–1049. https://doi.org/10.1177/0956797619847989.
Buckley, L., Broadley, M., & Cascio, C. N. (2019). Socio-economic status and the developing brain in adolescence: A systematic review. *Child Neuropsychology*, *25*(7), 859–884.
Callaghan, B. L., & Tottenham, N. (2016). The stress acceleration hypothesis: Effects of early-life adversity on emotion circuits and behavior. *Current Opinion in Behavioral Sciences*, *7*, 76–81.
Cao, M., Huang, H., Peng, Y., Dong, Q., & He, Y. (2016). Toward developmental connectomics of the human brain. *Frontiers in Neuroanatomy*, *10*, 25.
Casey, B., Cannonier, T., Conley, M. I., Cohen, A. O., Barch, D. M., Heitzeg, M. M., et al. (2018). The adolescent brain cognitive development (ABCD) study: Imaging acquisition across 21 sites. *Developmental Cognitive Neuroscience*, *32*, 43–54.
Chan, M. Y., Na, J., Agres, P. F., Savalia, N. K., Park, D. C., & Wig, G. S. (2018). Socioeconomic status moderates age-related differences in the brain's functional network organization and anatomy across the adult lifespan. *Proceedings of the National Academy of Sciences of the United States of America*, *115*(22), E5144–E5153.
Conejero, Á., Guerra, S., Abundis-Gutiérrez, A., & Rueda, M. R. (2018). Frontal theta activation associated with error detection in toddlers: Influence of familial socioeconomic status. *Developmental Science*, *21*(1) e12494.
Cremers, H. R., Wager, T. D., & Yarkoni, T. (2017). The relation between statistical power and inference in fMRI. *PLoS One*, *12*(11) e0184923.
Dufford, A. J., Bianco, H., & Kim, P. (2019). Socioeconomic disadvantage, brain morphometry, and attentional bias to threat in middle childhood. *Cognitive, Affective, & Behavioral Neuroscience*, *19*(2), 309–326.
Dufford, A. J., & Kim, P. (2017). Family income, cumulative risk exposure, and white matter structure in middle childhood. *Frontiers in Human Neuroscience*, *11*, 547.
Duval, E. R., Garfinkel, S. N., Swain, J. E., Evans, G. W., Blackburn, E. K., Angstadt, M., et al. (2017). Childhood poverty is associated with altered hippocampal function and visuospatial memory in adulthood. *Developmental Cognitive Neuroscience*, *23*, 39–44.
Ellwood-Lowe, M. E., Sacchet, M. D., & Gotlib, I. H. (2016). The application of neuroimaging to social inequity and language disparity: A cautionary examination. *Developmental Cognitive Neuroscience*, *22*, 1–8.

Evans, G. W. (2004). The environment of childhood poverty. *American Psychologist*, *59*(2), 77.
Evans, G. W., Li, D., & Whipple, S. S. (2013). Cumulative risk and child development. *Psychological Bulletin*, *139*(6), 1342.
Farah, M. J. (2018). Socioeconomic status and the brain: Prospects for neuroscience-informed policy. *Nature Reviews Neuroscience*, *19*(7), 428–438.
Farah, M. J., Shera, D. M., Savage, J. H., Betancourt, L., Giannetta, J. M., Brodsky, N. L., et al. (2006). Childhood poverty: Specific associations with neurocognitive development. *Brain Research*, *1110*(1), 166–174.
Gao, W., Alcauter, S., Elton, A., Hernandez-Castillo, C. R., Smith, J. K., Ramirez, J., et al. (2014). Functional network development during the first year: Relative sequence and socioeconomic correlations. *Cerebral Cortex*, *25*(9), 2919–2928.
Gianaros, P. J., Horenstein, J. A., Hariri, A. R., Sheu, L. K., Manuck, S. B., Matthews, K. A., et al. (2008). Potential neural embedding of parental social standing. *Social Cognitive and Affective Neuroscience*, *3*(2), 91–96.
Gianaros, P. J., Kuan, D. C.-H., Marsland, A. L., Sheu, L. K., Hackman, D. A., Miller, K. G., et al. (2017). Community socioeconomic disadvantage in midlife relates to cortical morphology via neuroendocrine and cardiometabolic pathways. *Cerebral Cortex*, *27*(1), 460–473.
Gianaros, P. J., Marsland, A. L., Sheu, L. K., Erickson, K. I., & Verstynen, T. D. (2012). Inflammatory pathways link socioeconomic inequalities to white matter architecture. *Cerebral Cortex*, *23*(9), 2058–2071.
Gilman, S. E., Kawachi, I., Fitzmaurice, G. M., & Buka, S. L. (2002). Socioeconomic status in childhood and the lifetime risk of major depression. *International Journal of Epidemiology*, *31*(2), 359–367.
Gogtay, N., Giedd, J. N., Lusk, L., Hayashi, K. M., Greenstein, D., Vaituzis, A. C., et al. (2004). Dynamic mapping of human cortical development during childhood through early adulthood. *Proceedings of the National Academy of Sciences of the United States of America*, *101*(21), 8174–8179.
Graham, A. M., Pfeifer, J. H., Fisher, P. A., Lin, W., Gao, W., & Fair, D. A. (2015). The potential of infant fMRI research and the study of early life stress as a promising exemplar. *Developmental Cognitive Neuroscience*, *12*, 12–39.
Haan, M., Kaplan, G. A., & Camacho, T. (1987). Poverty and health prospective evidence from the alameda county study. *American Journal of Epidemiology*, *125*(6), 989–998.
Hackman, D. A., Farah, M. J., & Meaney, M. J. (2010). Socioeconomic status and the brain: Mechanistic insights from human and animal research. *Nature Reviews Neuroscience*, *11*(9), 651.
Hagmann, P., Cammoun, L., Gigandet, X., Gerhard, S., Grant, P. E., Wedeen, V., et al. (2010). MR connectomics: Principles and challenges. *Journal of Neuroscience Methods*, *194*(1), 34–45.
Hair, N. L., Hanson, J. L., Wolfe, B. L., & Pollak, S. D. (2015). Association of child poverty, brain development, and academic achievement. *JAMA Pediatrics*, *169*(9), 822–829.
Hanson, J. L., Chandra, A., Wolfe, B. L., & Pollak, S. D. (2011). Association between income and the hippocampus. *PLoS One*, *6*(5) e18712.
Hanson, J. L., Hair, N., Shen, D. G., Shi, F., Gilmore, J. H., Wolfe, B. L., et al. (2013). Family poverty affects the rate of human infant brain growth. *PLoS One*, *8*(12) e80954.
Harrison, C., Loxton, H., & Somhlaba, N. Z. (2019). Stress and coping: Considering the influence of psychological strengths on the mental health of at-risk south African adolescents. *Child Care in Practice*, *25*, 1–15.
Huttenlocher, P. R. (1984). Synapse elimination and plasticity in developing human cerebral cortex. *American Journal of Mental Deficiency*, *88*, 488–496.
Huttenlocher, P. R., De, C. C., Garey, L. J., & der Loos Van, H. (1982). Synaptic development in human cerebral cortex. *International Journal of Neurology*, *16*, 144–154.

Javanbakht, A., King, A. P., Evans, G. W., Swain, J. E., Angstadt, M., Phan, K. L., et al. (2015). Childhood poverty predicts adult amygdala and frontal activity and connectivity in response to emotional faces. *Frontiers in Behavioral Neuroscience*, *9*, 154.

Jednoróg, K., Altarelli, I., Monzalvo, K., Fluss, J., Dubois, J., Billard, C., et al. (2012). The influence of socioeconomic status on children's brain structure. *PLoS One*, 7(8) e42486.

Jernigan, T. L., Brown, T. T., Hagler, D. J., Jr., Akshoomoff, N., Bartsch, H., Newman, E., et al. (2016). The pediatric imaging, neurocognition, and genetics (PING) data repository. *NeuroImage*, *124*, 1149–1154.

Jivraj, S., Goodman, A., Ploubidis, G. B., & de Oliveira, C. (2017). Testing comparability between retrospective life history data and prospective birth cohort study data. *The Journals of Gerontology: Series B, Psychological Sciences and Social Sciences*, gbx042. https://doi.org/10.1093/geronb/gbx042.

Johnson, M. H. (2005). Sensitive periods in functional brain development: Problems and prospects. *Developmental Psychobiology*, *46*(3), 287–292.

Johnson, S. B., Riis, J. L., & Noble, K. G. (2016). State of the art review: Poverty and the developing brain. *Pediatrics*, *137*(4) e20153075.

Khundrakpam, B., Choudhury, S., Vainik, U., Al-Sharif, N., Bhutani, N., & Evans, A. (2019). Non-linear effects of socioeconomic status on brain development: associations between parental occupation, cortical thickness and language skills in childhood and adolescence. *bioRxiv*. https://doi.org/10.1101/575993.

Kievit, R. A., Brandmaier, A. M., Ziegler, G., Van Harmelen, A.-L., de Mooij, S. M., Moutoussis, M., et al. (2018). Developmental cognitive neuroscience using latent change score models: A tutorial and applications. *Developmental Cognitive Neuroscience*, *33*, 99–117.

Kim, P., Evans, G. W., Angstadt, M., Ho, S. S., Sripada, C. S., Swain, J. E., et al. (2013). Effects of childhood poverty and chronic stress on emotion regulatory brain function in adulthood. *Proceedings of the National Academy of Sciences of the United States of America*, *110*(46), 18442–18447.

Kim, P., Evans, G. W., Chen, E., Miller, G., & Seeman, T. (2018). How socioeconomic disadvantages get under the skin and into the brain to influence health development across the lifespan. In *Handbook of life course health development* (pp. 463–497). Cham: Springer.

Knickmeyer, R. C., Gouttard, S., Kang, C., Evans, D., Wilber, K., Smith, J. K., et al. (2008). A structural MRI study of human brain development from birth to 2 years. *Journal of Neuroscience*, *28*(47), 12176–12182.

Knickmeyer, R. C., Xia, K., Lu, Z., Ahn, M., Jha, S. C., Zou, F., et al. (2016). Impact of demographic and obstetric factors on infant brain volumes: A population neuroscience study. *Cerebral Cortex*, *27*(12), 5616–5625.

Krishnadas, R., McLean, J., Batty, G. D., Burns, H., Deans, K. A., Ford, I., et al. (2013). Socioeconomic deprivation and cortical morphology: Psychological, social, and biological determinants of ill health study. *Psychosomatic Medicine*, *75*(7), 616–623.

Lajud, N., & Torner, L. (2015). Early life stress and hippocampal neurogenesis in the neonate: Sexual dimorphism, long term consequences and possible mediators. *Frontiers in Molecular Neuroscience*, *8*, 3.

Lawson, G. M., Duda, J. T., Avants, B. B., Wu, J., & Farah, M. J. (2013). Associations between children's socioeconomic status and prefrontal cortical thickness. *Developmental Science*, *16*(5), 641–652.

Lebel, C., Gee, M., Camicioli, R., Wieler, M., Martin, W., & Beaulieu, C. (2012). Diffusion tensor imaging of white matter tract evolution over the lifespan. *NeuroImage*, *60*(1), 340–352.

Lebel, C., Treit, S., & Beaulieu, C. (2019). A review of diffusion MRI of typical white matter development from early childhood to young adulthood. *NMR in Biomedicine*, *32*(4) e3778.

Lee, H., Andrew, M., Gebremariam, A., Lumeng, J. C., & Lee, J. M. (2014). Longitudinal associations between poverty and obesity from birth through adolescence. *American Journal of Public Health*, *104*(5), e70–e76.

Li, G., Wang, L., Yap, P.-T., Wang, F., Wu, Z., Meng, Y., et al. (2019). Computational neuroanatomy of baby brains: A review. *NeuroImage*, *185*, 906–925.

Luby, J., Belden, A., Botteron, K., Marrus, N., Harms, M. P., Babb, C., et al. (2013). The effects of poverty on childhood brain development: The mediating effect of caregiving and stressful life events. *JAMA Pediatrics*, *167*(12), 1135–1142.

Marshall, P. J., & Fox, N. A. (2007). Infant EEG and ERP in relation to social and emotional development. In *Infant EEG and event-related Potentials* (pp. 227–250). Hove, East Sussex: Psychology Press.

Maxwell, S. E., & Cole, D. A. (2007). Bias in cross-sectional analyses of longitudinal mediation. *Psychological Methods*, *12*(1), 23.

McEwen, B. S. (2008). Understanding the potency of stressful early life experiences on brain and body function. *Metabolism*, *57*, S11–S15.

McEwen, B. S. (2012). Brain on stress: How the social environment gets under the skin. *Proceedings of the National Academy of Sciences of the United States of America*, *109*(Suppl. 2), 17180–17185.

McLaughlin, K. A., Sheridan, M. A., & Lambert, H. K. (2014). Childhood adversity and neural development: Deprivation and threat as distinct dimensions of early experience. *Neuroscience & Biobehavioral Reviews*, *47*, 578–591.

McLoyd, V. C. (1998). Socioeconomic disadvantage and child development. *American Psychologist*, *53*(2), 185.

Merz, E. C., Tottenham, N., & Noble, K. G. (2018). Socioeconomic status, amygdala volume, and internalizing symptoms in children and adolescents. *Journal of Clinical Child & Adolescent Psychology*, *47*(2), 312–323.

Miller, G. E., & Chen, E. (2013). The biological residue of childhood poverty. *Child Development Perspectives*, *7*(2), 67–73.

Miller, G. E., Chen, E., Fok, A. K., Walker, H., Lim, A., Nicholls, E. F., et al. (2009). Low early-life social class leaves a biological residue manifested by decreased glucocorticoid and increased proinflammatory signaling. *Proceedings of the National Academy of Sciences*, *106*(34), 14716–14721.

Nagy, Z., Westerberg, H., & Klingberg, T. (2004). Maturation of white matter is associated with the development of cognitive functions during childhood. *Journal of Cognitive Neuroscience*, *16*(7), 1227–1233.

Natu, V. S., Gomez, J., Barnett, M., Jeska, B., Kirilina, E., Jaeger, C., et al. (2019). Apparent thinning of human visual cortex during childhood is associated with myelination. *Proceedings of the National Academy of Sciences of the United States of America*, *116*(41), 20750–20759.

Nie, J., Li, G., & Shen, D. (2013). Development of cortical anatomical properties from early childhood to early adulthood. *NeuroImage*, *76*, 216–224.

Noble, K. G., Houston, S. M., Brito, N. H., Bartsch, H., Kan, E., Kuperman, J. M., et al. (2015). Family income, parental education and brain structure in children and adolescents. *Nature Neuroscience*, *18*(5), 773.

Noble, K. G., Houston, S. M., Kan, E., & Sowell, E. R. (2012). Neural correlates of socioeconomic status in the developing human brain. *Developmental Science*, *15*(4), 516–527.

Noble, K. G., Norman, M. F., & Farah, M. J. (2005). Neurocognitive correlates of socioeconomic status in kindergarten children. *Developmental Science*, *8*(1), 74–87.

Noble, K. G., Wolmetz, M. E., Ochs, L. G., Farah, M. J., & McCandliss, B. D. (2006). Brain–behavior relationships in reading acquisition are modulated by socioeconomic factors. *Developmental Science*, *9*(6), 642–654.

Oomen, C. A., Soeters, H., Audureau, N., Vermunt, L., Van Hasselt, F. N., Manders, E. M., et al. (2010). Severe early life stress hampers spatial learning and neurogenesis, but improves hippocampal synaptic plasticity and emotional learning under high-stress conditions in adulthood. *Journal of Neuroscience*, *30*(19), 6635–6645.

Palma-Gudiel, H., Córdova-Palomera, A., Leza, J. C., & Fananás, L. (2015). Glucocorticoid receptor gene (NR3C1) methylation processes as mediators of early adversity in stress-related disorders causality: A critical review. *Neuroscience & Biobehavioral Reviews*, *55*, 520–535.

Panizzon, M. S., Fennema-Notestine, C., Eyler, L. T., Jernigan, T. L., Prom-Wormley, E., Neale, M., et al. (2009). Distinct genetic influences on cortical surface area and cortical thickness. *Cerebral Cortex*, *19*(11), 2728–2735.

Paus, T. (2010). Population neuroscience: Why and how. *Human Brain Mapping*, *31*(6), 891–903.

Perry, R. E., Finegood, E. D., Braren, S. H., Dejoseph, M. L., Putrino, D. F., Wilson, D. A., et al. (2019). Developing a neurobehavioral animal model of poverty: Drawing cross-species connections between environments of scarcity-adversity, parenting quality, and infant outcome. *Development and Psychopathology*, *31*(2), 399–418.

Picard, R. R., & Cook, R. D. (1984). Cross-validation of regression models. *Journal of the American Statistical Association*, *79*(387), 575–583.

Raizada, R. D., Richards, T. L., Meltzoff, A., & Kuhl, P. K. (2008). Socioeconomic status predicts hemispheric specialisation of the left inferior frontal gyrus in young children. *NeuroImage*, *40*(3), 1392–1401.

Rodier, P. M. (1994). Vulnerable periods and processes during central nervous system development. *Environmental Health Perspectives*, *102*(Suppl. 2), 121–124.

Rubinov, M., & Sporns, O. (2010). Complex network measures of brain connectivity: Uses and interpretations. *NeuroImage*, *52*(3), 1059–1069.

Sameroff, A. J., Seifer, R., Zax, M., & Barocas, R. (1987). Early indicators of developmental risk: Rochester longitudinal study. *Schizophrenia Bulletin*, *13*(3), 383–394.

Santos, A., Mier, D., Kirsch, P., & Meyer-Lindenberg, A. (2011). Evidence for a general face salience signal in human amygdala. *NeuroImage*, *54*(4), 3111–3116.

Satterthwaite, T. D., Elliott, M. A., Ruparel, K., Loughead, J., Prabhakaran, K., Calkins, M. E., et al. (2014). Neuroimaging of the Philadelphia neurodevelopmental cohort. *NeuroImage*, *86*, 544–553.

Scholtens, L. H., & van den Heuvel, M. P. (2018). Multimodal connectomics in psychiatry: Bridging scales from micro to macro. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *3*(9), 767–776.

Sharma, S., Mustanski, B., Dick, D., Bolland, J., & Kertes, D. A. (2019). Protective factors buffer life stress and behavioral health outcomes among high-risk youth. *Journal of Abnormal Child Psychology*, *47*, 1289–1301.

Sheridan, M. A., How, J., Araujo, M., Schamberg, M. A., & Nelson, C. A. (2013). What are the links between maternal social status, hippocampal function, and HPA axis function in children? *Developmental Science*, *16*(5), 665–675.

Sheridan, M. A., Sarsour, K., Jutte, D., D'Esposito, M., & Boyce, W. T. (2012). The impact of social disparity on prefrontal function in childhood. *PLoS One*, *7*(4) e35744.

Spann, M. N., Bansal, R., Hao, X., Rosen, T. S., & Peterson, B. S. (2019). Prenatal socioeconomic status and social support are associated with neonatal brain morphology, toddler language and psychiatric symptoms. *Child Neuropsychology*, *6*, 1–19.

Sripada, R. K., Swain, J. E., Evans, G. W., Welsh, R. C., & Liberzon, I. (2014). Childhood poverty and stress reactivity are associated with aberrant functional connectivity in default mode network. *Neuropsychopharmacology*, *39*(9), 2244.

Staff, R. T., Murray, A. D., Ahearn, T. S., Mustafa, N., Fox, H. C., & Whalley, L. J. (2012). Childhood socioeconomic status and adult brain size: Childhood socioeconomic status influences adult hippocampal size. *Annals of Neurology*, *71*(5), 653–660.

Stiles, J., & Jernigan, T. L. (2010). The basics of brain development. *Neuropsychology Review*, *20*(4), 327–348.
Stringer, S., & Tommerdahl, J. (2015). Building bridges between neuroscience, cognition and education with predictive modeling. *Mind, Brain, and Education*, *9*(2), 121–126.
Swartz, J. R., Hariri, A. R., & Williamson, D. E. (2017). An epigenetic mechanism links socioeconomic status to changes in depression-related brain function in high-risk adolescents. *Molecular Psychiatry*, *22*(2), 209.
Taylor, J. M., Ankerst, D. P., & Andridge, R. R. (2008). Validation of biomarker-based risk prediction models. *Clinical Cancer Research*, *14*(19), 5977–5983.
Tomalski, P., & Johnson, M. H. (2010). The effects of early adversity on the adult and developing brain. *Current Opinion in Psychiatry*, *23*(3), 233–238.
Tomalski, P., Moore, D. G., Ribeiro, H., Axelsson, E. L., Murphy, E., Karmiloff-Smith, A., et al. (2013). Socioeconomic status and functional brain development–associations in early infancy. *Developmental Science*, *16*(5), 676–687.
Tomatis, L. (1997). Poverty and cancer. *Sociological Methods and Research*, *160*(150), 140.
Tooley, U. A., Mackey, A. P., Ciric, R., Ruparel, K., Moore, T. M., Gur, R. C., et al. (2019). Associations between neighborhood SES and functional brain network development. *Cerebral Cortex*.
Tottenham, N., & Sheridan, M. A. (2010). A review of adversity, the amygdala and the hippocampus: A consideration of developmental timing. *Frontiers in Human Neuroscience*, *3*, 68.
Tryon, W. W. (2018). Mediators and mechanisms. *Clinical Psychological Science*, *6*(5), 619–628.
Uludağ, K., & Roebroeck, A. (2014). General overview on the merits of multimodal neuroimaging data fusion. *NeuroImage*, *102*, 3–10.
Ursache, A., Noble, K. G., & Pediatric Imaging, Neurocognition and Genetics Study. (2016). Socioeconomic status, white matter, and executive function in children. *Brain and Behavior*, *6*(10) e00531.
Uzgiris, I. C. (1973). Patterns of cognitive development in infancy. *Merrill-Palmer Quarterly of Behavior and Development*, *19*(3), 181–204.
van Marle, H. J., Hermans, E. J., Qin, S., & Fernández, G. (2009). From specificity to sensitivity: How acute stress affects amygdala processing of biologically salient stimuli. *Biological Psychiatry*, *66*(7), 649–655.
VanTieghem, M. R., & Tottenham, N. (2017). Neurobiological programming of early life stress: Functional development of amygdala-prefrontal circuitry and vulnerability for stress-related psychopathology. In *Behavioral neurobiology of PTSD* (pp. 117–136): Springer.
Versace, A., Acuff, H., Bertocci, M. A., Bebko, G., Almeida, J. R., Perlman, S. B., et al. (2015). White matter structure in youth with behavioral and emotional dysregulation disorders: A probabilistic tractographic study. *JAMA Psychiatry*, *72*(4), 367–376.
Vyas, A., Mitra, R., Rao, B. S., & Chattarji, S. (2002). Chronic stress induces contrasting patterns of dendritic remodeling in hippocampal and amygdaloid neurons. *Journal of Neuroscience*, *22*(15), 6810–6818.
Wadsworth, M. E., Evans, G. W., Grant, K., Carter, J. S., & Duffy, S. (2016). Poverty and the development of psychopathology. In D. Cicchetti (Ed.), *Developmental psychopathology* (pp. 136–179): John Wiley & Sons Inc.
Wang, Z., Dai, Z., Gong, G., Zhou, C., & He, Y. (2015). Understanding structural-functional relationships in the human brain: A large-scale network perspective. *The Neuroscientist*, *21*(3), 290–305.
Weissman, D. G., Conger, R. D., Robins, R. W., Hastings, P. D., & Guyer, A. E. (2018). Income change alters default mode network connectivity for adolescents in poverty. *Developmental Cognitive Neuroscience*, *30*, 93–99.

Westermann, G., Mareschal, D., Johnson, M. H., Sirois, S., Spratling, M. W., & Thomas, M. S. (2007). Neuroconstructivism. *Developmental Science*, *10*(1), 75–83.
Wierenga, L. M., Langen, M., Oranje, B., & Durston, S. (2014). Unique developmental trajectories of cortical thickness and surface area. *NeuroImage*, *87*, 120–126.
Wong, F. C., Chandrasekaran, B., Garibaldi, K., & Wong, P. C. (2011). White matter anisotropy in the ventral language pathway predicts sound-to-word learning success. *Journal of Neuroscience*, *31*(24), 8780–8785.
Woo, C.-W., Chang, L. J., Lindquist, M. A., & Wager, T. D. (2017). Building better biomarkers: Brain models in translational neuroimaging. *Nature Neuroscience*, *20*(3), 365.
Ziegler, G., Moutoussis, M., Hauser, T. U., Fearon, P., Bullmore, E. T., Goodyer, I. M., et al. (2019). Childhood socio-economic disadvantage predicts reduced myelin growth across adolescence and young adulthood. *bioRxiv*.
Zuo, X.-N., He, Y., Betzel, R. F., Colcombe, S., Sporns, O., & Milham, M. P. (2017). Human connectomics across the life span. *Trends in Cognitive Sciences*, *21*(1), 32–45.

Further reading

Hackman, D. A., & Farah, M. J. (2009). Socioeconomic status and the developing brain. *Trends in Cognitive Sciences*, *13*(2), 65–73.