Developmental Trajectories of Brain Structure, Motor, and Cognitive Functions from Infancy to Early Childhood and the Impact of SES

by

Julia Montagner Sassi

A dissertation submitted to the Graduate Faculty of
Auburn University
in partial fulfillment of the
requirements for the Degree of
Doctor of Philosophy

Auburn, Alabama
August 6, 2022

Keywords: Brain development, Infancy, Motor development,
Cognitive development, Income, Parental stress

Copyright 2022 by Julia Montagner Sassi

Approved by

Dr. Melissa Pangelinan, Chair, Associate Professor of Kinesiology
Dr. Danielle Wadsworth, Associate Professor of Kinesiology
Dr. Matthew Miller, Associate Professor of Kinesiology
Dr. William Murrah, Associate Professor of Educational Foundations, Leadership, and Technology

Abstract

During the first years of life, there are significant brain, cognitive, and motor development changes. Although studies have suggested a bidirectional relationship between the brain and these functional outcomes, few studies have directly examined their relationships. Moreover, the literature has suggested that socioeconomic status (SES) and related variables impact the brain, cognitive, language, and motor development. Additionally, parental stress has been associated with negative impacts on child development. However, there are knowledge gaps concerning the longitudinal relationships between the brain, motor, and cognitive development during the first few years of life, as well as the influence of socioeconomic factors and parental stress and their impact on these domains. Therefore, the overarching purpose of this dissertation was to address these knowledge gaps by examining the developmental trajectories of brain structure, motor skills, and cognitive function and their relationships from infancy to early childhood (i.e., birth – 2.5 years). In addition, this study examined the impact of adjusted household income and parental stress on the development of each domain. Lastly, we determined if changes in brain structure mediated the effect of adjusted household income and parental stress on this population's motor skills and cognitive function. To this end, a secondary data analysis was conducted using data from the National Institute of Health Study of Normal Brain Development – Object 2. We verified a significant positive relationship between average cortical thickness (CT) and BSID-II motor scale scores; however, there was an inverse relationship between average CT and BSID-II mental scale scores. Moreover, total cortical grey matter (GM) volume was not a significant predictor of motor or cognitive development. In addition, adjusted household income was a significant predictor of total cortical GM volume, and parental stress significantly predicted average CT and total cortical GM volume. However, these variables were not significant predictors of motor or cognitive development. Given the lack of relationship between the adjusted income and parental stress on the behavioral outcomes, the mediation analyses were not supported. Indeed, if total cortical GM volume or average CT were included in the model, there was still no evidence of a relationship between household income or parental stress on motor or cognitive development. Future directions and limitations are discussed. The study provided evidence regarding the developmental trajectories of each domain and the impact of income and parental stress. This study represents an important step in understanding infant development from a more comprehensive perspective.

Acknowledgements

I would like to thank my committee members for their feedback and support throughout this process. Dr. Matthew Miller, for not just providing feedback on this project but giving me the first opportunity to work with research. Dr. Wadsworth for always providing feedback, teaching, and rooting for me. Dr. Hamilton for providing me with insights and feedback. Dr. Murrah, for agreeing to be part of this project and teaching me more about statistics. Dr. Dede Yildirim, for agreeing to be my outside reader and being so understanding throughout this process. Lastly, I would like to thank Dr. Rudisill for all the support and opportunities during my academic trajectory.

I would also like to thank the Neurocognition and Imaging Research Lab at the University of North Carolina, Chapel Hill, for their help with processing the data, especially Dr. Wang and Dr. Wu, for always taking the time to reply to ALL my emails in a timely manner and make this dissertation possible.

A special thanks to my lab mates, who could not be more helpful! Danielle Lang, Emily Munn, Adefunke DadeMatthews, Janette Hynes, and Davis Dyke. Thank you all so much for always providing support and feedback and being the best motivators! Also, a special thanks to former lab mates that were very important on my trajectory until now, Dr. Robyn Feiss and Dr. Loriane Hill.

I would also like to thank my family and friends for their unconditional support. Special thanks to my family in Brazil, always cheering for me in the distance. Of course, a very special thanks to my husband, Marcos Daou, who has been very supportive since day one and has always believed in me and pushed me to be a better person.

Finally, a very special thanks to my mentor, Dr. Melissa Pangelinan, who has been a family to me all these years. Thank you for guiding me on this journey as a graduate student and preparing me for what is coming next. Thank you for making each student in your lab a priority and feeling appreciated. Thanks, Saphina, Andrew, and Connor, for sharing Dr. P. with us, especially for the last months!

Table of Contents

List of Tables

List of Figures

List of Abbreviations

BSID - II	Bayley Scales of Infant Development – Second Edition
CT	Cortical Thickness
GM	Grey Matter
PSI	Parent Stress Index
SES	Socioeconomic Status
SA	Surface Area
WM	White Matter

Chapter 1 – Introduction

Section 1: Overview

During the first years of life there are significant changes in the brain structure (Gilmore et al., 2007, 2012; Girault et al., 2020; Lyall et al., 2015; Knickmeyer et al., 2008), cognitive (Gerber et al., 2010; Johnson & Blasco, 1997; Blaga et al., 2009), and motor development (Gerber et al., 2010; Johnson & Blasco, 1997; WHO Multicentre Growth Reference Study Group, 2006). Although studies have suggested a bidirectional relationship between the brain and these functional outcomes, few studies have directly examined their relationships. Moreover, environmental factors, including poverty, have profound impacts on the structural changes in the brain (Johnson, Riis & Noble, 2016; Hanson et al., 2013; Jah et al., 2019) as well as development of motor (Clearfield, Stanger & Jenne, 2015); Fink, McCoy & Yousafzai, 2020; Black, Hess & Berenson-Howard, 2000) and cognitive skills (Rhoades et al., 2011; Suor et al., 2015; Blair et al., 2011). However, there are knowledge gaps concerning the *longitudinal* relationships between brain, motor, and cognitive development *from birth to early childhood*, as well as the influence of socioeconomic factors and their impact on these domains.

Therefore, the overarching purpose of this dissertation was to examine the developmental trajectories of and relationships between brain structure, motor skills, and cognitive function from infancy to early childhood (i.e., birth – 2.5 years). In addition, I examined the impact of household income on the development of each domain. Lastly, we examined if changes in brain structure mediate the impact of adjusted household income or parental stress on motor skills and cognitive function. To this end, a secondary data analysis was conducted using a dataset from the National Institute of Health Study of Normal Brain Development – Object 2 (Almli et al., 2007).

The purpose of this chapter is to provide a brief introduction to the key concepts that serve as the foundation for the specific aims and hypotheses.

Section 2: Brain Development

2.1. Grey Matter (GM) and White Matter (WM) volume

The first years of life are considered a critical window during which there are substantial changes in brain structure (Gilmore et al., 2007, 2012; Girault et al., 2020; Lyall et al., 2015) and behavior (i.e., motor and cognitive development; Girault et al., 2020; Shaw et al., 2006). By 3 months of age, infant brain volume grows from 33% to 54% of the adult brain (Holland et al., 2014). During the first year of life, growth in terms of brain volume is driven mainly by changes in gray matter (GM) (Gilmore et al., 2012; Knickmeyer et al., 2008). GM consists of neuronal cell bodies and dendrites in the brain and spinal cord, where the processing occurs, while WM refers to the commissures and axon tracts, facilitating the communication of GM areas. Its name is due to the light color resulting from the lipid content of myelin (Purves et al., 2012). Indeed, total GM volume increases by 149%, while white matter (WM) volume increases by only 11% during the first year (Knickmeyer et al., 2008). In addition, the changes in total GM volume differ by sex, where female brains reach 80% of the peak GM volume (i.e., 630 cm^3) around 14.4 months of age, while males reach 80% peak GM volume (i.e., 670 cm^3) around 10 months (Groeschel et al., 2010). Sex differences in WM volume have been reported, but the age at 80% peak WM volume (i.e, 330 cm^3, 390 cm^3) was observed around 6.52 years in females and 8.51 years in males, respectively (Groeschel et al., 2010). These data suggest a more gradual and protracted development of WM, extending well beyond infancy.

In addition to global changes in GM and WM volume, Gilmore et al. (2007) reported regional changes in cortical GM volume during the first 2 years of life. Specifically, during the first year of life (i.e., gestational age 38.8 to 47.8 weeks) occipital and parietal lobes, which mediate basic sensory processes, exhibit faster growth rates in GM volume compared to the prefrontal cortex, which mediates higher order cognitive functions (Gilmore et al., 2007). However, GM developmental trajectories continue to change throughout the first 2 years. By the end of the first year of life, the regions exhibiting faster growing rates are specific to visceral sensations and autonomic control, language, visual processing, and face recognition (i.e., insula, inferior frontal gyrus and angular gyrus, inferior temporal gyrus and fusiform gyrus, respectively). During the second year of life, faster growth rates in GM volume are observed in the frontal lobe (i.e., dorsolateral, and medial superior frontal gyri, and middle frontal gyrus), parietal lobe (i.e., inferior, angular, and supramarginal gyri), and temporal lobe (temporal pole of the middle temporal gyrus; Gilmore et al., 2012). Thus, the rapid changes in regional GM development during the first year of life may underlie developmental changes in sensory processing and language, while regional growth in GM volume during the second year of life may underlie the development changes in sensory integration, motor planning and coordination, and higher-order cognitive processes (Gilmore et al., 2012; Knickmeyer et al., 2008).

Infancy represents an important window for brain development that may underlie the development of motor and cognitive functions. Indeed, the total volume in frontal regions measured within the first 6 weeks of life is positively correlated to motor skills at 18 months, while volumes of temporal and occipital regions within the first 6 weeks are positively correlated with cognitive scores at 6, 24, and 18 months of age (Spann et al., 2014). Although these findings provide support of a directional relationship between early brain development and the subsequent development of motor and cognitive skills, there is a lack of studies directly investigating the relationship between brain volume and motor or cognitive abilities from a longitudinal perspective especially after age 2 (i.e., from birth to preschool years).

2.2. Cortical Thickness (CT)

GM volume is a product of cortical thickness (CT) and surface area (SA). Thus, it is not surprising that rapid changes in these other indices of structural brain development are also observed during the first years of life. From birth to 2 years of age, overall CT increases by 36.08% on average, with regional growth of CT increasing by 31% in the first year and 4.3% in the second (Lyall et al., 2015). Similar findings were reported with a larger sample (n= 73, compared with n = 40) by Li et al. (2015); CT increased by 42.4% during the first year with a more subtle increase of 0.7% during the second year. The frontal and temporal lobes exhibited overall thickest cortices in the first 2 years of life (Li et al., 2015). According to Wang et al. (2019), overall CT starts to decrease after reaching a plateau at about 14 months of age, however the sensorimotor, superior frontal, and superior parietal areas continue to increase slowly from 1 to 2 years of age. The authors hypothesized that the developmental changes in these areas correspond with changes in fine motor control and cognitive outcomes during the second year of life.

Developmental changes in CT may underlie the development of motor and cognitive abilities early in life. For example, thicker and larger cortices in infancy are related to better performance on cognitive and motor tasks at age 2 (Girault et al., 2020). Relationships among CT, cognitive, and motor skills would likely continue throughout early and late childhood. Indeed, intelligence was found to be related to the trajectory of CT, particularly in the prefrontal cortex and the left/superior/middle temporal gyri in children ages 3-18 years (Shaw et al., 2006). Specifically, superior levels of IQ were related to accelerated increase in cortical thickness during childhood, followed by rapid thinning by early adolescence (i.e., around 11.2 years; Shaw et al., 2006). However, very few studies have bridged the gap between infancy and those observed in later childhood with respect to the relationship between CT and motor and cognitive development

2.3. Surface Area (SA)

Corresponding changes in SA have also been reported during the first two years of life. Overall, brain surface area almost doubles in size from birth to 1 year of age (Li et al., 2013). More specifically, at birth, the mean SA of the left hemisphere is 361 cm^2, and the right hemisphere is 356 cm^2, whereas at 1 year the values are 640 cm^2 and 641 cm^2, respectively (Li et al., 2013). Cortical SA continues to increase in the second year of life, but the changes are smaller compared to the first year (i.e., mean for the left hemisphere: 770 cm^2; right hemisphere: 771 cm^2; Li et al., 2013). Therefore, the overall expansion in SA during the first 2 years of life is primarily due to the growth rates during the first year (Lyall et al., 2015).

The patterns of SA expansion are consistent with the findings related to the regional rate of growth of GM volumes during the first 2 years of life (Gilmore et al., 2012). During the first year, the regions that expand to a greater extent (i.e., exhibit faster-growing rates) include the parietal, temporal, and occipital lobes, compared to the frontal lobe. While from 1 to 2 years of age, parietal, temporal, and frontal lobes show larger expansion, compared to the occipital lobe (Li et al., 2013). Consistent with the findings from GM/WM volume and CT, developmental changes in SA likely underlie the development of behavioral functions such as cognitive and motor skills during infancy and across childhood. However, previous studies have not observed cross-sectional or longitudinal relationships between SA and behavior (Girault et al., 2020). For example, although relationships between neonatal, year 1, and year 2 SA and cognitive scores and year 1 and year 2 SA and fine motor scores were observed, after controlling for all covariates (e.g., age and sex), these relationships were no longer statistically significant (Girault et al., 2020). Similar patterns were observed between regional SA and cognitive scores at birth, 1 year and 2 years of age. However, these relationships were no longer statistically significant when considering all covariates with the exception of the relationship between visual reception and the right middle temporal gyrus (Girault et al., 2020). Taken together, it appears that SA is not as tightly linked to behavioral outcomes as GM and CT. Additional studies are needed to confirm the existence or lack of relationship between overall and regional SA and behavioral outcomes during the first two years of life.

2.4. Summary of Brain Development

The studies presented in this section provide evidence of structural brain development and suggest that changes observed during the first two years of life underlie functional changes across infancy. However, only a small number of studies have directly examined the relationships between brain structure and the development of motor and cognitive abilities from infancy to early childhood. Moreover, there is a large knowledge gap regarding the continued development of the brain and behavior in early childhood and how early changes in brain development during infancy may lead to different long-term developmental trajectories in brain and cognitive and motor development. Longitudinal evaluations are needed to determine if surface area, CT, and GM/WM volume indeed predict behavioral performance beyond the first two years of life.

Section 3: Motor Development

Motor milestones have been established based on the normative pattern of gross and fine motor skills to enable parents and clinicians to know what movements are expected during infancy. Gross motor skills are related to movements involving the whole body (balance, locomotor, and object control skills) while fine motor skills involve the upper extremities to manipulate and interact with the environment (Gerber et al., 2010).

Some of the gross motor milestones considered universal and fundamental to the acquisition of locomotion by the second year of life are: sitting without support (mean onset = 6 months); hands-and-knees crawling (mean onset = 8.5 months); standing with assistance (mean onset =7.6 months); walking with assistance (mean onset = 9.2 months); standing alone (mean onset = 11 months); and walking alone (mean onset = 12.1 months) (WHO Multicentre Growth Reference Study Group, 2006). In addition, infants can roll to the side (~3 months); run well (~18 months); walk upstairs with rail, alternating feet (~33 months); go up the stairs, alternating feet without rail, and walks heel to toe (~3 years); and balance on one foot (~4 years) (Johnson & Blasco, 1997; Gerber et al., 2010). These gross motor milestones enable the child to explore the environment and interact with other people and objects, and in doing so, improve motor as well as linguistic and cognitive abilities.

Some of the fundamental fine motor milestones are described as: hands fisted near the face (~1 month); hands unfisted and inspects objects (~3 months); transfer hand-hand and reach with one hand (~6 months); radial-digital grasp of cube (~9 months); fine pincer grasp of pellet (~12 months); release pellet into a bottle (~15 months); complete a square pegboard (~20 months); imitate circle and horizontal lines (~24 months); copy circle and strings small beads well (~3 years); write part of first name, and tie single knots (~4 years); cut with scissors and can use clothes-pins to transfer small objects (~5 years) (Johnson & Blasco, 1997; Gerber et al., 2010). Importantly, developmental changes in fine motor skills facilitate object exploration/manipulation between birth and 6 months of age and include mouthing, banging, and transferring objects (Lobo et al., 2014).

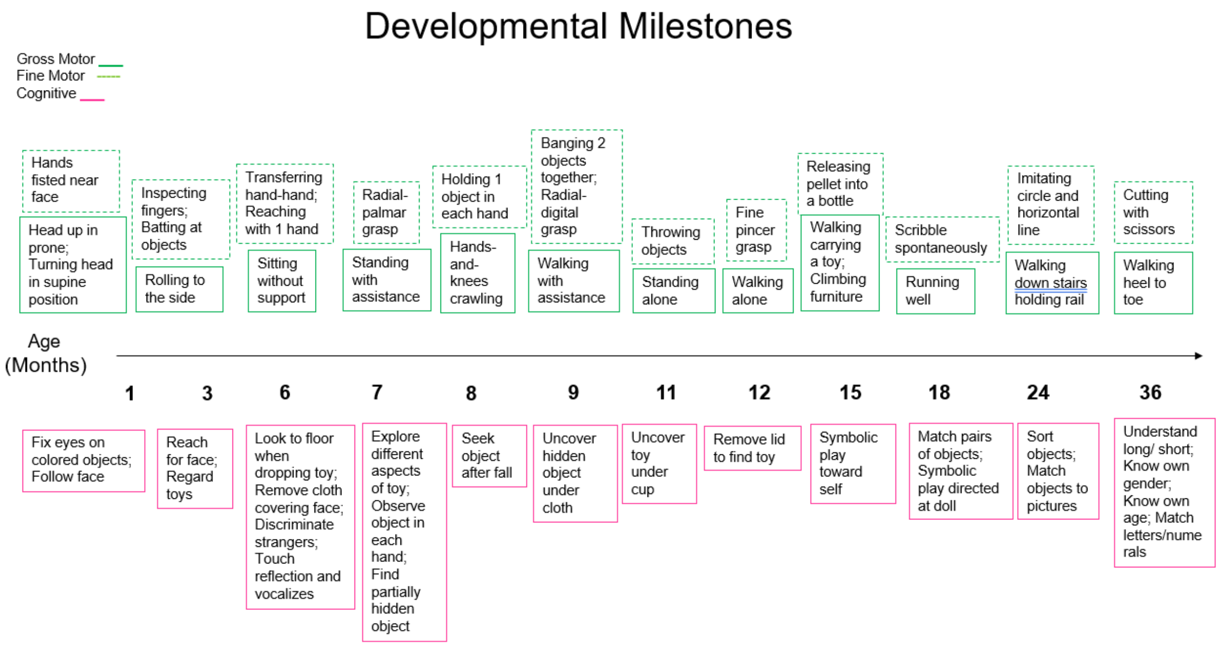
Gross and fine motor milestones are evaluated in common, standard assessments, such as the Bayley Scales of Infant Development or the Mullens Scales of Early Learning. Moreover, the development of gross and fine motor skills during infancy lay the foundation for future motor skill acquisition during early childhood. Indeed, 47% of the variance of gross motor skills at 3.5 years old is explained by early motor milestones, such as sitting, upright posture, and walking followed by reaching and grasping (Viholainen et al., 2006). Moreover, some motor skills are necessary precursors for future motor milestones (Adolph & Robinson, 2015). For example, difficulty achieving postural control (i.e., head, neck, trunk stability) can delay crawling or walking, which may reduce meaningful interactions with the environment and people. Specifically, when walking, toddlers can explore the environment, which provides opportunities to discover and develop new skills (Clark & Metcalfe, 2002). Independent locomotion also enables social exchanges that lead to language development (Iverson, 2010) as well as perceptual and cognitive development (Thelen, 2000; Adolph & Robinson, 2015).

Section 4: Cognitive Development

During the first four years of life, infants and young children experience exponential growth in their cognitive function. Some of the important cognitive milestones during the first year of life include: fix eyes on colored objects and follows face (~ 1 month); reach for face, regards toys (~ 3 months); remove cloth covering face, touch reflection and vocalize, bang and shake objects (~ 6 months); uncover hidden object (~ 9 months); remove lid to find toy (~ 12 months; Gerber et al., 2010; Johnson & Blasco, 1997). By two years, infants can: match pairs of objects, engage in symbolic play directed at doll (~ 18 months); deduce location of hidden objects (~ 20 months); sort objects, match objects to pictures, use familiar objects (~ 24 months; Gerber et al., 2010; Johnson & Blasco, 1997). By age 4, young children: knows own gender and age, match letter/numerals, understands long/short (~ 3 years); and understands simple analogies (e.g., ceiling/up; ice/cold), identify up to six colors, letters, and numerals (~ 4 years; Gerber et al., 2010; Johnson & Blasco, 1997). Figure 1 shows the motor and cognitive milestones from 1 month to 36 months. Those milestones include foundational skills relevant for later cognitive function and academic achievement. Importantly, imbedded in the performance of cognitive skills are fine and gross motor skills (e.g., moving eyes/hands, manipulating objects).

Figure 1

Motor and Cognitive Milestones From 1 to 36 Months



A central theory of cognitive development was proposed by Piaget (1952) in which cognitive structures become more sophisticated with experience and interaction with the environment. Acquisition of motor skills, such as crawling, standing, and walking during the first eighteen months of life allows children to explore the environment from different perspectives.

These skills enable infants to manipulate toys and interact with people, providing opportunities for language acquisition and communicative development, among other developing systems (Iverson, 2010). Through experience and exploration of their surroundings, infants learn that each action has an effect (i.e., the concept of causality). The infants understand that varying an action will result in different/novel outcomes (Johnson & Blasco, 1997). This concept is crucial for social development because the infant learns to manipulate the environment, either by crying or smiling, to elicit reactions by caregivers (Johnson & Blasco, 1997).

4.1. Relationship Between Motor and Cognitive Development

It is clear that motor and cognitive domains are interconnected and may develop together during infancy and early childhood (Diamond, 2000). Longitudinal studies have found that during the first year of life, motor, and cognitive domains, as measured by the Bayley Scales of Infant Development – II, appear to develop synchronously from the sixth month onward (Campos et al., 2012). Using this same assessment, a cross-sectional study observed that gross motor skills were positively associated with cognitive development in infants from 11 to 29 months of age (Veldman et al., 2019). Specifically, children that showed above-average scores for both locomotion and object manipulation skills also showed better cognitive skills, compared to those with below-average motor skills (Veldman et al., 2019). Although there is evidence that motor and cognitive domains develop concurrently, most studies employ cross-sectional designs. Therefore, additional longitudinal studies are needed to examine developmental trajectories of and the longitudinal relationship between motor and cognitive skills.

Interestingly, one study focused on a subset of cognitive skills, executive function including working memory and inhibitory control. Although executive function is believed to follow a protracted developmental timeline (i.e., not well developed until later childhood/adolescence), Wu et al. (2017) found that fine and gross motor abilities at age 2 were directly related to executive function skills at age 2. In addition to those concurrent associations, the development of motor skills and achievement of specific motor milestones are associated with cognitive and academic achievement later in childhood and early adolescence. Specifically, motor ability at age 1 also had a significant indirect effect on inhibitory control at age 3 via cognitive ability at age 2 and working memory at age 3, while fine and gross motor ability at age 2 had a significant direct effect on inhibitory control at age 3 (Wu et al., 2017). In a retrospective study, delayed achievement of the motor milestone "standing with assistance" (i.e., 2.1 months later than the average of the sample) was associated with lower adaptive and cognitive skills at age 4 (Ghassabian et al., 2016). Similarly, motor maturity (i.e., balance and movement – prelocomotion, locomotion, and sitting) and exploratory activity at 5 months of age predicted intellectual functioning at 4 and 10 years and academic achievement at 10 and 14 years (Bornstein, Hahn & Suwalsky, 2013). Together, these studies provide consistent evidence that early motor development influences later cognitive abilities during early and late childhood.

4.2. Summary of Motor and Cognitive Development

Taken together, there is evidence of simultaneous development of motor and cognitive domains as well as time-lagged relationships in which motor development predicts later cognitive development. However, there is a lack of studies investigating the contribution of brain development to these relationships from birth to early childhood. Therefore, the present study addressed this knowledge gap by examining the developmental trajectories of brain structure, motor skills, and cognitive function and the relationships between these factors from infancy to early childhood (i.e., birth – 3 years).

Section 5: Influence of Socioeconomic Status on Brain, Motor, and Cognitive Development

Research has shown that SES and related variables impact brain development, as well as cognitive, language, and motor development (Johnson, Riis & Noble, 2016; Hanson et al., 2013; Jah et al., 2019, Hair et al., 2015; Noble et al., 2015; Fink, McCoy & Yousafzai, 2020; Black, Hess & Berenson-Howard, 2000). Income has been associated with changes in brain growth, such that children from low-income households (defined as 200% below the federal poverty line) show lower average total gray matter volumes compared to their peers from higher income households between 13.5 months (mean age) until 4 years and 5 months of age (Hanson et al., 2013). During infancy and early childhood (newborn through 4.5 years of age), children from lower income families also show slower trajectories of brain growth (Hanson et al., 2013). The structural brain changes associated with income are more prominent in the most impoverished children (Hanson et al., 2013), which is consistent with studies examining this relationship with older children (Hair et al., 2015; Noble et al., 2015).

Other variables related to SES (e.g., parental education) have been identified as predictors of changes of average neonatal CT but not SA (Jah et al., 2019). Specifically, paternal education was negatively associated with average neonatal CT (i.e., a 1-year increase in paternal education was associated with a 0.13% decrease in average CT). On the other hand, when examining older children (i.e., mean age = 11.9 years), parent education is positively associated with SA in regions related to language and executive function (Noble et al., 2015). In addition, SA seems to mediate the relationship between income and inhibitory control and working memory (Noble et al., 2015). Based on these findings, it is not clear if the relationship between parental education and CT/ SA changes as a function of age. Alternatively, discrepancies between studies may be due to the way in which parental education was evaluated (i.e., averaging maternal and paternal education or considering only paternal or maternal education).

Discrepant findings have been reported regarding the relationship between socioeconomic factors and cognitive and motor development. For example, infants from low-income backgrounds do not differ in their mental and motor scales (BSID-II) compared to the standardized sample, while toddlers from low-income background exhibited lower scores compared to the standardized sample (Black, Hess & Berenson-Howard, 2000). Other studies have found that infants from low-SES backgrounds explored less and used less sophisticated behaviors during object exploration than infants from high-SES background at 12 months of age (Clearfield, Stanger & Jenne, 2015). It is possible that these discrepant results may be due to inconsistencies in the definitions of SES and related factors (e.g., income defined as 200% below or above the federal poverty line; split into categories low, medium, high; or as a continuous variable; as well as confounded with other factors such as parental education or race and ethnicity), or the age of the children evaluated, similar to what is observed for brain development. However, there is an overall lack of studies to critically evaluate the impact of SES on both the brain and behavior during infancy and early childhood.

SES factors are also linked to the presence of stressors (e.g., material deprivation, toxic stress related to parenthood, and environmental toxins), which are associated with adverse structural changes in the brain (Johnson, Riis & Noble, 2016). These changes can lead to poorer behavioral outcomes including reading/language, motor abilities and executive function. For example, salivary cortisol levels, an indicator of stress hormone concentrations, are higher in toddlers (~36 months of age) living below the poverty line (Blair et al., 2011). Moreover, salivary cortisol was also inversely related to executive function in this sample (Blair et al., 2011). However, additional studies are needed to determine the unique contribution of stress-related factors, beyond those associated with SES, on brain and behavioral development.

Taking in consideration the studies presented in this section, it is still unclear what the unique contributions are of SES-related variables on structural changes in the brain and how they impact cognitive and motor development during infancy and early childhood. Therefore, the present study addressed this knowledge gap by examining the effects of SES (e.g., adjusted household income) and parental stress on the development of brain, cognitive, and motor functions from infancy to early childhood (e.g., birth – 2.5 years).

Section 6: Specific Aims and Hypothesis

Considering the limitations of the studies mentioned in this chapter, there are knowledge gaps that need to be addressed to understand the differences in the long-term developmental trajectory of brain and behavioral development in infancy and early childhood. Moreover, there is a need to disentangle the unique effects of SES-related variables and parental stress and how these environmental factors impact brain, cognitive, and motor during this important period of development.

This study addressed these knowledge gaps by examining the developmental trajectories of brain structure, motor skills, and cognitive function and the relationships between these factors from infancy to early childhood. The study also examined SES (adjusted household income) and parental stress and how they uniquely impact brain, cognitive, and motor development during infancy to early childhood (i.e., birth – 2.5 years). To this end, a secondary data analysis was conducted using data acquired by the National Institute of Health Study of Normal Brain Development – Object 2 (Almli et al., 2007). Longitudinal data were collected from a large and representative sample of 106 participants from birth to age 4.5 years. In this dissertation, a sample of 87 participants from birth to 2.5 years of age was included. Due to differences in the number and interval between repeated measures, linear-mixed effect analysis was conducted to examine the following specific aims and hypotheses.

Specific Aim 1: To examine the relationships between brain, cognitive, and motor development from birth to 2.5 years.

- Greater Total Cortical GM Volume (mm^3) and overall Average CT (mm) will be associated with better performance on the Bayley Scales of Infant Development-II (BSID-II Mental and Motor scales), after accounting for age and sex.
- Motor development (BSID-II, Motor scale) will be positively associated with the cognitive development (BSID -II, Mental scale), after accounting for age and sex.

Specific Aim 2: To determine the effect of SES (Adjusted Household Income) and Parental Stress on brain, cognitive, and motor functions.

- Adjusted Household Income will be positively associated with Total Cortical GM Volume (mm^3), Average CT (mm), and BSID-II Motor and Mental scales, after controlling for age and sex.
- Parental Stress (PSI scores) will be negatively associated with Total Cortical GM Volume (mm^3), Average CT (mm), and BSID-II Mental and Motor subscales, after controlling for age and sex.

Specific Aim 3: To determine if changes in the brain mediate the relationship between SES and parental stress in motor and cognitive development.

- The positive relationship between SES (Adjusted Household Income) and BSID-II (Mental and Motor scales) will be mediated by Total Cortical GM Volume (mm^3) and overall Average CT (mm).

- The negative relationship between Parental Stress Index (PSI) and BSID-II (Mental and Motor scales) will be mediated by Total Cortical GM Volume (mm^3) and overall Average CT (mm).

6.1. Limitations

First, this is a secondary data analysis of previously acquired data from the National Institute of Health Study of Normal Brain Development. Data were acquired between 2001 and 2007 and utilized an older version of the assessments currently available (i.e., the researchers used Bayley Scales of Infant Development (BSID-II) and the BSID-IV is currently available). The older version of the assessment consisted of 3 domains (i.e., mental, motor and behavior rating scale) and did not provide standard scores for separate subscales (i.e., fine, and gross motor subscales). The updated version has 5 domains (i.e., cognitive, language, motor, social-emotional, and adaptive behavior) with the language scale divided into 2 subscales (receptive and expressive communication) and the motor scale divided into 2 subscales (i.e., fine, and gross motor). Therefore, it is not possible to compare the findings from this study with studies employing the newer version of the assessments.

Although the NIH Study of Normal Brain Development aimed to reflect the demographics of the US at the time of data collection, the sample lacked sufficient variability in some of the SES-related variables. Most of the children were White and Non-Hispanic and there was no variability in the level of parental education (high school degree (n = 83, maternal, n = 81, paternal, N = 87). However, adjusted household income had sufficient variability to examine its impact on brain, motor, and cognitive development, but the present analyses could not disambiguate differences related to parental education or parental occupation and SES.

Chapter 2 – Literature Review

Section 1: Brain Development

The first years of life are a critical period for postnatal brain development which may impact the development of cognitive and motor functions (Gilmore et al., 2007, 2012; Girault et al., 2020; Shaw et al., 2006). Studies investigating the structural development of the brain during this period found that during the first 3 months of life, neonates' brains grow from 33.5% to 54.9% of the adult brain size, with male brains growing slightly more rapidly than in females (66% and 63%, respectively; Holland et al., 2014). Additionally, differences in growth rates between gray and white matter have been identified during the first weeks after birth (e.g., 38.8 – 47.8 weeks), where total GM showed rapid growth compared to WM, with occipital and parietal regions growing significantly faster than prefrontal regions (Gilmore et al., 2007). Furthermore, during the first year of life, total cortical GM increased 108% and about 19% in the second year. Moreover, during the first year, the volume of the subcortical structures increased at a similar rate ranging between 104% and 107%, while in the second year, the growth rate was more variable (Gilmore et al., 2012). These changes in GM development during the first years of life may underlie developmental changes in sensory processing and language, followed by sensory integration, motor planning and coordination, and higher-order cognitive processes (Gilmore et al., 2012; Knickmeyer et al., 2008).

A similar rate of growth was observed in a previous study (Knickmeyer et al. 2008), where between 2 to 4 weeks of age total brain volume was around 36% of adult volume, at 1 year of age around 72%, and at 2 years around 83 % of adult volume. Hence, during the first year of life, the total brain volume increased by 101%, while in the second year it increased by 15%. Those growth rates reflected differences in GM compared with WM volumes. For example, the total GM increased by 149% in the first year and 14% in the second, while WM volume increased by 11% during the first year and 19% in the second (Knickmeyer et al., 2008). Congruent with Knickmeyer et al. (2008), Groeschel et al. (2010) verified the age at which 80% of the maximum GM volume is reached very early in life; 670 cm^3 was reached around 10 months for males and 630 cm^3 was reached around 14.4 months for females. On the other hand, 80% of the WM volume is reached at an older age for both males and females; 390 cm^3 at 8.51 years for males and 330 cm^3 at 6.52 years for females (Groeschel et al., 2010). These data suggest a more gradual development of WM, extending beyond infancy.

Relationships between brain development and behavioral functions were observed by Spann et al. (2014). Specifically, the frontal and occipital regions volume from scans obtained within the first 6 weeks were positively correlated with motor scores at 18 months, while temporal and occipital regions correlated significantly with cognitive scores at 6, 18, and 24 months of age (Spann et al., 2014). Indeed, the frontal lobe is related to planning, control, and short-term memory, participating in the control of motor behavior in different ways. These results make sense given the role of these brain regions in different behavioral functions. The parietal lobe is related to recognition (forming a body and relating it to an extrapersonal space), construction of spatial representations (that can guide attention and movement), and somatic sensation; the occipital lobe with vision; and the temporal lobe with hearing, learning, emotion and memory (Kandel et al., 2013). Therefore, the changes in GM volumes may underlie the capacity of acquiring and refining behaviors from birth throughout the lifespan (Purves et al., 2012). Although these findings provided support of a directional relationship between early brain development and the subsequent development of motor and cognitive skills, there is a lack of studies investigating the developmental trajectories and direct relationships, especially after 24 months.

Congruent with the differences in rate of growth GM volumes, during the first 2 years of life, the constituent components of GM, namely cortical thickness (CT) and surface area (SA) also show significant age-related changes during the first two years of life. For example, CT increased 36.08% on average over the first two years of life; a more robust growth was observed during the first year (averaging 31%) compared to the second year (i.e., averaging 4.3%; Lyall et al., 2015). Additionally, findings have suggested that although the total brain average CT increases rapidly during the first years of life, it reaches a plateau around 14 months (Wang et al., 2019), and appears to decrease the overall growth rate around 18 months (Wang et al., 2019).

With respect to regional changes, during the first 2 years frontal and temporal lobes achieve thicker cortices compared to occipital lobe (Li et al., 2015). CT increased around 0.1 mm per month during the first 2 years, where the prefrontal cortex (medial part) had the highest velocity between 0 and 12 months, followed by lateral frontal, posterior temporal, and lateral occipital cortices. The visual and sensorimotor cortices showed the slowest growth velocities during this period. From 12 and 24 months, superior frontal, superior parietal and sensorimotor showed slow and continuous increase (Wang et al., 2019). Those developmental changes may be compatible with changes in motor and cognitive outcomes during the second year of life.

The relationship between changes in CT and behavior have been examined. Girault et al. (2020), found that thicker cortices during infancy are correlated to better cognitive performance and gross motor skills at 1 year of age. But there is a lack of studies investigating the relationship between brain, cognitive and motor development and developmental trajectories across infancy and toddlerhood. Those addressing the relationship between the development of these domains are frequently looking at correlations at specific ages, which does not provide evidence of directional interactions. Thus, it is necessary to implement other statistical approaches to understand the longitudinal relationships between the brain and behavior.

With respect to developmental changes in SA, a similar growth pattern was observed, where during the first year there was an average growth of 76.35%, while in the second was 22.51% (Lyall et al., 2015). Furthermore, findings have suggested that the overall cortical SA expansion ranges from 20% to 108% between 1 and 6 years of age (Remer et al., 2017). Moreover, consistent with previous findings of regional changes in GM volumes, during the first year of life, the expansion of SA was larger in the parietal, temporal, and occipital lobes compared to frontal region. SA in the parietal, frontal and temporal lobes grow relatively fast in the second year of life as well (Gilmore et al., 2012; Li et al., 2013). Additional studies are needed to determine the relationship between overall and regional SA and behavioral outcomes during infancy and early childhood.

1.1. Brain development and SES

Socioeconomic factors are associated with adverse structural changes in the brain (Johnson, Riis & Noble, 2016). It is hypothesized that the impact of SES is due to adverse and stressful environmental exposures (e.g., many people living in the same house, family conflicts, neighborhood disorder, violence, or separation; Johnson, Riis & Noble, 2016). Young children from low-income backgrounds seem to have slower trajectories of brain growth during infancy and early childhood (e.g., 5 months to 4 years of age; Hanson et al., 2013). Infants from low-income families showed lower overall GM volume, in addition to lower average frontal and parietal GM volumes (Hanson et al., 2013). Those findings were significant among the children from the lowest SES.

The differences in GM volumes among poor and non-poor children were associated with disruptive behavioral problems (e.g., excessive aggression, hyperactivity, and rule breaking) by 4 years of age, which makes sense since these areas are responsible for cognitive flexibility, problem solving, and inhibitory control (Hanson et al., 2013). Those findings were consistent with studies examining the impact of SES on brain and behavior in older children (Hair et al., 2015; Noble et al., 2015). Indeed, during early childhood (e.g., 4-5 years of age), poverty was related to structural differences in brain areas associated with school readiness, especially for children from the lowest SES (Hair et al., 2015). Children from families with incomes 1.5 times below the federal poverty line exhibited GM volumes below the developmental norm and lower scores on standardized tests (Hair et al., 2015). Similarly, Noble et al. (2015) found that small differences in income were associated with large differences in SA, especially for children from low SES backgrounds. Although, overall SA partially accounted for association between family income and children's cognitive scores (e.g., inhibitory control and working memory), this association was not present between family income and CT (Noble et al., 2015). Taken together, these findings collectively suggest that the impact of income is most apparent in children from the most impoverished backgrounds and manifests in brain and behavioral outcomes.

Other variables related to SES (e.g., parental education) have been identified as predictors of change for neonatal CT but not SA (Jha et al., 2019). Specifically, paternal education was negatively associated with average CT (i.e., a 1-year increase in paternal education was associated with a 0.13% decrease in average CT). In another study examining older children and adolescents (4:6 and 18:3 years), Lawson et al. (2013) verified that CT in the right anterior cingulate gyrus and left superior frontal gyrus were predicted by parental education, where the increase of parental education (in years) predicted thicker cortices. Based on these findings, it is not clear if the relationship between parental education and CT/ SA changes as a function of age.

The studies presented in this section provide evidence of structural brain development and suggest that changes observed during the first two years of life may underlie functional changes during infancy. However, only a small number of studies have directly examined the relationships between brain structure and the development of motor and cognitive abilities from infancy to early childhood. It is unclear how early changes in brain development during infancy may lead to different long-term developmental trajectories in brain and behavioral development. Moreover, there are discrepancies in the literature regarding the impact of SES-related variables (e.g., income and maternal/paternal education) on the brain and relationships between the brain and behavior. Lastly, it is unclear if the effect of SES-related variables may indeed be due to adverse environments and to elevated parental and child stress.

Section 2: Motor Development

Changes in motor development throughout lifespan have been described using a mountain metaphor, considering the role of individual differences, task constraints, and the environment on the achievement of motor skills (Clark & Metcalfe, 2002). Over time, movements become more efficient and consistent, early involuntary/spontaneous movements are progressively transformed into goal-directed actions. The changes from one stage of motor development to the next are not based strictly on age but rather the emergence of different sets of skills with different goals. For example, from birth until about 2 weeks of life marks the “reflexive phase” during which reflexive and spontaneous movements are commonly observed. During the “preadapted phase”, infants begin using these reflexive and spontaneous movements to learn about their environment and begin developing the ability to execute goal-directed behaviors (e.g., holding their head up, reaching, crawling, walking, etc.). The "preadapted period" marks the onset of the infant gaining independence through locomotor (e.g., crawling/walking) and manipulative skills (e.g., feeding oneself). During the "fundamental motor patterns phase", which takes place between 1-7 years of age, children learn a broad range of motor skills that serve as the basis for participation in physical activities and sports (e.g., running, jumping, throwing, kicking, striking, etc.; Clark &Metcalfe, 2002). Importantly, during this early period of infant and child development, the motor abilities developed during one phase serve as the foundation for subsequent phases.

Another metaphor for motor development, proposed by Gallahue et al. (2012), represents motor development as a triangulated hourglass. This model goes from more reflexive and rudimentary phases to fundamental and specialized movement phases. Similar to the mountain metaphor, there is a sequential progression reflecting the stages and phases of motor development, which will vary depending on individual characteristics, environment, and task. Reflexes are involuntary movements, they are the first movements performed in-utero, and they are the way infants recognize their surroundings including their own body, and information about the environment, such as sound, light, and touch, they reflect the overall movement repertoire, and they reflect the first phase of movement development. Reflexes are divided into primitive and postural. Primitive reflexes are related to mechanisms of survival (e.g., sucking and rooting reflexes and their importance for feeding), and postural reflexes are precursors for later voluntary movements (e.g., palmar grasping and later grasping behavior, or primary stepping reflex and later walking behavior). This phase goes from in utero to up to one year of age.

The next phase reflects the rudimentary movements, which are basic voluntary movements required for survival that are usually performed up to two years of age, such as stability movements (i.e., head and neck control), manipulative movements (e.g., reaching and grasping), and locomotor movements (e.g., crawling and walking). This phase is divided into two stages, the first stage consists of the inhibition of the primitive and postural reflexes, the difference between the two phases on this first stage is very subtle because the infant's neuromotor control is in a rudimentary stage of development as well. In the next stage of this phase (around one year of age), the infants can control their movement with more precision, it is in this stage that they learn how to maintain balance, manipulate objects and finally explore the environment by crawling and walking.

With the “foundation” of the rudimentary movements, next comes the fundamental movement skills phase. In this phase, children learn how to respond with motor control and movement competence to different stimuli related to constraints and variations on the environment and on the task (e.g., level of difficulty). The acquisition of fundamental movements in early childhood is crucial for daily living activities throughout life. This phase is divided into three stages, the initial stage (usually between two to three years of age) consists of the first goal-oriented attempts to performing fundamental skills; the emerging stage (usually between three to five years of age) when the performance of fundamental movements involves coordination and greater motor control, and the proficient stage is the last of the fundamental skills phase (usually between five to six years of age), followed by the specialized movement phase (from seven and up) (Gallahue et al., 2012).

Empirical studies of motor development typically examine three main functional categories: stabilizing movement or movement related to balance or equilibrium, locomotor movement or movements that require a change in position/location of the body (i.e., walking, running, jumping), and manipulative movements involving interaction with objects (Goodway et al.,2019). Motor milestones are specific movement skills that follow a fairly stable developmental trajectory across early childhood and lead to upright posture, reaching, and locomotion (Haywood & Getchell, 2020). As mentioned in the first chapter, motor milestones have been established based on the normative pattern of gross motor skills (i.e., movements involving the whole body, balance, locomotor, and object control skills) and fine motor skills (i.e., movements involving the upper extremities to manipulate and interact with the environment). Normative patterns of the acquisition of motor milestones enable parents and clinicians to know what movements are expected and at what point during infancy (Gerber et al., 2010).

Some of the gross motor milestones considered universal and fundamental to the acquisition of locomotion by the second year of life are: sitting without support (mean onset = 6 months); hands-and-knees crawling (mean onset = 8.5 months); standing with assistance (mean onset =7.6 months); walking with assistance (mean onset = 9.2 months); standing alone (mean onset = 11 months), and walking alone (mean onset = 12.1 months; (WHO Multicentre Growth Reference Study Group, 2006). The average age of onset for some of those milestones were congruent with findings of the Bayley Scales of Infant Development (1936): sitting without support (mean = 6.6 months); standing alone (mean = 11 months) and walking alone (mean = 11.7 months) (Haywood & Getchell, 2020). In addition, infants can roll to the side (~3 months); run well (~18 months); walk upstairs with rail, alternating feet (~33 months); go up the stairs, alternating feet without rail, and walk heel to toe (~3 years) (Johnson & Blasco, 1997; Gerber et al., 2010). These gross motor milestones enable the child to explore the environment and interact with other people and objects, thus creating opportunities to develop language and cognitive skills.

Some of the fundamental fine motor milestones include: hands fisted near the face (~1 month); hands unfisted and inspects objects (~3 months); transfer hand-hand and reach with one hand (~6 months); radial-digital grasp of a cube (~9 months); fine pincer grasp of a pellet (~12 months); release pellet into a bottle (~15 months); complete a square pegboard (~20 months); imitate circle and horizontal lines (~24 months); copy circle and strings small beads well (~3 years); write part of the first name, and tie single knots (~4 years); cut with scissors and can use clothes-pins to transfer small objects (~5 years) (Johnson & Blasco, 1997; Gerber et al., 2010). Importantly, developmental changes in fine motor skills facilitate object exploration/manipulation, which also may provide opportunities for language and cognitive development.

Longitudinal studies have examined motor milestones from birth to early childhood. In a large sample (N= 135, from birth to 3.5 years of age), 47% of the variance of gross motor skills was explained by early body control (e.g., upright posture, sitting, and walking), and early hand control (e.g., reaching and grasping; Viholainen et al., 2006). Moreover, some motor skills are necessary precursors for future motor milestones (Adolph & Robinson, 2015). For example, difficulty achieving postural control (i.e., head, neck, trunk stability) can delay crawling or walking, which may reduce meaningful interactions with the environment and people. Additionally, the major milestones identified by the WHO (2006) study were reported by mothers at ages 4, 8, 12, 18, and 24 months and were analyzed with later Battelle Developmental Inventory second edition (BDI-2) scores (personal/social, adaptive, motor, communication, and cognitive domains) at 4 years of age (Ghassabian et al., 2016). Associations were observed between lower total developmental skills and an older age at which motor milestones were achieved. For example, children that achieved the milestone of standing with assistance 2.1

months later than the mean of the sample (8.9 months), showed a decrease of BDI-2 scores by 21.9 scores, and those associations were driven mainly by differences and cognitive and adaptive skills. Although these previous studies employed large samples and longitudinal designs, the milestones were identified by parent reports, which might lead to issues regarding reliability and generalizability.

Motor and cognitive domains are interconnected and may develop together during infancy and early childhood (Diamond, 2000). Indeed, early motor milestones have been associated with later academic achievement (Bornstein, Hahn & Suwalsky, 2013). Infants that were more motorically mature (e.g., prelocomotion upper and lower body, locomotion, and sitting) and actively explored the environment by 5 months showed higher intellectual functioning at 4 and 10 years, as well as higher academic achievement at 10 and 14 years of age (Bornstein, Hahn & Suwalsky, 2013). Further, Wu et al. (2017) conducted a longitudinal study to assess cognitive and motor abilities at 1 and 2 years, and executive functions at 3 years of age. The authors reported concurrent and time-lagged relationships between motor, cognitive, and executive skills. For example, motor ability at 1 year was related to general cognitive ability at 2 years. Higher gross motor scores at 2 years were associated with better inhibitory control at age 2. Further, fine motor and cognitive ability at 2 were related to inhibitory control and working memory at 3 years. Overall, the infants that had higher scores for motor abilities developed higher cognitive abilities (Wu et al., 2017). In another longitudinal study examining the relationship between motor and cognitive domains, performance on the motor and mental scales of the Bayley Scales of Infant Development – II showed a similar pattern of development from 6-months to 12 months (Campos et al., 2012). Furthermore, in a cross-sectional study (Veldman et al., 2019), locomotion was associated with object manipulation and cognition in toddlers between 11 and 29 months. Collectively, these findings suggest that opportunities to develop gross motor skills may positively impact cognitive development during the first years of life. Taken together, there is evidence of simultaneous development of motor and cognitive domains as well as time-lagged relationships in which motor development predicts later cognitive development. However, there is a lack of studies investigating the contribution of brain development to these relationships from birth to early childhood.

2.1. Motor Development and SES

Research has shown that socioeconomic status (SES) and related variables impact motor development (Johnson et al., 2016; Fink, McCoy & Yousafzai, 2020; Black, Hess & Berenson-Howard, 2000); but there are discrepancies reported. For example, infants (mean = 5.5 months) from low-income backgrounds do not differ in their motor scales (BSID-II) compared to the standardized sample (which had only 30% variability in ethnicity and race, and about 17% with parental education as less than high school, and no indicators of poverty), while toddlers (mean = 19.7 months) from low-income backgrounds exhibited lower scores compared to the standardized sample (Black, Hess & Berenson-Howard, 2000). Other studies have found that infants from low-SES backgrounds explored less and used less sophisticated behaviors during object exploration than infants from a high-SES background at 12 months of age (Clearfield et al., 2014). Congruent with those findings, Tacke et al. (2015) found that when exploring rigid versus flexible objects and surfaces, high-SES infants chose more rigid objects and surfaces (and banged objects into the surface more often) compared to low-SES infants. The choice of interacting with rigid objects/surfaces represented a more sophisticated behavior; the sound of the object on the surface created new opportunities for object exploration (suggesting preference for novel objects/environments). Comparing the major motor milestones (i.e., sit independently, stand without support, walk without support, and run without falling), although on average children in low Human Development Index countries demonstrated lower motor scores than children from high-HDI countries, those children that grew up in stimulating environments (measured with parent reports about the interactions between caregiver and child) appear to perform equally well across the globe (Fink, McCoy & Yousafzai, 2020). It is possible that these discrepant results may be due to inconsistencies in the definitions of SES and related factors as well as differences in the age of the participants and tasks evaluated.

Taking into consideration the studies presented in this section, it is still unclear what the unique contributions are of SES-related variables (i.e., income, parental education) and parental stress on motor functions from infancy to early childhood (e.g., birth-2.5 years).

Section 3: Cognitive Development

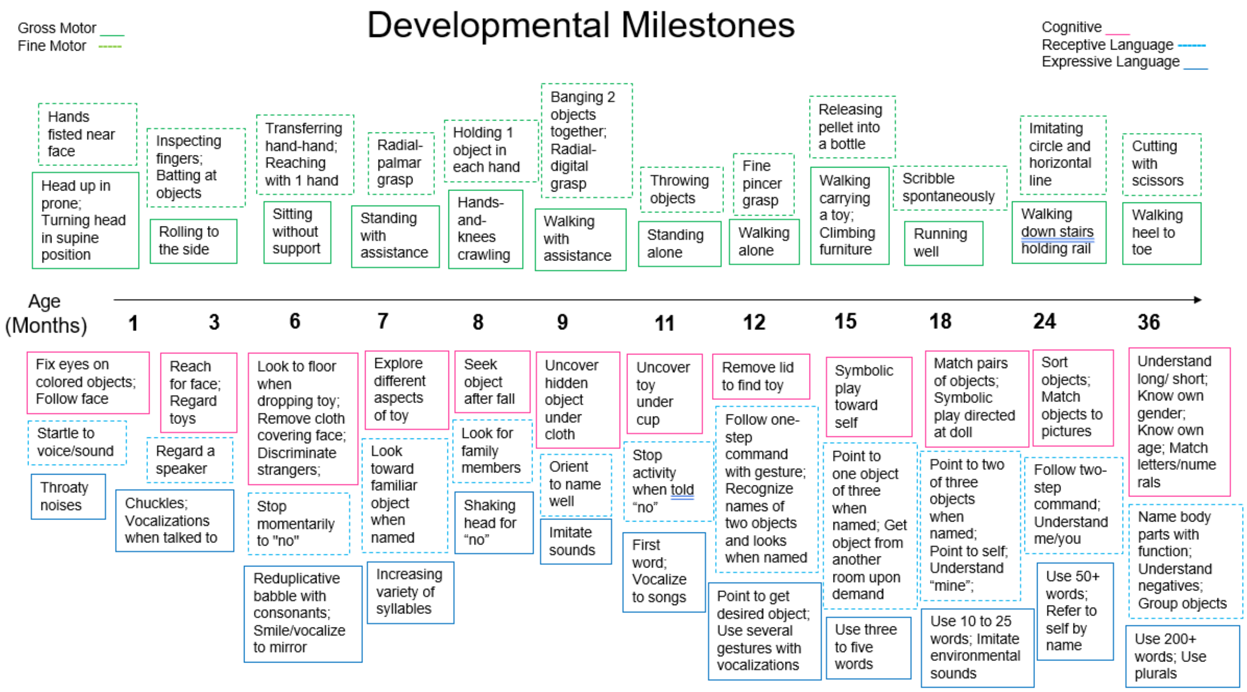
During the first years of life, infants and young children experience exponential growth in their cognitive function. Some of the important cognitive milestones during the first year of life include: look at black-white objects, fix eyes on colored objects, and follow face (~ 1 month); reach for face, observe objects in a circle, regard toys (~ 3 months); remove the cloth covering the face, touch reflection and vocalizes, bang and shake objects, look to the floor when drops a toy, and attain partially hidden object (~ 6 months); ring bell uncover hidden object, pull string to obtain ring (~ 9 months); rattle spoon in a cup and remove the lid to find toy (~ 12 months; Gerber et al., 2010; Johnson & Blasco, 1997). Toddlers can: match pairs of objects, engage in a symbolic play directed at doll (~ 18 months); deduce the location of hidden objects (~ 20 months); sort objects, match objects to pictures, show use of familiar objects (~ 24 months; Gerber et al., 2010; Johnson & Blasco, 1997). Young children: know their gender and age, match letter/numerals, understand long/short (~ 3 years); and understand simple analogies (e.g., ceiling/up; ice/cold), point up to six colors, letters and numerals (~ 4 years; Gerber et al., 2010; Johnson & Blasco, 1997). Those milestones include foundational skills relevant for later cognitive function and academic achievement.

Similarly, the language system undergoes considerable development during the first 4 years of life. Concerning receptive language during the first year of life infants: startle to voice/sound (~ 1 month); regard a speaker (~ 3 months); stop momentarily to "no," gestures for "up" (~ 6 months); enjoy gesture games, orients to the bell, orient to name (~ 9 months); and look when named (~ 12 months; Gerber et al., 2010). Toddlers can: point to 2 of 3 objects when named, points to self, understands "mine," points to familiar people when named (~ 18 months); and understands me/you, points to 5 to 10 pictures (~ 24 months; Gerber et al., 2010). Around 3 years, young children can: point to parts of images (e.g., nose, door), name body parts with function, group objects (e.g., toys, food), and understand negatives (Gerber et al., 2010).

Concerning expressive language, during the first year of life, infants exhibit: throaty noises (~ 1 month); chuckles, vocalizations when talked to (~ 3 months); listen then vocalize when adult stops; smile/vocalize to mirror, discriminate strangers (~ 6 months); imitate sounds, say "mama" (~ 9 months); use gestures with vocalizations and point to get desired object (~ 12 months). Toddlers can: imitate environmental sounds, use 10 to 25 words (~ 18 months); and refer to self by name (24 months; Gerber et al., 2010). Between 3 and 4 years, young children can: produce 3-word sentences, name body parts by use, ask to be read to, and use plurals (~ 3 years; Gerber et al., 2010). Please, see figure 2. The milestones for receptive and expressive language consist of essential skills for communication and interactions. These skills consequently influence other domains of development (e.g., social, emotional, and academic achievement).

Figure 2

Developmental milestones from 1 month to 36 months



Additional studies have examined how cognitive and language milestones influence social behavior and learning. For example, Flavell (1999) reviewed the evidence regarding cognitive milestones during the first two years of life; 5- to 8-week-old infants responded differently to people than objects because they expected them to behave differently. Specifically, infants would mimic mouth openings produced by people, but they would not mimic characteristics or similar-looking behaviors produced by an object. Additionally, infants (~ 12 months) expected a person to reach for an item they were looking for with positive affect, while older infants (~ 18 months) seemed to understand that if the experimenter reacted with happiness versus disgust towards food, the infant regarded that food with similar happiness, even if it was not the infant's preferred food (Flavell, 1999). Those findings are congruent with the expected cognitive milestones for this period for cognition and bring attention to the importance of socialization and interactions in this process.

Through experience and exploration of their surroundings, infants learn that each action has an effect (i.e., the concept of causality). The infants understand that varying an action will result in different/novel outcomes (Johnson & Blasco, 1997). This concept is crucial for social development because the infant learns to manipulate the environment, either by crying or smiling, to obtain the caregivers' desired reaction (Johnson & Blasco, 1997). According to Wellman and Gelman (1992), social interactions in infancy are first evident from 9 to 12 months, where the infants seem to understand the difference between self and others. These findings are in line with the cognitive and language milestones expected at those specific ages.

Two theories of cognitive development are essential in linking cognitive and motor development. The first was proposed by Vygotsky (1978) and states that cognition is influenced by culture, values, and beliefs transmitted to children through interaction with parents and peers. In this theory, language plays an essential role since caregivers/parents verbally teach the tools and strategies from their culture for thinking, adaptation, and problem-solving. The second was proposed by Piaget (1952), in which cognitive structures become more sophisticated with experience and interaction with the environment. This theory is based on the child’s capacity to adjust or adapt the existing knowledge to new situations, acquire new knowledge, and develop more complex or sophisticated thoughts. In both theories, infants and toddlers need to interact with other people and the environment to create opportunities to improve the development of not just cognitive, but other domains such as language and motor.

According to Piaget, cognitive development progresses across four different stages: sensorimotor, pre-operational, concrete operational, and formal operational. The first two stages take place during infancy and early childhood and are relevant to this study. The sensorimotor stage takes place during infancy (0-2 years of age) and is based on experiences and physical interactions with the environment. Knowledge is acquired through sensory experiences and the manipulation of objects. Object permanence, which is a foundational aspect of memory, is achieved around seven months, while language abilities are obtained by the end of this period. In addition, eye-hand coordination enables the infant to develop intellectual abilities (e.g., goal orientation and intentionality) around 8- to 12-months-of-age. The pre-operational stage takes place during toddlerhood and early childhood (from 2- to 7-years-of-age). In this stage, children are not able to mentally manipulate information nor understand concrete logic. This stage is divided into 2 other substages, the symbolic function substage (about 2- to 4-years-of-age) and the intuitive thought substage (about 4- to 7- years of age). During the symbolic function substage, children engage in pretend play or symbolic play (playhouse, role-play with friends, or develop imaginary friends), which reflects their level of creativity and ability to connect with other people. However, thinking in this stage is considered nonlogical, and it is more egocentric (e.g., concerning own body; Piaget, 1952). The intuitive thought substage is identified by the emergence of the interest in reasoning, where children start asking questions and begin using primitive reasoning (Piaget, 1952). Some of the characteristics of these two stages (sensorimotor and pre-operational) are considered cognitive milestones across infancy and early childhood and are evaluated using standardized assessments like the Bayley Scales of Infant Development (1969).

Current research has built upon Piaget's notion that physical interaction with the environment enables the development of different interacting systems. Indeed, cognitive and motor systems have been found to be interconnected and develop together (Diamond, 2000). For example, Thelen (2000) demonstrated that movement provides children with the opportunity to experience the environment around them, thereby increasing their attention to perceptual information, discrimination ability, and memory. Iverson (2010) argues that the acquisition of motor skills, such as crawling, standing, and walking during the first eighteen months of life allows children to explore the environment from different perspectives. These skills enable infants to manipulate toys and interact with people, providing opportunities for language acquisition and communicative development, among other developing systems. Furthermore, Goldin-Meadow (2014) demonstrated a developmental cascade in which parents' speech is not only related to the child's language skills but also the child's cognitive skills. Indeed, according to Meadows (2006), language is an auditory, cognitive, and motor skill. Hence, language development is integrated with social, cognitive, and motor skills/abilities. Blaga et al. (2009) investigated the interaction between cognitive and language skills in a large sample (n = 166 children); early cognitive function (measured by Bayley-II at 12 months) had a significant indirect effect on verbal and nonverbal scores at 48 months (Peabody Picture Vocabulary Test – Third Edition (PPVT-III), and Stanford-Binet Fourth Edition (SB4E)). The interdependence of problem-solving and language development becomes more prominent as the child begins to label objects and actions (Johnson & Blasco, 1997). Furthermore, according to Deak (2014), understanding language means understanding the development and recruitment of cognitive and learning processes, therefore, language processing might be understood as a form of cognition.

Despite the similarity in developmental processes and interaction amongst the motor, cognitive, and language domains, common assessments, like the Bayley Scales of Infant Development-II (BSID-II; 1969), typically split infant abilities into discrete domains (e.g., mental and motor scales). The mental domain of the BSID-II for example, consists of problem-solving and language tasks involving receptive and expressive language. The motor domain of the BSID-II is comprised of fine and gross tasks. Although the BSID-II distinguishes between language and cognitive function on one hand and fine and gross motor on the other, it is very likely that the developmental trajectories in both domains will be highly connected/correlated.

Evidence presented in this chapter has suggested that changes in cognition (and language processes) occur in parallel with structural changes in the brain and might be interrelated with motor abilities. There is a lack of studies examining the relationships among the development of those domains from birth to early childhood. Therefore, studies should address the developmental trajectories and relationship between brain structure and behavioral changes during infancy and toddlerhood.

3.1. Cognitive Development and SES

Many studies have examined the impact of SES and related factors on cognitive and language development. Hart & Risley (1995) found that on average children from low-income families exhibited smaller vocabularies at school entry than children from higher SES families. In a more recent longitudinal study, although Goldin-Meadow (2014) did not find a significant variation in vocabulary across SES, the impact of SES on child gesture was mediated by parent gesture and speech, and child gesture was related to later child vocabulary and cognitive skills. Congruent with these findings, Jeon et al. (2013) reported that parental supportiveness at 14 months old in infants at-risk for developmental delays due to poverty was positively related to cognitive development at 24 and 36 months. These studies suggest that SES may influence or reflect how parents and/or caregivers create environments that may hinder or enhance language and cognitive development through their interactions with their children.

One important limitation of the studies examining low-SES families is that the samples consisted of mostly African American and Hispanic families. Given that race and ethnicity influence culture, including parenting styles, the findings from these studies might not reflect the role of SES alone. Indeed, a mediation analysis focused on identifying risk factors for executive function skills in 36-month-old children (Rhoades et al., 2011) showed that the strongest predictor of poor executive function skills was exposure to poverty. Although SES can influence the child's overall development, the impact of each SES factor may play a different role when analyzed independently (e.g., income, parental education, and parental occupation), it also must be disambiguated from race and other relevant demographic factors that are part of SES.

In addition, poverty is associated with adverse environmental effects, such as material deprivation, malnutrition, toxic stressors, and environmental toxins. These may lead to structural and functional changes in the brain that impact many domains of child development, including cognitive, motor, and linguistic development (Johnson et al., 2016). In addition, differences in the stress response and the impact on development may be due to differences in children's experiences (Suor et al., 2015). Yet, the unique effects of parental stress have not been examined while parsing out the effects of SES.

Chapter Summary

Taken together, the studies presented in this chapter provide insights into the importance of investigating the developmental trajectories of and relationships between cognition, motor, and brain structure from birth to early childhood. Each section highlights the importance of considering the impacts of socioeconomic status-related variables and stress on the developmental trajectory of brain and behavior.

Chapter 3 – Developmental Trajectories of Brain Structure, Motor, and Cognitive Functions from Infancy to Early Childhood and the Impact of SES

Introduction

During the first years of life there are significant changes in the brain (Gilmore et al., 2007, 2012; Girault et al., 2020; Lyall et al., 2015; Knickmeyer et al., 2008), cognitive development (Gerber et al., 2010; Johnson & Blasco, 1997; Blaga et al., 2009), and motor development (Gerber et al., 2010; Johnson & Blasco, 1997; WHO Multicentre Growth Reference Study Group, 2006). Although studies have suggested a bidirectional relationship between the brain and these functional outcomes, few studies have directly examined their relationships. Moreover, environmental factors, including poverty, have profound impacts on structural changes in the brain (Johnson, Riis & Noble, 2016; Hanson et al., 2013; Jah et al., 2019) as well as development of motor (Clearfield, Stanger & Jenne, 2015; Fink, McCoy & Yousafzai, 2020; Black, Hess & Berenson-Howard, 2000) and cognitive skills (Rhoades et al., 2011; Suor et al., 2015; Blair et al., 2011) during childhood. However, there are knowledge gaps concerning the *longitudinal* relationships between brain, motor, and cognitive development *during the first few years of life*, as well as the influence of socioeconomic factors on these domains.

Growth of brain volume is driven mainly by changes in gray matter (GM) in the first year of life (Gilmore et al., 2012; Knickmeyer et al., 2008). Indeed, total GM volume increases by 149%, while white matter (WM) volume increases by only 11% (Knickmeyer et al., 2008). Furthermore, GM volume is a product cortical thickness (CT) and surface area (SA). Thus, rapid changes in these corresponding indices of structural brain development are also observed during the first years of life. From birth to 2 years of age, overall CT increases on average by 36.08% and is mainly driven by larger growth rates during the first year (Lyall et al., 2015). However, only a small number of studies have directly examined the relationships between brain structure and the development of motor and cognitive abilities from infancy to early childhood. Moreover, there is a knowledge gap regarding the continued development of the brain and behavior in early childhood and how early changes in brain development during infancy may lead to different long-term developmental trajectories in brain and behavioral development.

The development of gross and fine motor skills during infancy lay the foundation for future motor skill acquisition during early childhood. Indeed, 47% of the variance of gross motor skills at 3.5 years old is explained by early motor milestones such as sitting, upright posture, walking, reaching, and grasping (Viholainen et al., 2006). The acquisition of motor milestones during infancy may contribute to the substantial changes in cognitive development experienced during the first four years of life. Indeed, the acquisition of independent locomotion is associated with perceptual and cognitive development (Thelen, 2000; Adolph & Robinson, 2015). The neural mechanisms linking motor and cognitive development have been proposed (e.g., changes in the cerebral cortex and subcortical structures), however, there is a lack of studies investigating the contribution of brain development to the relationship between motor and cognitive development during the first few years of life.

Socioeconomic status (SES) and related variables impact brain (Johnson et al., 2016; Hanson et al., 2013; Jah et al., 2019, Hair et al., 2015; Noble et al., 2015), cognitive, and motor development (Fink, McCoy & Yousafzai, 2020; Black, Hess & Berenson-Howard, 2000). For example, household income is positively related to changes in brain growth in 1- to 4.5-year-olds; children from low-income households exhibit lower average total gray matter volume compared to their peers from higher income households (Hanson et al., 2013). Infants and young children from lower income families also show slower trajectories of brain growth (Hanson et al., 2013).

However, discrepant findings have been reported regarding the impact of socioeconomic factors on cognitive and motor development (Black, Hess & Berenson-Howard, 2000; Clearfield, Stanger & Jenne, 2015). It is possible that these discrepant results may be due to inconsistencies in the definitions of SES and related factors (e.g., low/high SES, household income, maternal education) as well as measurement of cognitive and motor development (e.g., parent report of milestones, measurement of task performance).

In addition to SES, research has shown that parental stress may negatively impact child development. Specifically, parental stress was found to be a predictor of children's maladaptive externalizing behaviors (Creasey & Jarvis, 1994; Bayer et al., 2008; Khoshkerdar, Baradaran, & Ranjbar Noushari, 2020), and maladaptive internalizing behaviors (Bayer et al., 2008). After accounting for demographic variables and SES (e.g., income and parental education), higher maternal parenting stress was associated with lower scores on cognitive and motor domains in 3 - 4-month-olds (Kim et al., 2016). However, there is an overall lack of studies that critically evaluate the impact of SES and higher levels of parental stress on both the brain and behavior during infancy and early childhood.

Therefore, the overarching purpose of this dissertation was to address these knowledge gaps by examining the developmental trajectories of brain structure, motor skills, and cognitive skills and their relationships from infancy to early childhood (e.g., birth – 2.5 years). In addition, this study examined the impact of socioeconomic status (i.e., household income) and parental stress on the development of each domain. Lastly, we determined if changes in brain structure mediate the impact of socioeconomic factors or parental stress on motor skills and cognitive skills during this period of development. To this end, a secondary data analysis was conducted to examine brain structure and behavioral performance data from the National Institute of Health

Study of Normal Brain Development – Object 2 (Almli et al., 2007) for children from birth to age 2.5 years.

Method

Database

The dataset was part of the NIH MRI Study of Normal Brain Development, which aimed to provide a large normative database of healthy infants' and children's brain and behavior for comparison with brain studies of children with developmental, psychiatric, and neurological disorders. Data were acquired between 2001 and 2007 from 6 sites across the United States. All participants were full term (i.e., greater than 37 weeks and 3 days), and the sample closely reflected the demographics distribution established by the United States Census (e.g., Census: 79.53% Caucasian, 18.25% African American, 1% Asian, .024% American Indian, and 1.03% Hispanic; Sample: 70% Caucasian, 14% African American, 4% Asian, 3% American Indian, and 9% Hispanic; Study Protocol; United States Census Bureau, 2000; Almli et al., 2007).

Data from Objective-2 are of interest to the present study and included children ranging from 10 days post-delivery until 4 years and 5 months of age (Study Protocol; Brain Development Cooperative Group, 2006. The data collection (scan + behavioral tests) targeted the following specific ages (and respective time windows): 3 months (0:3; 2 weeks); 6 and 9 months (0:6-0:9; 2 weeks); 12 and 15 months (0:12- 0:15; 2 weeks); 18, 24 and 30 months (0:18-0:24-0:30; 4 weeks); 36 months (0:36; 4 weeks); and 48 months (0:48; anytime between 48 months and 54 months; Procedure Manual Objective 2). The total number of participants collected for Objective 2 was 107.

Participants

The present analysis included a subset of participants from Objective-2 with complete data for the independent and dependent variables of interest. A total of 87 participants (38 females/49 males) met inclusion (see Figure 3). Table 1 presents the participant details for this sample for all variables of interest. The maternal race (provided via the demographics questionnaire) for the sample included: White (*n* = 76), African American (*n* = 6), and Asian (*n* = 5). The level of maternal and paternal education (provided via demographics questionnaire) was: Less than High School (0 maternal/2 paternal), High School Degree (83 maternal/81 paternal), College Degree (1 maternal/1 paternal), and Graduate Degree (3 maternal/2 paternal). The adjusted household income ranged between $2,101 and $135,401, with a median income of $66,225.

Figure 3

Flow Chart of the Participant Demographics

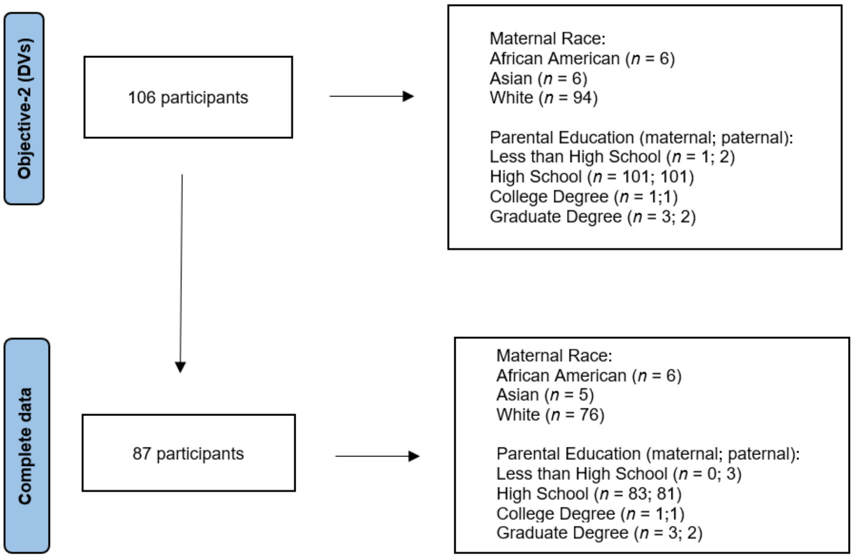


Table 1

Participant Details

	Number of Visits	Age (months)	Household Income	PSI	Total Cortical GM Volume (mm^3)	Average CT (mm)	BSID-II Mental Scale Raw Score	BSID-II Motor Scale Raw Score
Median	2	15.0	$66,225	187.5	364,612	2.2	97.0	68.0
Minimum	1	2.6	$2,101	126.0	217,066	1.8	26.0	18.0
Maximum	7	31.2	$135,401	258.0	523,601	2.4	154.0	97.0

Assessments

Bayley Scales of Infant Development – II (BSID-II). This assessment evaluates children between 1 month and 42 months of age and consists of three scales: Mental (178 items), Motor (111 items), and Behavior Rating (30 items rated by a 5-point scale). The administration time is 30-90 minutes, depending on the age of the child (Bayley, 1993). For the present study, the raw scores for the Mental and Motor Scale Scores were analyzed. The Mental Scale Score includes abilities such as: memory, learning and problem-solving, sensory/perception acuities, acquisition of object constancy, vocalization, beginning of verbal communication, habituation, mental mapping; etc. The Motor Scale Score includes abilities such as: fine motor skills, body control, coordination, etc. (Bayley, 1993; Black & Matula, 2000; Study Protocol). Test-retest reliability coefficients are reported as ICC = .87 for the Mental Scale Score and ICC = .78 for the Motor Scale Score (Study Protocol).

Parenting Stress Index (PSI). This self-report parent questionnaire is appropriate for children between 1 month and 10 years of age. The PSI has 120 items (19 optional items), with each question rated on a 5-point Likert-scale (e.g., Strongly Agree, Agree, Not Sure, Disagree, and Strongly Disagree). The assessment can be completed in 30 minutes. The PSI is divided in Child Domain scores (adaptability, mood, reinforces parent, distractibility/hyperactivity, demandingness, and acceptability), Parent Domain scores (spouse, role restriction, depression, attachment, isolation, competence, and health), Total Stress Score. A Total Score between the

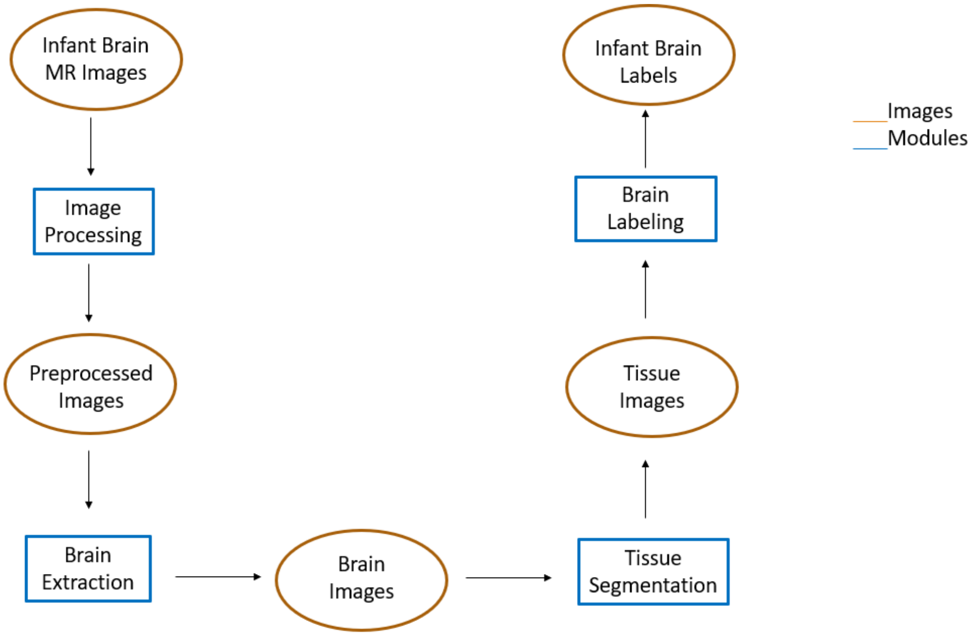
15th and 80th percentile is considered within the normal range (Abidin, 1995; Study Protocol). For the present study, the Total Stress Score was examined. Test-retest reliability for PSI (total scores) was reported as $\alpha = .96$ and internal reliability as $\alpha = .95$; and validity was reported as 0.90 (Abidin, 1995).

MRI. The MRI scans lasted around 30–45 minutes on a 1.5 Tesla (T) scanner with a 2D sequence that minimized scan duration. Infants were scanned during natural sleep without sedation. The axial scans consisted of a 2D T1-weighted spin echo and a T2-weighted 2D Fast Turbo spin echo sequence. MRI scans were acquired using 2 different scanners - General Electric scanner (Signa Excite) in Boston and a Siemens Medical Systems scanner (Sonata, Magnetom) in St. Louis; the scans from St. Louis provided the majority of the data for Objective-2 ($n = 60$; Brain Development Cooperative Group, 2006; Almli et al., 2007; Sanchez et al., 2012).

MRI data were processed at the University of North Carolina, Chapel Hill in the Neurocognition and Imaging Research Lab. The data processing pipeline was conducted in the Infant Brain Extraction and Analysis Toolbox (iBEAT; Dai et al., 2013) software, and includes the following steps: image quality analysis, longitudinal data registration, linear and non-linear registration of images to a standard infant template, image intensity corrections, tissue classification, segmentation of cortical and subcortical regions, segmentation of cortical mantle, and extraction of Total Cortical GM and Average CT (see figure 4; Dai et al., 2013). Additional details about the data processing pipeline are provided in Li et al. (2013; 2016), Wang et al. (2014), and Dai et al., 2013

Figure 4

MRI Data Processing Pipeline (Dai et al., 2013)



Statistical Approach

All analyses were conducted using R-Studio (version 1.4.1717) and R (version 4.1.1). Prior to the statistical analyses, all data were screened using Excel (version 2018) to remove errors/inconsistencies in parent reported data or data entry. Due to differences in the number and time interval between repeated measures, linear mixed effects regressions (LMER) using the "lme4", "nlme", "lmerTest", "AICcmodavg" packages were conducted to examine the specific aims and hypotheses below. A random intercept was modeled for each participant. The best fit model was determined based on a significant difference in the model fit statistics by maximum likelihood (i.e., reduction in Akaike Information Criterion (AIC) or Bayesian Information Criterion (BIC)) using a threshold of $p < .05$. Each random and fixed effect were added iteratively using the likelihood ratio test performed by the analysis of variance to compare models, and the most parsimonious and best fit model was selected. If there was concern regarding collinearity (based on correlations amongst factors), fixed effects were mean centered.

Specific Aim 1: To examine the relationships between brain, cognitive, and motor development from birth to 2.5 years.

H1 - Greater Total Cortical GM Volume and Average CT will be associated with better performance on the Bayley Scales of Infant Development-II (BSID-II Mental and Motor Scale Score), after accounting for age and sex.

The following equation will address this hypothesis:

$$\text{Equation 1: } Y_{ij} = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \gamma_i + \varepsilon_{ij}$$

where:

Y_{ij} observed BSID Mental or Motor Scale scores for individual i at time j

β_0, β_1, β_2, and β_3, regression coefficients

X_1, X_2, and X_3, age, sex, and Total Cortical GM Volume

γ_i is the random intercept for subject i, with $\gamma_i \sim N(0, \sigma_r^2)$

ε_{ij} residuals, with $\varepsilon_{ij} \sim N(0, \sigma^2)$, ε_{ij} and ε_{il} are independent

In this equation β_0 is the intercept parameter. β_1, β_2, and β_3 are the slope parameters for age, sex, and Total Cortical GM Volume, respectively. Interactions among fixed effects will also be modelled.

To address the relationship between BSID Motor/Mental and Average CT, Equation 1 will be used. Y_{ij} will represent BSID Mental/Motor, β_3 the slope parameter for Average CT, and X_3 will represent Average CT.

Note: The best-fit model for the developmental trajectory will be determined by modelling age as linear, squared, and cubic terms, consistent with the literature examining infant development (Haywood & Getchell, 2020; Ducharme et al., 2016). Interactions between these terms and sex will also be modelled. Total Cortical GM Volume or Average CT will be added to the best fit developmental trajectory. GM and CT will be modeled separately since each parameter may provide different insights into cortical growth. Although GM is a product of CT and SA, the relationship between behavior and those parameters might differ, as the literature suggests.

> H2 – Cognitive development (BSID-II Mental Scale Score) will be positively associated with motor development (BSID-II Motor Scale Score), after accounting for age and sex.

To address the relationship between BSID Mental Scale Score and BSID Motor Scale Score, Equation 1 will be used. Y_{ij} will represent BSID Mental Scale, β_3 the slope parameter for BSID Motor Scale, and X_3 will represent BSID Motor Scale.

Specific Aim 2: To determine the effect of SES (Adjusted Household Income) and PSI on brain, cognitive, and motor functions.

> H3 - Adjusted Household Income will be positively associated with Total Cortical GM Volume, Average CT, and BSID-II Mental and Motor Scale Scores, after controlling for Age and Sex.

To address the relationship between the dependent variables (Total Cortical GM Volume, Average CT, BSID Mental and Motor Scales) and Adjusted Household Income, Equation 1 will be used for each variable. Y_{ij} will represent each dependent variable, β_3 the slope parameter for Adjusted Household Income, and X_3 will represent Adjusted Household Income.

> H4 - Parental stress (PSI scores) will be negatively associated with Total Cortical GM Volume, Average CT, and BSID-II Mental and Motor Scale Scores, after controlling for age and sex.

To address the relationship between the dependent variables (Total Cortical GM Volume, Average CT, BSID Mental and Motor Scales) and PSI, Equation 1 will be used for each variable.

Y_{ij} will represent each dependent variable, β_3 the slope parameter for PSI, and X_3 will represent PSI scores.

Specific Aim 3: To determine if changes in the brain mediate the relationship between SES and parental stress in motor and cognitive development.

H5 - The positive relationship between SES (Adjusted Household Income) and BSID-II (Mental and Motor Scale Scores) will be mediated by Total Cortical GM Volume and Average CT.

H5a: Income and BSID-II Mental mediated by Total Cortical GM Volume:

To address this hypothesis, Equation 1 will be used. Y_{ij} will represent BSID Mental Scale, β_3 the slope parameter for Adjusted Household Income, and X_3 will represent Adjusted Household Income. In addition, the following equation will be used:

$$\text{Equation 2: } Y_{ij} = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_4 X_4 + \gamma_i + \varepsilon_{ij}$$

Where:

Y_{ij}, observed BSID Mental Scale scores for individual i at time j

X_1, X_2, X_3, X_4, age, sex, Adjusted Household Income, Total Cortical GM Volume

H5b: Income and BSID-II Motor mediated by Total Cortical GM Volume:

To address this hypothesis, Equation 1 will be used. Y_{ij} will represent BSID Motor Scale, β_3 the slope parameter for Adjusted Household Income, and X_3 will represent Adjusted Household Income. In addition, the following equation will be used:

$$\text{Equation 2: } Y_{ij} = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_4 X_4 + \gamma_i + \varepsilon_{ij}$$

Where:

Y_{ij}, observed BSID Motor Scale scores for individual i at time j

X_1, X_2, X_3, X_4, age, sex, Adjusted Household Income, Total Cortical GM Volume

H5c: Income and BSID-II Mental mediated by Average CT:

To address this hypothesis, Equation 1 will be used. Y_{ij} will represent BSID Mental Scale, β_3 the slope parameter for Adjusted Household Income, and X_3 will represent Adjusted Household Income. In addition, the following equation will be used:

Equation 2: $Y_{ij} = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_4 X_4 + \gamma_i + \varepsilon_{ij}$

Where:

Y_{ij}, observed BSID Mental Scale scores for individual i at time j

X_1, X_2, X_3, X_4, age, sex, Adjusted Household Income, Average CT

H5d: Income and BSID-II Motor mediated by overall Average CT:

To address this hypothesis, Equation 1 will be used. Y_{ij} will represent BSID Motor Scale, β_3 the slope parameter for Adjusted Household Income, and X_3 will represent Adjusted Household Income. In addition, the following equation will be used:

Equation 2: $Y_{ij} = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_4 X_4 + \gamma_i + \varepsilon_{ij}$

Where:

Y_{ij}, observed BSID Mental Scale scores for individual i at time j

X_1, X_2, X_3, X_4, age, sex, Adjusted Household Income, Average CT

H6 - The negative relationship between parent stress and BSID-II (Mental and Motor Scale Scores) will be mediated by Total Cortical GM Volume and overall Average CT.

H6a: PSI and BSID-II Mental mediated by Total Cortical GM Volume:

To address this hypothesis, Equation 1 will be used. Y_{ij} will represent BSID Mental Scale, β_3 the slope parameter for PSI, and X_3 will represent PSI scores. In addition, the following equation will be used:

$$\text{Equation 2: } Y_{ij} = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_4 X_4 + \gamma_i + \varepsilon_{ij}$$

Where:

Y_{ij}, observed BSID Mental Scale scores for individual i at time j

X_1, X_2, X_3, X_4, age, sex, PSI, Total Cortical GM Volume

H6b: For PSI and BSID-II Motor mediated by Total Cortical GM Volume:

To address this hypothesis, Equation 1 will be used. Y_{ij} will represent BSID Motor Scale, β_3 the slope parameter for PSI, and X_3 will represent PSI scores. In addition, the following equation will be used:

$$\text{Equation 2: } Y_{ij} = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_4 X_4 + \gamma_i + \varepsilon_{ij}$$

Where:

Y_{ij}, observed BSID Motor Scale scores for individual i at time j

X_1, X_2, X_3, X_4, age, sex, PSI, Total Cortical GM Volume

H6c: PSI and BSID-II Mental mediated by overall Average CT:

To address this hypothesis, Equation 1 will be used. Y_{ij} will represent BSID Mental Scale, β_3 the slope parameter for PSI, and X_3 will represent PSI scores. In addition, the following equation will be used:

$$\text{Equation 2: } Y_{ij} = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_4 X_4 + \gamma_i + \varepsilon_{ij}$$

Where:

Y_{ij}, observed BSID Mental Scale scores for individual i at time j

X_1, X_2, X_3, X_4, age, sex, PSI, Average CT

H6d: PSI and BSID-II Motor mediated by overall Average CT:

To address this hypothesis, Equation 1 will be used. Y_{ij} will represent BSID Motor Scale, β_3 the slope parameter for PSI, and X_3 will represent PSI scores. In addition, the following equation will be used:

Equation 2: $Y_{ij} = \beta_0 + \beta_1X_1 + \beta_2X_2 + \beta_3X_3 + \beta_4X_4 + \gamma_i + \varepsilon_{ij}$

Where:

Y_{ij}, observed BSID Motor Scale scores for individual i at time j

X_1, X_2, X_3, X_4, age, sex, PSI, Average CT

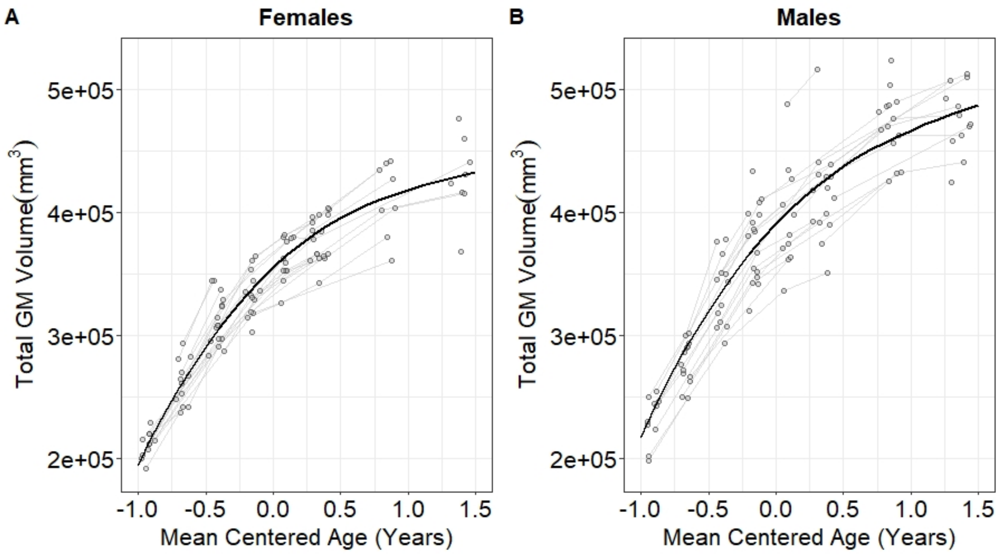
Results

The assumptions for the LMER were checked via inspection of the residuals (homogeneity of variance and normality); there was no indication that these assumptions were violated (see Appendix A)**.** In addition, we conducted a sensitivity analysis for each hypothesis to identify the effect size required to observe as statistically significant result with 70% power (see Appendix B).

Figure 5 presents the Total Cortical GM Volume by age and sex. The best fit model is overlaid. The final model for Total Cortical GM Volume included a random intercept. Mean Centered Age was modeled as linear ($F(1,128) = 1275.554$, $p < .001$), squared ($F(1,121) = 393.675$, $p < .001$), and cubic terms ($F(1,124) = 13.482$, $p < .001$). There was a main effect of sex ($F(1,84) = 36,574$, $p < .001$), and an interaction between Sex and the Mean Centered linear Age ($F(1, 143) = 16.352$, $p < .001$).

Figure 5

Total Cortical GM Volume for Females (A) and Males (B) as a Function of Mean Centered Age

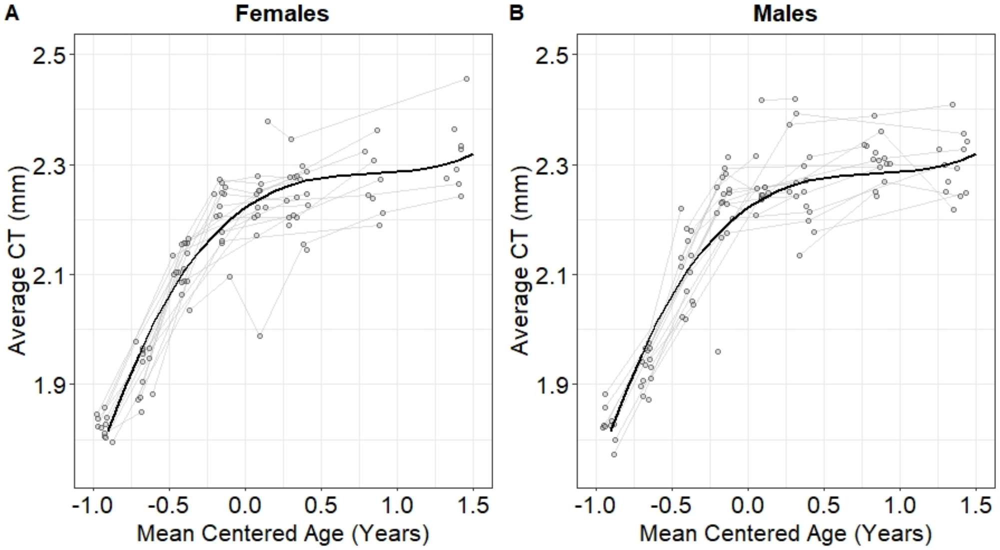


Note. The predicted developmental trajectories are depicted in a solid thick line by the following equations: Predicted Total Cortical GM Volume (Females) = 355284.89 + 101516.11*Mean Centered Age - 48759.72* Mean Centered Age^2 + 10303.76* Mean Centered Age^3; predicted Total Cortical GM Volume (Males) = 355284.89 + 101516.11* Mean Centered Age - 48759.72* Mean Centered Age^2 + 10303.76* Mean Centered Age^3 + 35516.17 + 12768.44* Mean Centered Age. Each participant's data are depicted by small circles connected with a gray line connecting repeated measures.

Figure 6 presents the Average CT by age and sex. The best fit model is overlaid. The final model for Average CT included a random intercept. Mean Centered Age was modeled as a linear ($F(1,169) = 231.251$, $p < .001$), squared ($F(1,150) = 395.890$, $p < .001$), and cubic term ($F(1,153) = 49.631$, $p < .001$). There was no significant main effect or interactions with Sex, therefore Sex was removed from the model.

Figure 6

Average CT for Females (A) and Males (B) as a Function of Mean Centered Age

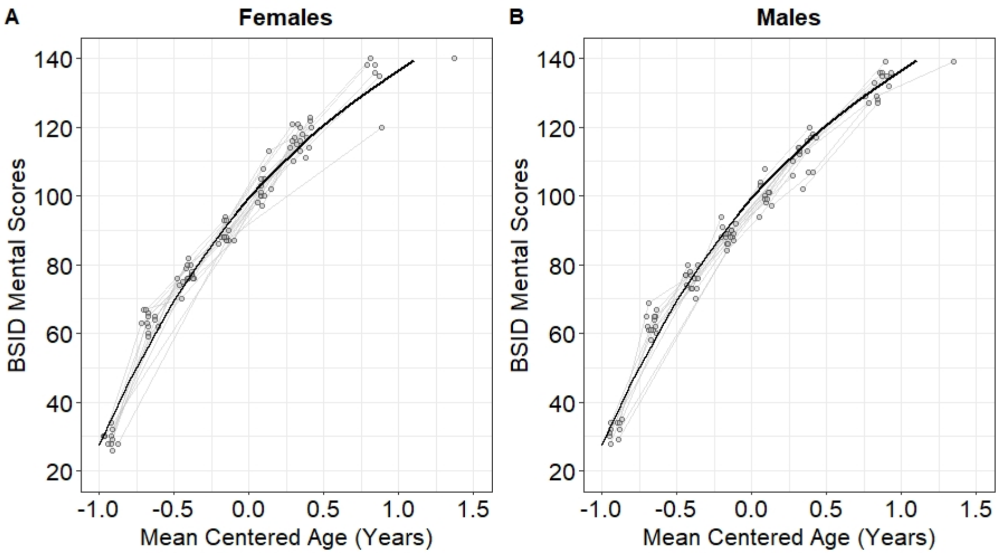


Note. The estimated developmental trajectories are depicted in a solid thick line by the following equation: Predicted Average CT = 2.221600 + 0.191795*Mean Centered Age - 0.211897 * Mean Centered Age^2 + 0.084979 * Mean Centered Age^3. Each participant's data are depicted by small circles connected with a gray line across repeated measures.

Figure 7 presents the BSID-II Mental Scale Score by age and sex. The best fit model is overlaid. The final model for BSID-II Mental Scale Score included a random intercept. Mean Centered Age was modeled as a linear ($F(1, 189) = 1850.800$, $p < .001$), squared ($F(1, 169) = 289.921$, $p < .001$) and cubic term ($F(1, 166) = 15.226$, $p < .001$). There was no significant main effect or interactions with Sex, therefore Sex was removed from the model.

Figure 7

BSID-II Mental Scale Score Raw Scores for Females (A) and Males (B) as a Function of Mean Centered Age

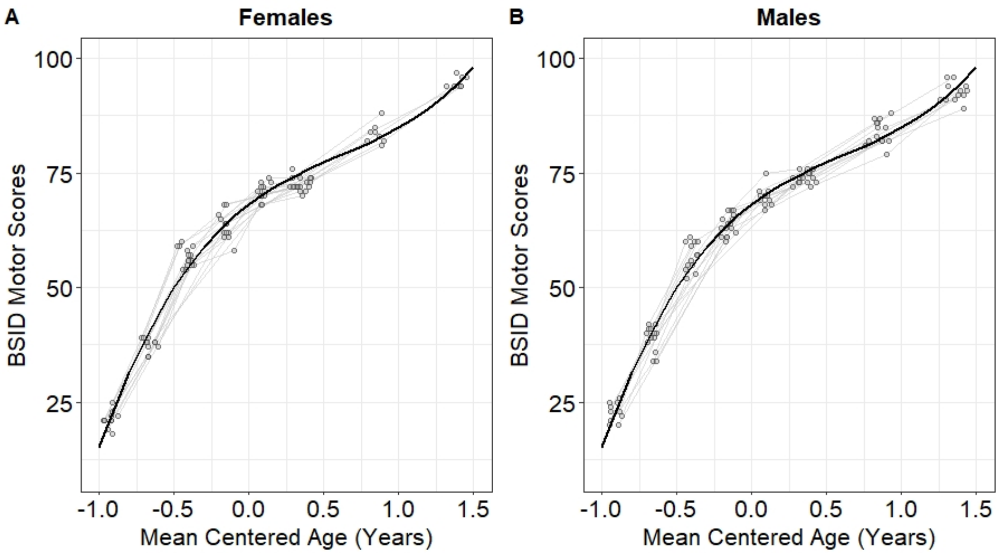


Note. The estimated developmental trajectories are depicted in a solid thick line by the following equation: Predicted BSID-II Mental Scale Score = 99.3288 + 50.0572*Mean Centered Age - 17.2805* Mean Centered Age^2 + 4.4817* Mean Centered Age^3. Each participant's data are depicted by small circles connected with a gray line across repeated measures.

Figure 8 presents the BSID-II Motor Scale Score by age and sex. The best fit model is overlaid. Similar to the model for BSID-II Mental Scale Score, the final model for BSID-II Motor Scale Score included a random intercept. Mean Centered Age was modeled as a linear ($F(1, 190) = 1364.32$, $p < .001$), squared ($F(1, 174) = 980.44$, $p < .001$) and cubic term ($F(1, 174) = 230.39$, $p < .001$). There was no significant main effect or interactions with Sex, therefore Sex was removed from the model.

Figure 8

BSID-II Motor Scale Score Raw Scores for Females (A) and Males (B) as a Function of Mean Centered Age

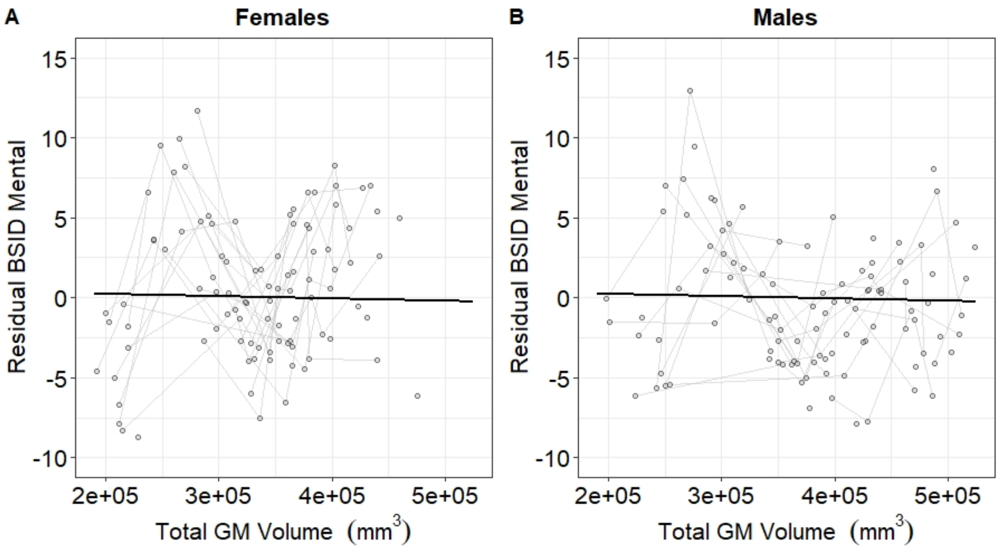


Note. The estimated developmental trajectories are depicted in a solid thick line by the following equation: Predicted BSID-II Motor Scale Score = 68.2205 + 24.8718*Mean Centered Age - 18.2781* Mean Centered Age^2 + 10.0226* Mean Centered Age^3. Each participant's data are depicted by small circles connected with a gray line across repeated measures.

To address Hypothesis 1, Total Cortical GM Volume was added as a fixed effect to the best fit model for the BSID-II Motor and Mental Scale Scores to determine its effect on these domains after accounting for age and sex. Contrary to what was expected, there was no significant effect of Total Cortical GM Volume for Mental ($F(1, 86) = 1.042$, $p = .310$) or Motor Scale Scores ($F(1, 113) = .421$, $p = .518$). Figures 9 and 10 depict the residual BSID-II Mental and Motor Scale Scores, respectively, as a function of Total Cortical GM Volume for males and females with the best fit regression line overlaid.

Figure 9

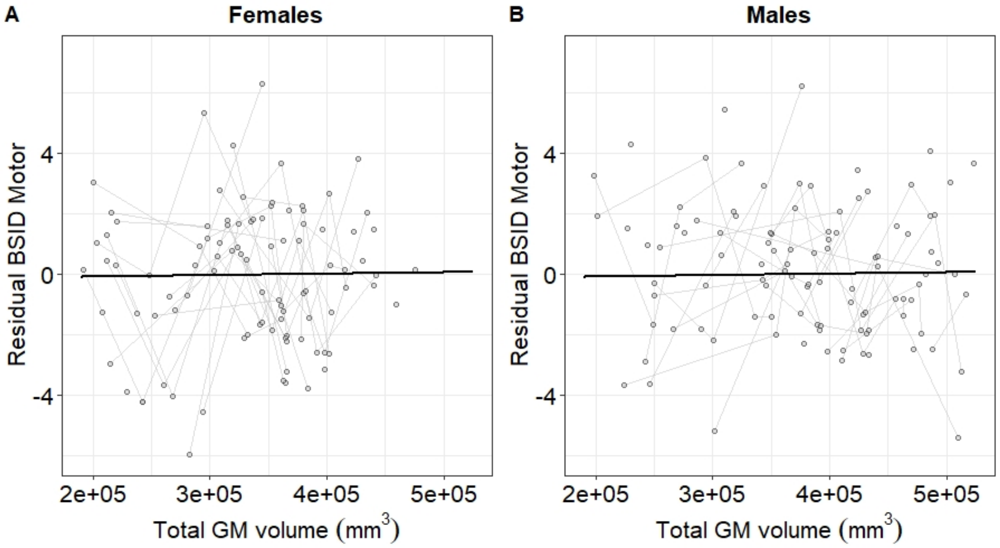
Residual BSID-II Mental Scale Score for Females (A) and Males (B) as a Function of Total Cortical GM Volume After Controlling for Mean Centered Age and Sex



Note. The estimated residual BSID-II Mental Scale Score is depicted in a solid thick line by the following equation: Predicted residual BSID-II Mental Scale Score = 0.5134 – 0.000001443*Total Cortical GM Volume. Each participant's data are depicted by small circles connected with a gray line across repeated measures.

Figure 10

Residual BSID-II Motor Scale Score for Females (A) and Males (B) as a Function of Total Cortical GM Volume After Controlling for Mean Centered Age and Sex

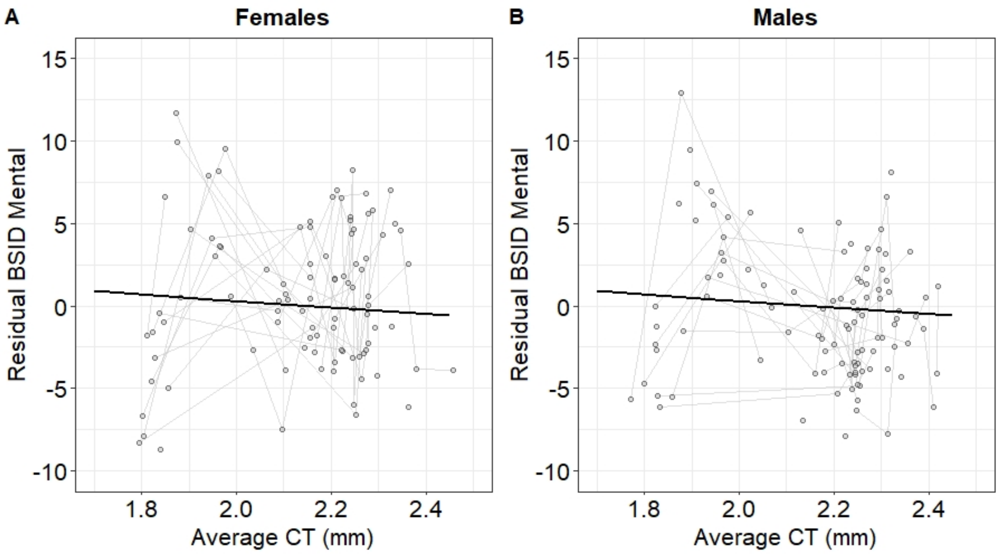


Note. The estimated residual BSID-II Motor Scale Score is depicted in a solid thick line by the following equation: Predicted residual BSID-II Motor Scale Score = - 0.1708 + 0.0000004802*Total Cortical GM Volume. Each participant's data are depicted by small circles connected with a gray line across repeated measures.

In addition, Averaged CT was added as a fixed effect to the best fit model for the BSID-II Mental and Motor Scale Scores to determine its effect on these domains after accounting for age and sex. Consistent with our hypothesis, Average CT was a significant predictor of BSID-II Mental ($F(1, 166) = 10.378$, $p = .002$), and Motor Scale Scores ($F(1, 180) = 8.897$, $p = .003$). However, the direction of the relationship differed by domain; for the BSID-II Mental Scale Score there was a negative relationship with Average CT, with thicker cortices associated with lower BSID Mental scores, and for the Motor Scale Score there was a positive relationship with Average CT, with thicker cortices associated with greater BSID Motor scores. Figures 11 and 12 depict the residual BSID-II Mental and Motor Scale Scores, respectively, as a function of Average CT for males and females with the best fit regression line overlaid.

Figure 11

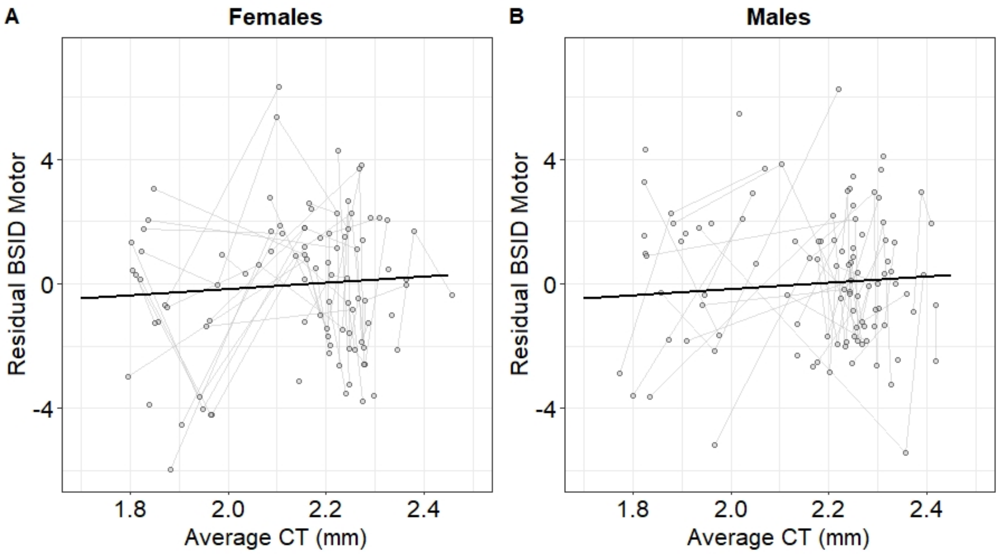
Residual BSID-II Mental Scale Score for Females (A) and Males (B) as a Function of Average CT After Controlling for Mean Centered Age and Sex



Note. The estimated residual BSID-II Mental Scale Score is depicted in a solid thick line by the following equation: Predicted residual BSID-II Mental Scale Score = 4.226 - 1.964 *Average CT. Each participant's data are depicted by small circles connected with a gray line across repeated measures.

Figure 12

Residual BSID-II Motor for Females (A) and Males (B) as a Function of Average CT After Controlling for Mean Centered Age and Sex

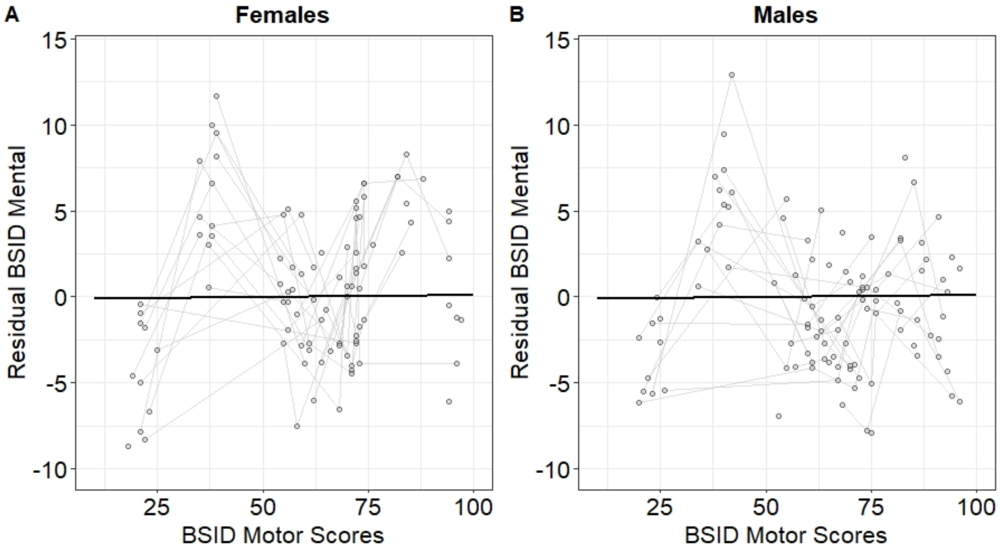


Note. The estimated residual BSID-II motor is depicted in a solid thick line by the following equation: Predicted residual BSID-II motor = - 2.1303 + 0.9901*Average CT. Each participant's data are depicted by small circles connected with a gray line across repeated measures.

To address Hypothesis 2, BSID-II Motor Scale Score Raw Score was added as a fixed effect to the best fit model for the BSID-II Mental Scale Score Raw Score to determine the relationship between motor and cognitive development after accounting for age and sex. Contrary to our hypothesis, the BSID-II Motor Scale Score was not a significant predictor of BSID-II Mental Scale Score ($F(1, 197) = 1.324$, $p = .251$). Figure 13 depicts the residual BSID-II Mental Scale Score as a function of BSID-II Motor Scale Score for males and females with the best fit regression line overlaid.

Figure 13

Residual BSID-II Mental for Females (A) and Males (B) as a Function of BSID-II Motor After Controlling for Mean Centered Age and Sex



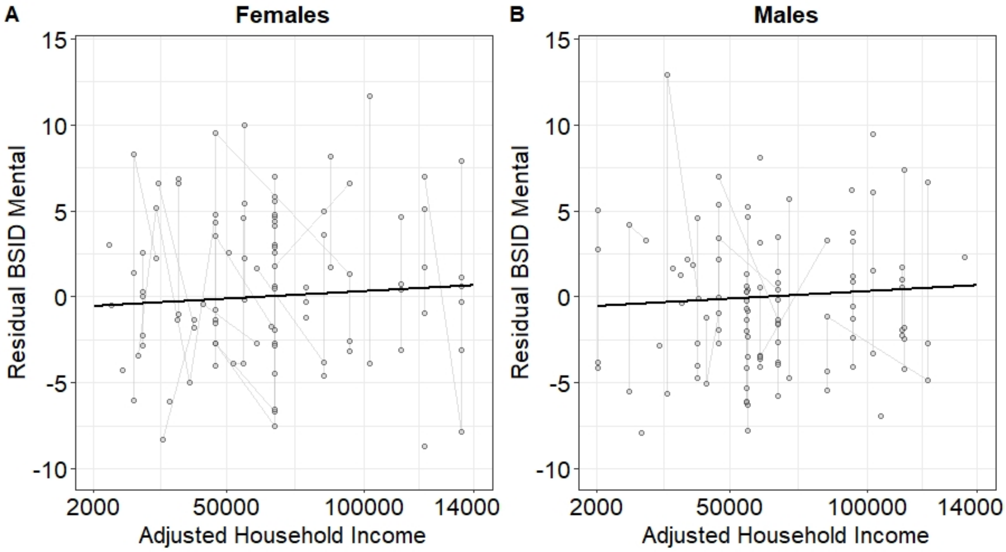
Note. The estimated residual BSID-II Mental Scale Score is depicted in a solid thick line by the following equation: Predicted residual BSID-II Mental Scale Score = - 0.145617 +

0.002326*BSID-II Motor. Each participant's data are depicted by small circles connected with a gray line across repeated measures.

To address Hypothesis 3, Adjusted Household Income was added as a fixed effect to the best fit model for each dependent variable to determine its effect on the development of each domain after accounting for age and sex. Contrary to our hypothesis, Adjusted Household Income was not a significant predictor of BSID-II Mental Scale Score (*F*(1, 67) = 1.107, *p* = .296; Figure 14), BSID-II Motor Scale Score (*F*(1, 91) = 1.772, *p* = .186; Figure 15), and Average CT (*F*(1, 110) = .826, *p* = .365; Figure 16). However, Adjusted Household Income was a significant predictor for Total GM Volume (*F*(1, 175) = 8.589, *p* = .004; Figure 17); there was a positive relationship between Adjusted Household Income and Total Cortical GM Volume after accounting for age and sex.

Figure 14

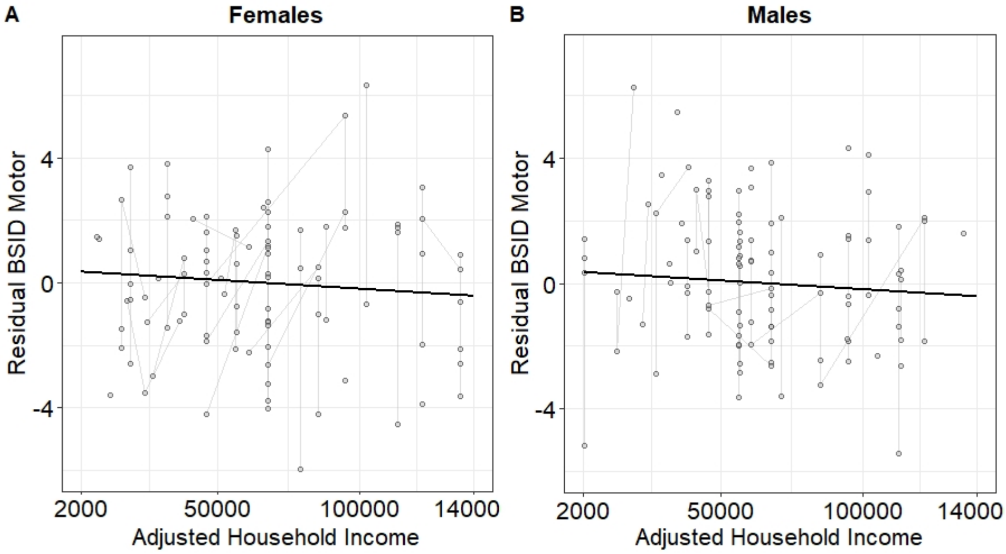
Residual BSID-II Mental Scale Score for Females (A) and Males (B) as a Function of Adjusted Household Income After Controlling for Mean Centered Age and Sex



Note. The estimated residual BSID-II Mental Scale Score is depicted in a solid thick line by the following equation: Predicted residual BSID-II Mental Scale Score = - 0.5676 + 0.000008756*Adjusted Household Income. Each participant's data are depicted by small circles connected with a gray line across repeated measures.

Figure 15

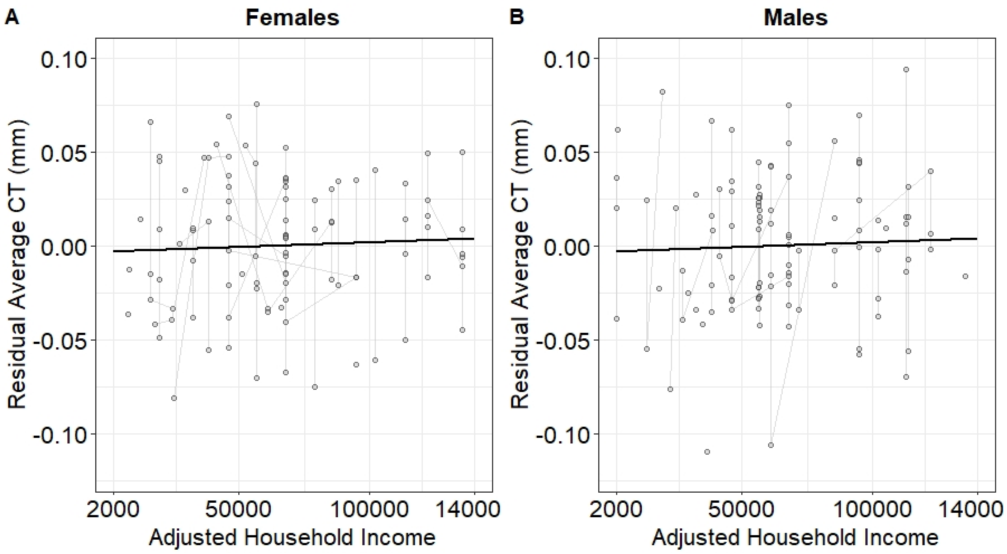
Residual BSID-II Motor Scale Score for Females (A) and Males (B) as a Function of Adjusted Household Income After Controlling for Mean Centered Age and Sex



Note. The estimated residual BSID-II Motor Scale Score is depicted in a solid thick line by the following equation: Predicted residual BSID-II Motor Scale Score = 0.3620 – 0.000005585 *Adjusted Household Income. Each participant's data are depicted by small circles connected with a gray line across repeated measures.

Figure 16

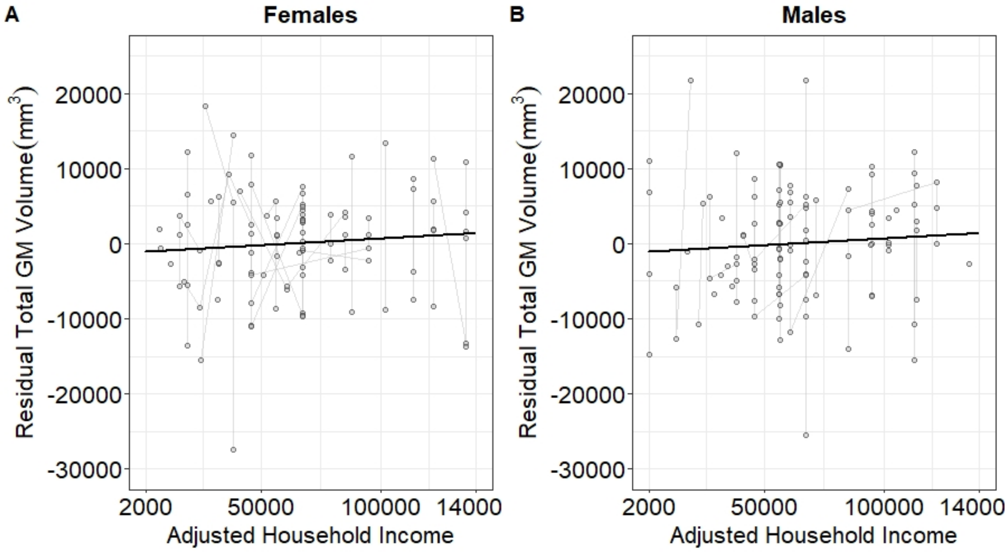
Residual Averaged CT for Females (A) and Males (B) as a Function of Adjusted Household Income After Controlling for Mean Centered Age and Sex



Note. The estimated residual Average CT is depicted in a solid thick line by the following equation: Predicted residual Average CT = - 0.003237 + 0.00000004994*Adjusted Household Income. Each participant's data are depicted by small circles connected with a gray line across repeated measures.

Figure 17

Residual Total Cortical GM Volume for Females (A) and Males (B) as a Function of Adjusted Household Income After Controlling for Mean Centered Age and Sex

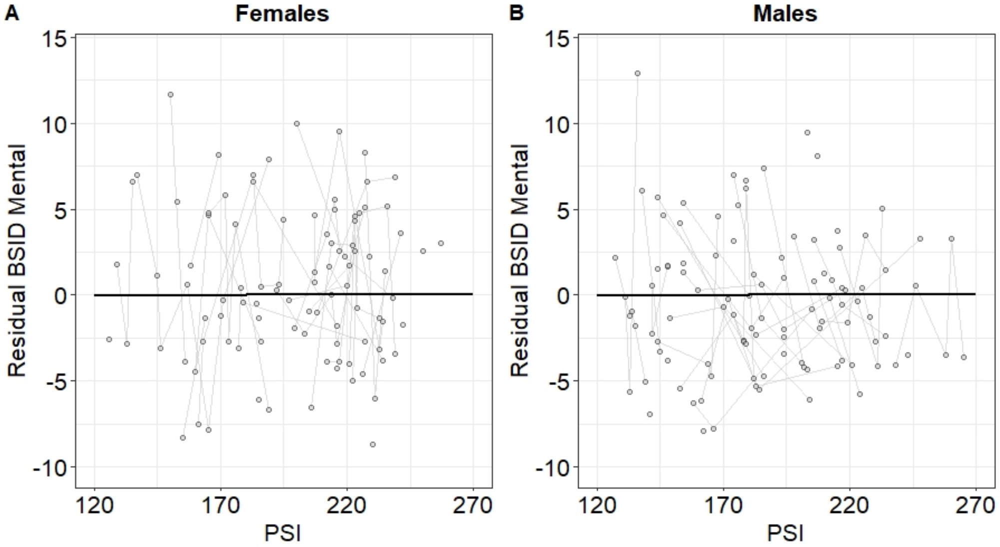


Note. The estimated residual Total Cortical GM Volume is depicted in a solid thick line by the following equation: Predicted residual Total Cortical GM Volume = - 1168 + 0.01802*Adjusted Household Income. Each participant's data are depicted by small circles connected with a gray line across repeated measures.

To address Hypothesis 4, Parental Stress Index (PSI) was added as a fixed effect to the best fit model for each dependent variable to determine its effect on the development of each domain after accounting for age and sex. Contrary to our hypothesis, PSI was not a significant predictor of BSID-II Mental Scale Score ($F(1, 89) = .002$, $p = .967$; Figure 18) or BSID-II Motor Scale Score ($F(1, 123) = .104$, $p = .748$; Figure 19). However, for Average CT there was a significant interaction between PSI and the linear term of Mean Centered Age ($F(1, 176) = 7.526$, $p = .007$; Figure 20); a positive relationship between PSI and CT was observed for younger children whereas a negative relationship between PSI and CT was observed for older children. Similarly, for Total Cortical GM Volume, there was a significant interaction between PSI and the linear term of Mean Centered Age ($F(1, 130) = 4.934$, $p = .028$; Figure 21), as well as an interaction between PSI and Sex ($F(1, 177) = 10.396$, $p = .002$); a positive relationship between PSI and Total Cortical GM Volume was observed for younger children whereas a negative relationship was observed for older children. Further, males do not show evidence of a relationship between PSI and GM, whereas females show a negative relationship between those variables

Figure 18

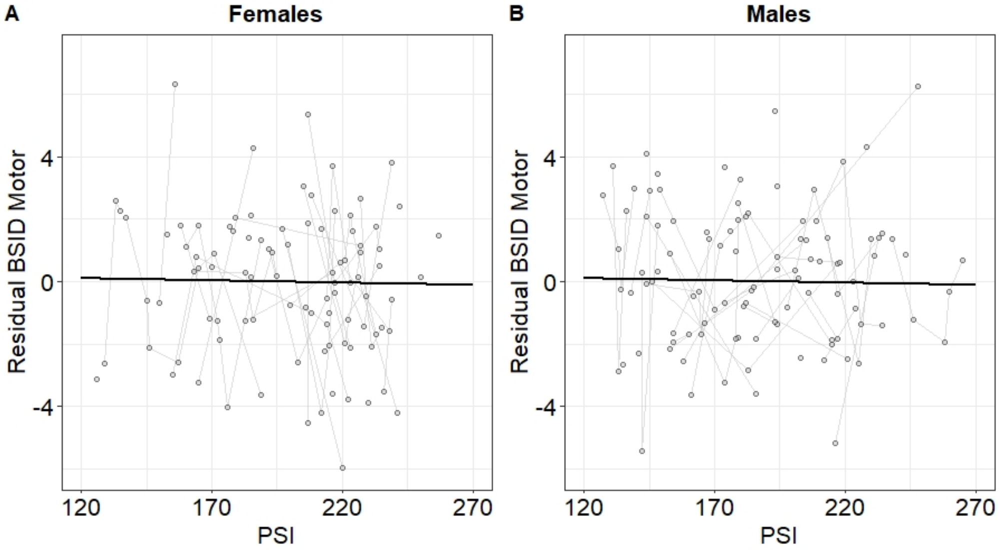
Residual BSID-II Mental for Females (A) and Males (B) as a Function of Parental Stress Index After Controlling for Mean Centered Age and Sex



Note. The estimated residual BSID-II Mental Scale Score is depicted in a solid thick line by the following equation: Predicted residual BSID-II Mental Scale Score = - 0.0653928 + 0.0003401*PSI. Each participant's data are depicted by small circles connected with a gray line across repeated measures.

Figure 19

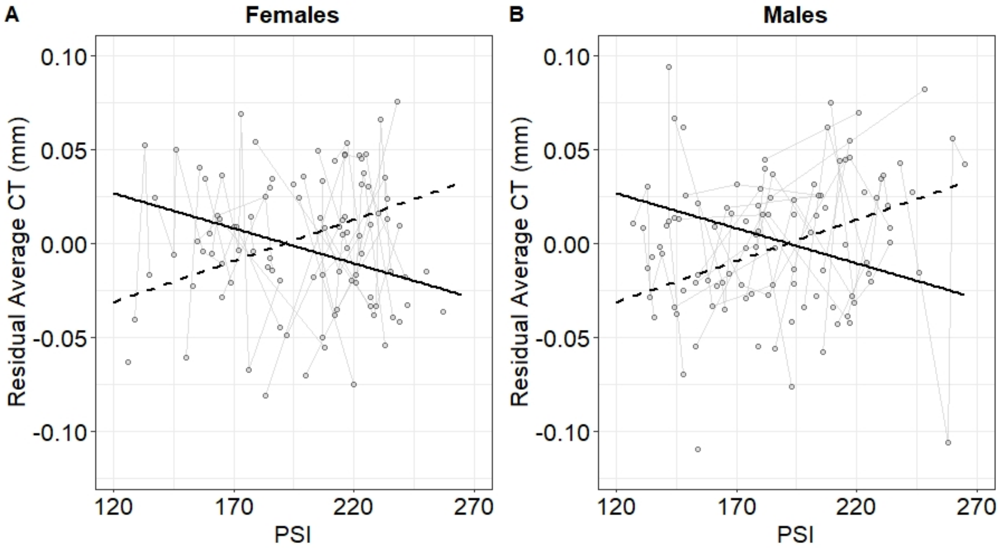
Residual BSID-II Motor Scale Score for Females (A) and Males (B) as a Function of PSI After Controlling for Mean Centered Age and Sex



Note. The estimated residual BSID-II Motor Scale Score is depicted in a solid thick line by the following equation: Predicted residual BSID-II Motor Scale Score = 0.275603 - 0.001434 *PSI. Each participant's data are depicted by small circles connected with a gray line across repeated measures.

Figure 20

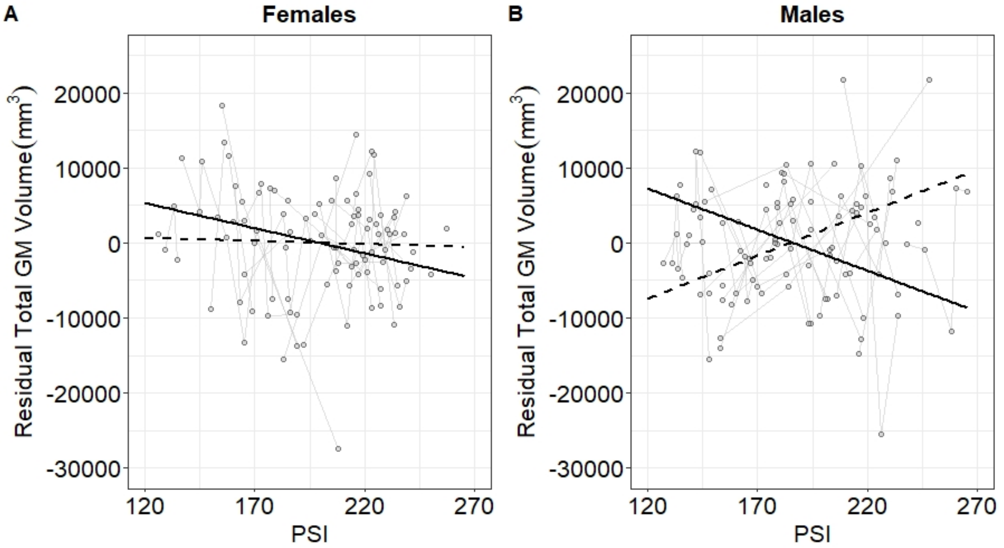
Residual Averaged CT for Females (A) and Males (B) as a Function of PSI After Controlling for Mean Centered Age and Sex



Note. The estimated residual Average CT is depicted in a dashed line for the minimal Mean Centered Age (-1) by the following equation: Predicted residual Average CT = - 0.02201 + 0.06235*-1 + 0.0001150*PSI + -1*PSI*- 0.0003259. The estimated residual Average CT is depicted in a solid thick line for the maximal Mean Centered Age (1.5) by the following equation: Predicted residual Average CT = - 0.02201 + 0.06235*1.5+ 0.0001150*PSI +1.5*PSI*- 0.0003259. Each participant's data are depicted by small circles connected with a gray line across repeated measures.

Figure 21

Residual Total Cortical GM Volume for Females (A) and Males (B) as a Function of PSI After Controlling for Mean Centered Age and Sex

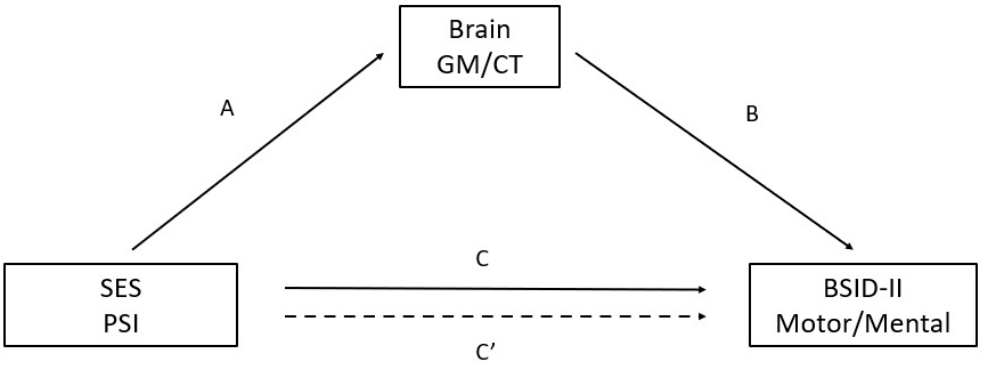


Note. For the Females, the estimated residual total cortical GM volume is depicted in a dashed line for the minimal mean centered age (-1) by the following equation: Predicted residual Total Cortical GM Volume = 6315.47 + 4666.20*-1 - 31.78*PSI -23.46*PSI*-1; while the solid thick line represents the estimated residual for the maximal Mean Centered Age (1.5) by the following equation: 6315.47 + 4666.20*1.5 - 31.78*PSI -23.46*PSI*1.5. For the Males, the estimated residual Total Cortical GM Volume is depicted in a dashed line for the minimal Mean Centered Age (-1) by the following equation: Predicted residual Total Cortical GM Volume = 6315.47 + 4666.20*-1 -10901.50 -31.78*PSI + 11981.21*-1 -23.46*-1*PSI + 56.85*PSI -66.34*-1*PSI; while the solid thick line represents the estimated residual Total Cortical GM Volume for the maximal Mean Centered Age (1.5) by the following equation: 6315.47 + 4666.20*1.5 -10901.50 -31.78*PSI + 11981.21*1.5 -23.46*1.5*PSI + 56.85*PSI -66.34*1.5*PSI. Each participant's data are depicted by small circles connected with a gray line across repeated measures.

Figure 22 depicts the general framework for the mediation analysis (Hypotheses 5 and 6). Tables 2 and 3 provide the path coefficients for the mediation analyses for SES (Adjusted Household Income) or PSI, Brain (Average CT and Total Cortical GM Volume), and BSID-II Mental Scale Score Scores, respectively. Tables 4 and 5 provide the path coefficients for the mediation analyses for SES (Adjusted Household Income) or PSI, Brain (Average CT and Total Cortical GM Volume), and BSID_II Motor Scale Scores. Each table is followed by a description of the results.

Figure 22

Mediation Model



Note. 'A' = direct effects of Adjusted Household Income and PSI on Average CT and Total Cortical GM volume. 'B' = direct effects of Average CT and Total Cortical GM Volume on BSID-II Mental and Motor Scale Scores. 'C' = direct effect of Adjusted Household Income and PSI on BSID-II Mental and Motor Scale Scores. 'C' = mediating effects of Average CT and Total Cortical GM Volume on Adjusted Household Income and PSI on BSID-II Mental and Motor Scale Scores. All models accounted for age and sex.

Table 2

Mediation Models for SES, Brain (Average CT and Total Cortical GM Volume), and BSID-II Mental Scale Score Scores

Variable/Path	Estimate (ß)	Standard Error	*p*
SES - CT – Mental			
Path A	1.575e-07	1.733e-07	.365
Path B	**-18.441**	**5.724**	**.002**
Path C	1.263e-05	1.200e-05	.296
Path C'	1.567e-05	1.208e-05	.199
SES – GM – Mental			
Path A	**.198**	**.067**	**.004**
Path B	-1.230e-05	1.205e-05	.310
Path C	1.263e-05	1.200e-05	.296
Path C'	1.692e-05	1.235e-05	.176

SES (Adjusted Household Income) to BSID-II Mental Scale Score Scores via Average CT

Path A was not significant indicating that there was no evidence of a relationship between Adjusted Household Income and Average CT, after accounting for age and sex. Path B was significant (ß = -18.441, SE = 5.724, *p* = .002); for every 1-unit increase in Average CT there was an 18.44-unit reduction in BSID-II Mental Scale Score Scores. Path C was not significant indicating that there was no evidence of a relationship between Adjusted Household Income and BSID-II Mental Scale Score Scores. Similarly, Path C' was not significant. Although there was a significant inverse relationship between Average CT and BSID-II Mental Scale Score, there was no evidence of a significant relationship between Adjusted Household Income and BSID-II Mental Scale Score after accounting for the age-related trajectories.

SES (Adjusted Household Income) to BSID-II Mental Scale Scores via Total Cortical GM Volume

Path A was significant (ß = .198, *SE* = .067, *p* = .004); for every 1 unit increase in Adjusted Household Income there was a .198-unit increase in Total Cortical GM Volume. However, Paths B, C, and C' were not significant. These results suggest that there was no evidence of a relationship between Total Cortical GM Volume and BSID-II Mental Scale Scores (B) or Adjusted Household Income and BSID-II Mental Scale Scores with or without accounting for total GM volume (C and C') after accounting for the age-related trajectories.

Table 3

Mediation Models for PSI, Brain (Average CT and Total Cortical GM Volume), and BSID-II Mental Scale Scores

Variable/Path	Estimate (ß)	Standard Error	*p*
PSI - CT – Mental			
Path A	2.498e-04	1.520e-04	.102
Path B	**-18.441**	**5.724**	**.002**
Path C	4.722e-04	.011	.967
Path C'	.005	.011	.664
PSI – GM – Mental			
Path A	-25.46	47.99	.596
Path B	-1.230e-05	1.205e-05	.310
Path C	4.722e-04	.011	.967
Path C'	-.001	.012	.926

PSI to BSID-II Mental Scale Scores via Average CT

Path A was not significant indicating that there was no evidence of a relationship between PSI and Average CT. Path B was significant (ß = -18.441, SE = 5.724, $p = .002$); for every 1-unit increase in Average CT there is an 18.44-unit reduction in BSID-II Mental Scale Scores. Path C was not significant indicating that there was no evidence of a relationship between PSI and BSID-II Mental Scale Score. Similarly, Path C' was not significant. Although there was a significant inverse relationship between Average CT and BSID-II Mental Scale Score, there was no evidence of a significant relationship between PSI and BSID-II Mental Scale Score after accounting for the age-related trajectories.

PSI to BSID-II Mental Scale Scores via Total Cortical GM Volume

None of the paths were significant suggesting that there was no evidence of a relationship between those variables.

Table 4

Mediation Models for SES, Brain (average CT and total cortical GM volume), and Motor scores

Variable/Path	Estimate (ß)	Standard Error	*p*
SES - CT – Motor			
Path A	1.575e-07	1.733e-07	.365
Path B	**10.118**	**3.392**	**.003**
Path C	-9.631e-06	7.235e-06	.186
Path C'	-1.089e-05	7.202e-06	.134
SES – GM – Motor			
Path A	**.198**	**.067**	**.004**
Path B	4.762e-06	7.337e-06	.518
Path C	-9.631e-06	7.235e-06	.128
Path C'	-1.153e-05	7.503e-06	.083

SES (Adjusted Household Income) to BSID-II Motor Scale Scores via Average CT

Path A was not significant indicating that there was no evidence of a relationship between Adjusted Household Income and Average CT. Path B was significant (ß = 10.118, SE = 3.392, *p* = .003); for every 1-unit increase in Average CT there was a 10.118-unit increase in BSID-II Motor Scale Scores. Path C was not significant indicating that there was no evidence of a relationship between Adjusted Household Income and BSID-II Motor Scale Score. Similarly, Path C' was not significant. Although there was a significant relationship between Average CT and BSID-II Motor Scale Score, there was no evidence of a significant relationship between Adjusted Household Income and BSID-II Motor Scale Score after accounting for the age-related trajectories.

SES (Adjusted Household Income) to BSID-II Motor Scale Scores via Total Cortical GM Volume

Path A was significant (ß = .198, *SE* = .067, *p* = .004); for every 1 unit increase in Adjusted Household Income there was a .198-unit increase in Total Cortical GM Volume. However, Paths B, C and C' were not significant. These results suggest that there was no evidence of a relationship between Total GM volume and BSID-II Motor Scale Score (B) or adjusted household income and BSID-II Motor Scale Scores with or without accounting for Total GM Volume (C and C’), after accounting for the age-related trajectories.

Table 5

Mediation Models for PSI, Brain (Average CT and Total Cortical GM Volume), and BSID-II Motor Scale Scores

Variable/Path	Estimate (ß)	Standard Error	*p*
PSI - CT – Motor			
Path A	2.498e-04	1.520e-04	.102
Path B	**10.118**	**3.392**	**.003**
Path C	-.002	.007	.748
Path C'	-.005	.007	.474
PSI – GM – Motor			
Path A	-25.46	47.99	.596
Path B	4.762e-06	7.337e-06	.518
Path C	-.002	.007	.748
Path C’	-.002	.007	.813

PSI to BSID-II Motor Scale Scores via Average CT

Path A was not significant indicating that there was no relationship between PSI and average CT. Path B was significant (ß = 10.118, SE = 3.392, *p* = .003); for every 1-unit increase in Average CT there is a 10.118-unit increase in BSID-II Motor Scale Scores. Path C was not significant indicating that there was no evidence of a relationship between PSI and BSID-II Motor Scale Score. Similarly, Path C’ was not significant. Although there was a significant relationship between Average CT and BSID-II Motor Scale Score, there was no evidence of a significant relationship between PSI and BSID-II Motor Scale Score after accounting for the age-related trajectories.

PSI to BSID-II Motor Scale Scores via Total Cortical GM Volume

None of the paths were significant suggesting that there was no evidence of a relationship between those variables.

Discussion

This study aimed to examine the relationships between the brain, cognitive, and motor development from birth to 2.5 years. Second, the study explored the effect of SES (adjusted household income) and parental stress on those domains. Last, the study examined if changes in the brain mediate the relationship between SES or parental stress and motor and cognitive development. Consistent with our hypotheses, there was a significant positive relationship between average CT and BSID motor scale. Although average CT was a significant predictor of BSID-II mental scale, the direction of this relationship was negative (i.e., thicker cortices associated with lower cognitive scores), which was contrary to our hypotheses. Moreover, we did not find evidence that total cortical GM volume was a significant predictor of motor or cognitive development. With respect to the impact of socioeconomic variables (household income) and parental stress, adjusted household income was a significant predictor of total cortical GM volume and PSI was a significant predictor of total cortical GM volume and average CT. Contrary to our hypothesis, we did not find evidence that these variables were significant predictors of motor or cognitive development. Given the lack of relationship between the socioeconomic variables on the behavioral outcomes, the mediation analyses did not support our hypotheses. Indeed, if total cortical GM volume or CT were included in the model, there still was no evidence of a relationship between household income or PSI on motor or cognitive development.

Developmental Trajectories

When modelling the developmental trajectories for each domain, the most parsimonious models included age (mean centered age in this case) as linear, squared, and cubic terms, which is consistent with the literature (Haywood & Getchell, 2020; Ducharme et al., 2016). Overall, total cortical GM volume had a greater increase in the first year of life and a more gradual increase over the second year. In addition, sex differences were present such that males had greater total cortical GM volume than females which became more pronounced after about 12 months of age. These findings are congruent with the literature (i.e., GM volume in males greater than in females, Gilmore et al., 2012; Knickmeyer et al., 2008; Groeschel et al., 2010). The developmental trajectory of average CT is also in line with the literature, with greater changes taking place in the first year of life compared to the second (Lyall et al., 2015; Li et al., 2015). For the BSID-II Mental Scale, the age-related trajectory showed rapid changes in the first year which tapered off towards the end of the age range. These results are congruent with the literature and compatible with the cognitive milestones during this period of development (Gerber et al., 2010; Johnson & Blasco, 1997). For the BSID-II Motor Scale, the trajectory was slightly different from the mental scale; although rapid changes occurred during the first year of life, there was also an increase towards the end of the age range (~24-30 months). Again, these findings are in line with previous literature and motor milestones during this period of development (WHO Multicentre Growth Reference Study Group, 2006).

Relationships Among Brain and Behavior

The lack of relationship between GM volume and the BSID mental and motor scales was surprising. In this study, we examined the total cortical GM volume, which might have obscured the relationship between GM growth of specific brain regions and motor or cognitive development. Indeed, developmental changes in language and sensory processing might be driven by changes in GM volume in occipital and parietal lobes (i.e., insula, inferior frontal gyrus, angular gyrus, inferior temporal gyrus, and fusiform gyrus) in the first year (Gilmore et al., 2007). In contrast, changes in sensory integration, motor planning, coordination, and higher-order cognitive processes would be driven by changes in GM volume in the frontal lobe (i.e., dorsolateral, and medial superior frontal gyri, and middle frontal gyrus), parietal lobe (i.e., inferior, angular, and supramarginal gyri), and temporal lobe in the second year (temporal pole of the middle temporal gyrus; Gilmore et al., 2012; Knickmeyer et al., 2008). Thus, an important next step is an examination of the relationship between specific brain regions and the age-related trajectories of motor and cognitive development.

A positive relationship between average CT and BSID motor scale was observed, which is in line with the literature (Girault et al., 2020). Although average CT was a significant predictor of the BSID mental scale, the direction of that relationship was not as expected (greater cortical thickness was related to poorer cognitive performance). Like the GM volume analysis, we examined the average CT, which might have obscured relationships between regional CT and cognitive development. Indeed, studies examining the regional CT found positive correlations between cognitive scores and CT in the right insula at age 2 years (Girault et al., 2020). Additionally, Shaw et al. (2006) examined the relationship between intelligence and cortical thickness. They verified a shift from a negative correlation between those variables in early childhood to a positive correlation at around seven years of age. Therefore, with the regional analysis of CT, different patterns might be identified, and the relationship between cognitive development might flip over time. Again, follow-up analyses with regional CT may shed additional light on its relationship and motor and cognitive development.

Surprisingly, we did not observe a significant relationship between BSID-II Mental and Motor Scales in our sample. One thing that might explain the lack of relationship is there may be a lag in the relationship between the two domains during this period of development (e,g., motor scores at 12 months predict cognitive scores at 18 months). The present analysis can only shed light on concurrent relationships across time. An examination of lagged relationships would require a greater number of participants with at least two data points, particularly time points towards the end of the age range. In addition to the performance on BSID-II Motor Scale, parent report of the age of onset for key motor milestones (e.g., sitting without support, walking without assistance) may align closer to results from previous literature suggesting a relationship between motor and cognitive development. For example, previous studies have found that sitting can enable reaching and object manipulation (Lobo et al., 2014; Veldman et al., 2019) and greater environmental exploration (Iverson, 2010). With that said, the use of parent reported age onsets for motor milestones can suffer from reliability and generalizability issues. Therefore, future studies would benefit from the use of both parent reported milestones and standardized performance assessments like the current version of the BSID.

Impact of Income on Behavior and Brain Development

The literature related to the impact of SES on motor and cognitive development in this age range is mixed. One reason for discrepant results is that the impact of SES may differ as a function of age. Indeed, Black, Hess & Berenson-Howard (2000) found that low income has a greater negative impact in toddlers compared to infants. In our study, adjusted household income was not a significant predictor of cognitive or motor development, which suggests that the age-related developmental changes observed using the BSID-II may be robust to income-related effects during this period of development. Examinations of early childhood (e.g., 2 years and older) may reveal a greater impact of adjusted household income on BSID performance.

It is also possible that household income might not impact behavioral development as much as other SES-related factors such as parent education and home environment (Fink, McCoy & Yousafzai, 2020; Noble et al., 2015). Unfortunately, variables related to the home environment or quality of caregiver interactions were not available in the present data set. Although maternal and paternal education were available in the present data set, these variables did not have sufficient variability to be included in the statistical analyses (i.e., out of 87 participants, 83 mothers and 81 fathers had high school degree). Additional studies are needed to determine if these other SES-related variables affect motor and cognitive development in infants.

With respect to brain development, this is the first study to examine the relationship between household income and multiple indices of brain development in infancy; Jha et al. (2019) examined CT while Hair et al. (2022) and Hanson et al. (2013) examined GM volume. The present results are consistent with Jha et al. (2019); adjusted household income was not a significant predictor of CT in neonates. However, Jha and colleagues (2019) did find a positive relationship between parental education and CT in neonates. These results suggest that during infancy other SES-related variables (e.g., parental education) may impact CT. Given the lack of variability in parental education in the present study, additional research is needed to confirm the impact of parental education and other SES-related variables on the trajectory of CT in infancy.

With respect to GM volume, the present results are consistent with Hair et al. (2022) and Hanson et al. (2013) in which income positively predicted GM volume. The consistency in results across these studies may be because these previous studies also used the NIH Study of Normal Brain Development Objectives 1 and 2 (Hair et al., 2022) and Objective 1 (Hanson et al., 2013). With that said, one important difference between the present study and previous studies is how income was treated statistically. In the present study, income was modelled as a continuous variable while Hair et al. (2022) dichotomized income as above/below 200% below the federal poverty line and Hanson et al. (2013) split income into three categories based on the federal poverty line. Although there is evidence to suggest that those from the lowest SES may be most negatively impacted, splitting income into categories makes it difficult to generalize to those at the edges of the categories. The present analysis allows us to estimate the impact of a unit increase in income on GM volume, which enables generalization across all income levels. These differences notwithstanding, higher income is associated with greater GM volumes suggesting that GM is more sensitive to the impact of income than the other variables (brain and behavior). Future studies are needed to verify the present findings and determine the mechanisms underlying the relationship between income and GM.

Impact of Parental Stress on Behavior and Brain Development

Similar to the results examining the relationship between SES and behavior, contrary to our hypotheses, parental stress was not a significant predictor of BSID-II mental and motor scales. These results differ from a previous study that found that maternal stress was associated with lower scores on parent-reported language, cognitive, and motor skills in 3- to 4-month-olds (Kim et al., 2016). The differences between this previous study and the present may be due the sample differences which may affect PSI responses (Grace et al., 2016). While Kim et al. (2016) included a large sample of mostly first-time Korean mothers with an average education of a college degree, the present sample included mostly multiparous Caucasian American parents with an average education of a high school degree. Given the lack of variability in race and ethnicity in our sample, our results suggest that for non-Hispanic, Caucasian, multiparous parents, the level of parental stress is not related to cognitive and motor development. Future studies are needed to confirm differences in the way in which race/ethnicity or family structure contribute to perceptions of stress and the effects of stress on behavior.

Interestingly, parental stress had a significant relationship with brain development, but this effect differed as a function of age. For both Averaged CT and Total Cortical GM Volume, for older infants, lower PSI scores were associated with thicker cortices and greater total GM volume. In contrast, for younger infants the relationship was inverse. These findings suggest that the parental stress may start to negatively affect brain development as children age. These results are consistent with studies of children suggesting a negative relationship between *prenatal maternal* stress and CT in 7-year-olds (Davis et al., 2020) and hippocampal volume (Moog et al., 2021). Future studies are needed to determine the impact of on-going/concurrent parental stress (using the PSI) to confirm the relationship with CT and GM volume observed presently in a larger age range (e.g., birth to school age) with a more diverse sample.

Limitations and Future Directions

Although the NIH Study of Normal Brain Development aimed to reflect the demographics of the US at the time of data collection, the final sample lacked sufficient variability in some of the SES-related variables and race/ethnicity. For example, parental education was almost exclusively High School degree and nearly all participants were Non-Hispanic Caucasians. With this said, by effectively holding parental education and race/ethnicity constant, we were able to determine the effects of income on the brain and behavior. To increase generalizability and confirm the results from the present study, future studies are needed with more diverse samples with respect to SES (variability in income, parental education, and parental occupation) and demographics (race and ethnicity).

There are several additional variables that may provide insights to behavioral and brain development and the impact of SES and related factors. For example, parent reports related to the age onset regarding key milestones would complement the performance outcomes of the BSID. Information about the caregiver/child interactions and home environment would be useful to determine if/how environmental factors, compared with income or parental stress, affect development.

The global measures of the brain development analyzed presently may have obscured potential relationships between regional brain development and behavior. As a future direction, we will run regional cortical analysis to determine the relationship between regional CT and regional cortical GM volume and cognitive and motor development. With this said, these data were acquired between 2001 and 2007 using a lower scan resolution which may affect the precision of the cortical segmentation and potentially affecting regional analyses.

The use of older version of the BSID (i.e., BSID-II vs. BSID-IV), again due to when these data were originally acquired, may also limit comparison with studies employing current versions. Specifically, the BSID-II consisted of 3 domains (i.e., mental, motor and behavior rating scale) and did not provide standard scores for separate subscales (i.e., fine and gross motor subscales). The updated version has five domains (i.e., cognitive, language, motor, social-emotional, and adaptive behavior), with the language scale divided into two subscales (receptive and expressive communication) and the motor scale also divided into two subscales (i.e., fine and gross motor). Therefore, it is not possible to directly compare the findings from this study with studies employing the newer version of the assessment.

These limitations notwithstanding, this study provided corroborating evidence regarding age-related trajectories of development in cognitive, motor, and brain development. This study also provided new evidence regarding the impact of income and parental stress on these domains. Together, this study represents an important step in understanding infant development from a more comprehensive perspective.

Chapter 4 – General Discussion

The present study adds to the literature by examining infant development from a comprehensive approach. Changes in global measures of GM volume, average CT, mental and motor abilities, their relationships, and the impact of adjusted family income and parental stress on those variables were systematically examined. Studies examining the relationship between brain and behavior and with large samples often implement purely cross-sectional designs or correlation analyses, which does not provide evidence of directional interactions. In this study, we were able to critically examine the longitudinal developmental trajectory of each domain, as well as their relationships from 2.6 to 31.2 months. Specifically, our sample consisted of 87 participants, 52 of which contributed at least 2 data points. The mixed-longitudinal sampling enabled us to address knowledge gaps using a robust longitudinal analysis with standardized assessments and MRI data.

Building upon this study, an important next step is to examine how motor development may lead to later cognitive development. An examination of time-lagged relationships may provide compelling evidence regarding developmental cascades in which the development of one domain influence future development of other domains. To this end, additional data would be useful to collect. Specifically, it is unclear how the results from the present study align with studies using parent reported age of onset for important motor and cognitive milestones during this period (i.e., birth to 2.5 years of age). Therefore, future studies should include parental reports of infant milestones in addition to standardized performance assessments. Additionally, the use of the current versions of the BSID may also enable a better understanding of subdomains of motor development (fine vs. gross) and how they relate to specific cognitive domains (i.e., cognitive, language, social-emotional, and adaptive behavior) and brain development. Indeed, one recent study examining brain and behavior found more correlations with gross motor and cognitive skills in the first year (Girault, 2020). Moreover, gross motor skills were positively associated with cognitive development in infants from 11 to 29 months of age, which is when milestones like standing alone and walking alone have emerged (Veldman et al., 2019).

A second immediate follow-up with our dataset would be to analyze the developmental trajectories of cortical regions of interest and their impact on behavior. As mentioned in the previous chapters, during the first year of life occipital and parietal GM volumes exhibit faster growth rates compared with brain regions mediating basic sensory processes. During the second year, frontal, parietal, and temporal GM exhibit faster growth rates; these regions underlie sensory integration, motor planning, coordination, and higher-order cognitive processes (Gilmore et al., 2007; Gilmore et al., 2012). Thus, developmental trajectories of GM volume in those regions would be examined, along with the changes in scores for BSID-II Mental and Motor Scales. Additionally, in this study, sex was a significant predictor of total cortical GM volume, with males presenting greater total GM volumes than females and increasing at a greater rate than females. There was no evidence indicating that total cortical GM volume was a significant predictor of behavior (cognitive and motor development). It is possible that the behavior milestones assessed were very strong during this time (birth to 2.5 years of age). Given that sex differences, as observed for total GM volume, are also observed in motor development (e.g., fundamental motor skills; Valentini et al., 2016) at school age, the relationship between total cortical GM volume and behavior might change with time.

The developmental trajectory for regional CT is slightly different than that observed for GM volume; CT increases first for frontal and temporal lobes compared with the occipital lobe.

Specifically, during the first year of life, there is an increase in CT in the medial frontal cortex, followed by lateral frontal, posterior temporal, and lateral occipital cortices. In the second year, there is a significant increase in CT in the superior frontal, superior parietal, and sensorimotor cortices (Wang et al., 2019). Those trajectories may also contribute to changes in cognitive and motor development, especially across the second year of life. Few studies have examined the relationship between the developmental trajectories of the brain and behavior using standardized assessments and those that do, often use a correlation approach. Therefore, using a similar statistical approach with the same longitudinal dataset but with regional GM volume and CT would represent a significant contribution to the literature.

SES is often confounded with other factors, such as race and ethnicity, in previous studies. Although race and ethnicity are important to cultural differences and family dynamics, they should be separated from SES. Moreover, SES is defined by three main factors: income, parental education, and parental occupation (National Center for Education Statistics, 2012). In the present study, we had a broad range of adjusted household income, but no variability of parental education and no information about parental occupation. Therefore, the present analyses strictly focused on adjusted household income as a proxy for SES. Total cortical GM volume was found to be the variable most influenced by adjusted income in our sample. Indeed, these results support evidence from previous studies in infants and young children suggesting that GM would be significantly impacted by income. On the other hand, most studies examining SES and CT found that parental education and not income significantly impacted CT in infancy and childhood. Although we replicated findings that CT was not significantly predicted by adjusted income, we were unable to assess the impact of parental education. In addition, although the literature regarding the impact of SES on motor and cognitive development is mixed, the studies that found an effect of SES typically examined participants from very impoverished backgrounds (below the federal poverty line) compared to those above the federal poverty line. Thoughtful data collection and stratification of the sample is necessary to disentangle SES variables (i.e., income, parental education, and parental occupation) to understand which factors impact domains of development.

A thorough understanding of the developmental trajectories of the brain, cognitive and motor behavior, and the impact of socioeconomic variables and parental stress enable us to identify a better approach and window to implement interventions to improve the development of those domains. In this study, income was a significant predictor of GM volume, and parental stress was a significant predictor for both brain variables analyzed (total cortical GM volume and average CT). Given that changes in the development of regional GM volume and CT are still expected to predict mental and motor development, an intervention aimed at underserved populations, which according to the literature, is often linked to increased parental stress, might have a greater impact on overall development. In addition, as mentioned previously, the literature examining the effect of SES and behavior is mixed. Research has suggested that home environment and parent interaction might play an essential role in development. Therefore, cost-effective interventions aimed at promoting an enriched and stimulating environment at home and also at daycare/school might alleviate the negative effect of parental stress and low income. The impact of those variables was significant specifically for older children in our sample (i.e., at the end of our age range). This finding may suggest that prolonged exposure to environmental factors (e.g., low income for GM and higher levels of PSI for GM and CT) lead to adverse effects on brain development and possibly later cognitive and motor development. Thus, interventions should be implemented as early as possible to attenuate those effects.

Although I have not collected the data analyzed in this dissertation, this project was a rich research experience where I had the opportunity to acquire knowledge that will be very important for my future experiences. As the data were part of an extensive data set, the first thing I needed to work on was extracting data, which required specific software. Next, I had to work on data organization, making sure there were no errors, and combine data sets (e.g., demographic information and measures for each dependent variable). As the Neurocognition and Imaging Research Lab had the appropriate pipeline to process infants' MRI data, we sent them the data. For that, I learned how to convert data and transfer using specific programs. While MRI data were being processed, I conducted the quality control of all images by checking if the tissue segmentation was appropriate, which I also learned how to do with this project. After that, all the cortical surface measures were extracted and sent to us. All transfers were secured, protecting data from unauthorized access. In the data analysis, I had more exposure to R and R-studio and learned how to conduct linear-mixed effect analysis appropriately. In addition, I became more able to critically examine the assessments and the literature, especially about how SES is confounded with other factors, and I became thoughtful about how to analyze this variable better. Therefore, this project provided me with learning opportunities that will lead to my future research experiences (e.g., project development, thoughtful stratification of the sample, MRI data analysis, and data management) and helped me to become a more thoughtful and independent researcher. Furthermore, this project has enabled me to continue researching infancy development and contribute to the literature.

References

Abidin, R. R. (1995). Parenting stress index. Psychological Assessment Resources, Inc. (3rd ed.). Florida: Odessa

Adolph, K., Robinson, S. (2015). Motor development. *Handbook of Childhood Psychology Development Science*, (113-157).

Almli, C.R., Rivkin, M. J., Mckinstry, R.C. (2007). The NIH MRI study of normal brain development (Objective-2): Newborns, infants, toddlers, and preschoolers. *NeuroImage, 35* (1), 308-325. https://doi.org/10.1016/j.neuroimage.2006.08.058.

Bayer, J. K., Hiscock, H., Ukoumunne, O. C., Price, A., & Wake, M. (2008). Early childhood aetiology of mental health problems: A longitudinal population-based study. *Journal of child psychology and psychiatry, and allied disciplines*, *49*(11), 1166–1174. https://doi.org/10.1111/j.1469-7610.2008.01943.x.

Bayley, N. (1969). *Manual for the Bayley Scales of Infant Development*. San Antonio, TX: Psychological Corporation.

Bayley, N. (1993). *Manual for the Bayley Scales of Infant Development* (2nd ed.). San Antonio, TX: Psychological Corporation.

Black, M. M., Matula, K. (2000). *Essentials of Bayley Scales of Infant Development assessment.* John Wiley & Sons Inc.

Black, M. M., Hess, C. R., Berenson-Howard, J. (2000). Toddlers from low-income families have below normal mental, motor, and behavior scores on the revised Bayley scales. *Journal of Applied Developmental Psychology, 21*(6), 655-666. https://doi.org/10.1016/S0193-3973(00)00059-9.

Blaga, O. M., Shaddy,D. J., Anderson, C. J., Kannass, K. N., Little, T. D., Colombo, J.(2009). Structure and continuity of intellectual development in early childhood. *Intelligence, 37*(1), 106-113. https://doi.org/10.1016/j.intell.2008.09.003.

Blair, C., Granger, D. A., Willoughby, M., Mills-Koonce, R., Cox, M., Greenberg, M. T., Kivlighan, K. T., Fortunato, C. K. (2011). Salivary cortisol mediates effects of poverty and parenting on executive functions in early childhood. *Child Development, 82* (6), 1970-1984. https://doi.org/10.1111/j.1467-8624.2011.01643.x

Bornstein, M. H., Hahn, C. S., & Suwalsky, J. T. D. (2013). Physically developed and exploratory young infants contribute to their own long-term academic achievement. *Psychological Science*, *24*(10), 1906–1917. https://doi.org/10.1177/0956797613479974

Brain Development Cooperative Group (2006). The MRI study of the normal brain development: Procedure Manual Objective 2.

Brain Development Cooperative Group (2006). The MRI study of the normal brain development: Study protocol.

Campos, D., Gonçalves, V. M. G., Guerreiro, M. M., Santos, D. C., Goto, M. M. F., Arias, A. V., & Campos-Zanelli, T. M. (2012). Comparison of motor and cognitive performance in infants during the first year of life. *Pediatric Physical Therapy*, *24*(2), 193–197. https://doi.org/10.1097/PEP.0b013e31824d2db7

Clark, J. E., Metcalfe, J. S. (2002). The mountain of motor development: A metaphor. *Motor Development: Research and Reviews*, *2*, 163-190.

Clearfield, M. W., Stanger, S. B., Jenne, H. K. (2015). Socioeconomic status (SES) affects means–end behavior across the first year. *Journal of Applied Developmental Psychology, 38*, 22-28. https://doi.org/10.1016/j.appdev.2015.02.001.

Creasey, G. L., & Jarvis, P. A. (1994). Relationships between parenting stress and developmental functioning among 2-year-olds. *Infant Behavior and Development,17* (4), 423-429. https://doi.org/10.1016/0163-6383(94)90034-5.

Dai, Y., Shi, F., Wang, L., Wu, G., & Shen, D. (2013). iBEAT: A toolbox for infant brain magnetic resonance image processing. *Neuroinformatics*, *11*(2), 211–225. https://doi.org/10.1007/s12021-012-9164-z

Davis, E. P., Hankin, B. L., Glynn, L. M., Head, K., Kim, D. J., & Sandman, C. A. (2020). Prenatal maternal stress, child cortical thickness, and adolescent depressive symptoms. *Child development*, *91*(2), e432–e450. https://doi.org/10.1111/cdev.13252

Deák, G. O (2014). Interrelations of language and cognitive development. In Brooks, P., & Kampe, V. (Eds.), *Encyclopedia of language development* (284 – 291). Sage. https://doi.org/ 10.4135/9781483346441.n91

Diamond A. (2000). Close interrelation of motor development and cognitive development and of the cerebellum and prefrontal cortex. *Child Development*, *71*, 44–56. https://doi.org/10.1111/1467-8624.00117

Diamond & Lee, 2016 - Diamond, A., and Ling, D. S. (2016). Conclusions about interventions, programs, and approaches for improving executive functions that appear justified and those that, despite much hype, do not. *Developmental Cognitive Neuroscience, 18*, 34–48. https://doi.org/10.1016/j.dcn.2015.11.005

Ducharme, S., Albaugh, M. D., Nguyen, T. V., Hudziak, J. J., Mateos-Pérez, J. M., Labbe, A., Evans, A. C., Karama, S., & Brain Development Cooperative Group (2016). Trajectories of cortical thickness maturation in normal brain development-The importance of quality control procedures. *NeuroImage*, *125*, 267–279. https://doi.org/10.1016/j.neuroimage.2015.10.010

Fink, G., McCoy, D.C., Yousafzai, A. (2020). Contextual and socioeconomic variation in early motor and language development. *Archives of Disease in Childhood, 105,* 421-427. http://dx.doi.org/10.1136/archdischild-2019-317849

Flavell, J. H. (1999). Cognitive Development: Children's knowledge about the mind. *Annual Review of Psychology, 50*, 21-45. https://doi.org/10.1146/annurev.psych.50.1.21

Gallahue, D. L., Ozmun, J. C., & Goodway, J. (2012). *Understanding Motor Development: Infants, Children, Adolescents, Adults*. McGraw-Hill.

Gerber, R. J., Wilks, T., Erdie-Lalena, C. (2010). Developmental milestones: Motor development. *Pediatrics in Review*, *32*, 267-277. https://doi.org/10.1542/pir.31-7-267

Ghassabian, A., Sundaram, R., Bell, E., Bello, S. C., Kus, C., & Yeung, E. (2016). Gross motor milestones and subsequent development. *Pediatrics*, *138*(1), 1-8. https://doi.org/10.1542/peds.2015-4372

Gilmore, J. H., Lin, W., Prastawa, M. W., Looney, C. B., Vetsa, Y. S. K., Knickmeyer, R. C., Evans, D. D., Smith, J. K., Hamer, R. M., Lieberman, J. A., & Gerig, G. (2007). Regional gray matter growth, sexual dimorphism, and cerebral asymmetry in the neonatal brain. *Journal of Neuroscience*, *27*(6), 1255–1260. https://doi.org/10.1523/JNEUROSCI.3339-06.2007

Gilmore, J. H., Shi, F., Woolson, S. L., Knickmeyer, R. C., Short, S. J., Lin, W., Zhu, H., Hamer, R. M., Styner, M., & Shen, D. (2012). Longitudinal development of cortical and subcortical gray matter from birth to 2 years. *Cerebral Cortex*, *22*(11), 2478–2485. https://doi.org/10.1093/cercor/bhr327

Girault, J. B., Cornea, E., Goldman, B. D., Jha, S. C., Murphy, V. A., Li, G., Wang, L., Shen, D., Knickmeyer, R. C., Styner, M., & Gilmore, J. H. (2020). Cortical Structure and Cognition in Infants and Toddlers. *Cerebral Cortex*, *30*(2), 786–800. https://doi.org/10.1093/cercor/bhz126

Goldin-Meadow, S., Levine, S. C., Hedges, L. V., Huttenlocher, J., Raudenbush, S. W., & Small, S. L. (2014). New evidence about language and cognitive development based on a longitudinal study: hypotheses for intervention. *The American psychologist*, *69*(6), 588–599. https://doi.org/10.1037/a0036886

Goodway, J. D., Ozmun, J. C., Gallahue, D. L. (2019). *Understanding motor development: Infants, children, adolescents, adults* (8th Ed.). Jones & Bartlett Learning.

Grace, T., Bulsara, M., Robinson, M., & Hands, B. (2016). The impact of maternal gestational stress on motor development in late childhood and adolescence: A longitudinal study. *Child development*, *87*(1), 211–220. https://doi.org/10.1111/cdev.12449

Groeschel, S., Vollmer, B., King, M. D., & Connelly, A. (2010). Developmental changes in cerebral grey and white matter volume from infancy to adulthood. *International Journal of Developmental Neuroscience*, *28*(6), 481–489. https://doi.org/10.1016/j.ijdevneu.2010.06.004

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. https://doi.org/10.1001/jamapediatrics.2015.1475

Hair N.L., Hanson J.L., Wolfe B.L., Pollak S.D. (2022) Low household income and neurodevelopment from infancy through adolescence. *PLoS ONE, 17*(1), e0262607. https:// doi.org/10.1371/journal.pone.0262607

Hanson, J.L., Hair, N., Shen, D.G., Shi, F., Gilmore, J.H., Wolfe, B.L., Pollak, S.D. (2013) Family poverty affects the rate of human infant brain growth. *PLoS ONE, 8*(12) e80954. https://doi.org/10.1371/journal.pone.0080954

Hart, B., & Risley, T. R. (1995). Meaningful differences in the everyday experiences of young children. Baltimore, MD*: Brookes*

Holland, D., Chang, L., Ernst, T. M., Curran, M., Buchthal, S. D., Alicata, D., Skranes, J., Johansen, H., Hernandez, A., Yamakawa, R., Kuperman, J. M., & Dale, A. M. (2014). Structural growth trajectories and rates of change in the first 3 months of infant brain development. *JAMA Neurology*, *71*(10), 1266–1274. https://doi.org/10.1001/jamaneurol.2014.1638

Haywood, K. M., & Getchell, N. (2020). *Life Span Motor Development* (7th ed.). Champaign, IL: Human Kinetics.

Iverson J. M. (2010). Developing language in a developing body: the relationship between motor development and language development. *Journal of child language*, *37*(2), 229–261. https://doi.org/10.1017/S0305000909990432

Jha, S. C., Xia, K., Ahn, M., Girault, J. B., Li, G., Wang, L., Shen, D., Zou, F., Zhu, H., Styner, M., Gilmore, J. H., Knickmeyer, R. C. (2019). Environmental influences on infant cortical thickness and surface area. *Cerebral Cortex*, *29* (3), 1139-1149. https://doi.org/10.1093/cercor/bhy020

Jeon, H., Peterson, C., DeCoster, J. (2013). Parent-child interaction, task-oriented regulation, and cognitive development in toddlers facing developmental risks. *Journal of Applied Developmental Psychology*, *34* (6), 257-267. https://doi.org/10.1016/j.appdev.2013.08.002

Johnson, C. P., & Blasco, P. A. (1997). Infant growth and development. *Pediatrics in Review*, *18*(7), 224–242. https://doi.org/10.1542/pir.18-7-224

Johnson, S., Riis, J., Noble, K. (2016). State of the Art Review: Poverty and the Developing Brain. *Pediatrics*, 137 (4). https://doi.org/10.1542/peds.2015-3075

Kandel, E. R., Schwartz, J. H., Jessell, T. M., Siegelbaum, S. A., Hudspeth, A. J. (Eds.). (2013). *Principles of neural science* (5th ed.). The McGraw-Hill Companies, Inc.

Khoshkerdar, S. F., Baradaran, M., Ranjbar Noushari, F. (2020). The role of parenting styles, parental stress and children's executive functions deficits in predicting the children's internalizing and externalizing problems. *Journal of Child Mental Health,7* (2),156-168. http://childmentalhealth.ir/article-1-927-en.html.

Kim, M., Kang, S. K., Yee, B., Shim, S. Y., & Chung, M. (2016). Paternal involvement and early infant neurodevelopment: The mediation role of maternal parenting stress. *BMC pediatrics*, *16*(1), 212. https://doi.org/10.1186/s12887-016-0747-y.

Knickmeyer, R. C., Gouttard, S., Kang, C., Evans, D., Wilber, K., Smith, J. K., Hamer, R. M., Lin, W., Gerig, G., & Gilmore, J. H. (2008). A structural MRI study of human brain development from birth to 2 years. *Journal of Neuroscience*, *28*(47), 12176–12182. https://doi.org/10.1523/JNEUROSCI.3479-08.2008

Lawson, G. M., Dada, 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. https://doi.org/10.1111/desc.12096

Li, G., Lin, W., Gilmore, J. H., & Shen, D. (2015). Spatial patterns, longitudinal development, and hemispheric asymmetries of cortical thickness in infants from birth to 2 years of age. *Journal of Neuroscience*, *35*(24), 9150–9162. https://doi.org/10.1523/JNEUROSCI.4107-14.2015

Li, G., Nie, J., Wang, L., Shi, F., Lin, W., Gilmore, J. H., & Shen, D. (2013). Mapping region-specific longitudinal cortical surface expansion from birth to 2 years of age. *Cerebral Cortex*, *23*(11), 2724–2733. https://doi.org/10.1093/cercor/bhs265

Li, G., Wang, L., Shi, F., Lyall, A. E., Ahn, M., Peng, Z., Zhu, H., Lin, W., Gilmore, J. H., & Shen, D. (2016). Cortical thickness and surface area in neonates at high risk for schizophrenia. *Brain structure & function*, *221*(1), 447–461. https://doi.org/10.1007/s00429-014-0917-3

Lobo, M. A., Kokkoni, E., de Campos, A. C., & Galloway, J. C. (2014). Not just playing around: Infants' behaviors with objects reflect ability, constraints, and object properties. *Infant Behavior and Development*, *37*(3), 334–351. https://doi.org/10.1016/j.infbeh.2014.05.003

Lyall, A. E., Shi, F., Geng, X., Woolson, S., Li, G., Wang, L., Hamer, R. M., Shen, D., & Gilmore, J. H. (2015). Dynamic development of regional cortical thickness and surface area in early childhood. *Cerebral Cortex*, *25*(8), 2204–2212. https://doi.org/10.1093/cercor/bhu027

Meadows, S. (2006). *The child as thinker: The Development and Acquisition of Cognition in Childhood* (2nd ed.). London: Routledge. https://doi.org/10.4324/9780203965207

Moog, N. K., Nolvi, S., Kleih, T. S., Styner, M., Gilmore, J. H., Rasmussen, J. M., Heim, C. M., Entringer, S., Wadhwa, P. D., & Buss, C. (2021). Prospective association of maternal psychosocial stress in pregnancy with newborn hippocampal volume and implications for infant social-emotional development. *Neurobiology of stress*, *15*, 100368. https://doi.org/10.1016/j.ynstr.2021.100368

National Center for Education Statistics. (2012). Improving the measurement of socioeconomic status for the national assessment of education progress: A theoretical foundation. *US Department of Education*. http://nces.ed.gov/nationsreportcard/pdf/researchcenter/Socioeconomic_Factors.pdf.

Noble, K., Houston, S., Brito, N., Bartsc, H., Kan, E., Kuperman, J. M., Ashhoomoff, N., Amaral, D. G., Bloss, C. S., Libiger, O., Schork, N. J., Murray, S. S., Casey, B. J., Chang, L., Ernst, T. M., Frazier, J. A., Gruen, J. R., Kennedy, D. N., Van Zijl, P., Mostofsky, S., Kaufmann, W. E., Kenet, T., Dales, A. M., Jernigan, T. L., Sowell, E. (2015). Family income, parental education and brain structure in children and adolescents. *Nature Neuroscience, 18* (5)**,** 773–778.https://doi.org/10.1038/nn.3983

Piaget, J. (1952). *The origins of intelligence in children*. New York: International Universities Press.

Purves, D., Augustine, G. J., Fitzpatrick, D., Hall, W. C., LaMantia, A., White, L. E. (Eds.). (2012). *Neuroscience* (5th ed.). Sinauer Associates, Inc.

Remer, J., Croteau-Chonka, E., Dean, D. C., 3rd, D'Arpino, S., Dirks, H., Whiley, D., & Deoni, S. (2017). Quantifying cortical development in typically developing toddlers and young children, 1-6 years of age. *NeuroImage*, *153*, 246–261. https://doi.org/10.1016/j.neuroimage.2017.04.010

Rhoades, B., Greenberg, M., Lanza, S., Blair, C. (2011). Demographic and familial predictors of early executive function development: Contribution of a person-centered perspective. *Journal of Experimental Child Psychology*, 108(3), 638-662. https://doi.org/10.1016/j.jecp.2010.08.004

Sanchez, C. E., Richards, J. E., Almli, R. (2012). Neurodevelopmental MRI brain templates for children from 2 weeks to 4 years of age. *Developmental Psychobiology, 54* (1), 77-91. https://doi.org/10.1002/dev.20579

Shaw, P., Greenstein, D., Lerch, J., Clasen, L., Lenroot, R., Gogtay, N., Evans, A., Rapoport, J., & Giedd, J. (2006). Intellectual ability and cortical development in children and adolescents. *Nature*, *440*(7084), 676–679. https://doi.org/10.1038/nature04513

Spann, M. N., Bansal, R., Rosen, T. S., & Peterson, B. S. (2014). Morphological features of the neonatal brain support development of subsequent cognitive, language, and motor abilities. *Human Brain Mapping*, *35*(9), 4459–4474. https://doi.org/10.1002/hbm.22487

Suor, J., Sturge-Apple, M., Davies, P., Cicchetti, D., Manning, L. (2015) Tracing differential pathways of risk: Associations among family adversity, cortisol, and cognitive functioning in childhood. *Child Development*, 86 (4), 1142-1158. https://doi.org/10.1111/cdev.12376

Tacke, N. F., Bailey, L. S., & Clearfield, M.W. (2015). Socio-economic status (SES) affects infants' selective exploration. *Infant and Child Development, 24* (6), 571-586. https://doi.org/10.1002/icd.1900

Thelen, E. (2000). Motor development as foundation and future of developmental psychology. *International Journal of Behavioral Development*, *24*(4), 385-397.

United States Census Bureau (2000). SF1 and SF4, retrieved from: http://factfinder.census.gov.

Valentini, N. C., Logan, S., Spessato, B., Souza, M. S., Pereira, K. G., Rudisill, M. E. (2016). Fundamental motor skills across childhood: Age, sex, and competence outcomes of Brazilian children. *Journal of Motor Learning and Development, 4*(1), 16-36. https://doi.org/10.1123/jmld.2015-0021

Veldman, S. L. C., Santos, R., Jones, R. A., Sousa-Sá, E., & Okely, A. D. (2019). Associations between gross motor skills and cognitive development in toddlers. *Early Human Development*, *132*, 39–44. https://doi.org/10.1016/j.earlhumdev.2019.04.005

Viholainen, H., Ahonen, T., Cantell, M., Tolvanen, A., & Lyytinen, H. (2006). The early motor milestones in infancy and later motor skills in toddlers: A structural equation model of motor development. *Physical and Occupational Therapy in Pediatrics*, *26*(1–2), 91–113. https://doi.org/10.1300/J006v26n01_07

Vygotsky, L.S. (1978). *Mind in society: The development of higher psychological processes.* Cambridge, MA*:* Harvard University Press.

Wang, L., Shi, F., Li, G., Gao, Y., Lin, W., Gilmore, J. H., & Shen, D. (2014). Segmentation of neonatal brain MR images using patch-driven level sets. *NeuroImage*, *84*, 141–158. https://doi.org/10.1016/j.neuroimage.2013.08.008

Wang, F., Lian, C., Wu, Z., Zhang, H., Li, T., Meng, Y., Wang, L., Lin, W., Shen, D., & Li, G. (2019). Developmental topography of cortical thickness during infancy. *Proceedings of the National Academy of Sciences of the United States of America*, *116*(32), 15855–15860. https://doi.org/10.1073/pnas.1821523116

Wass, S., Porayska-Pomsta, K., & Johnson, M. H. (2011). Training Attentional Control in Infancy. *Current Biology, 21* (18), 1543-1547. https://doi.org/10.1016/j.cub.2011.08.004.

Wellman, H. M., & Gelman, S. A. (1992). Cognitive Development: Foundational theories of core domains. *Annual Review of Psychology, 43* (1), 337 – 375. https://doi.org/10.1146/annurev.ps.43.020192.002005

WHO Multicentre Growth Reference Study Group, Onis, M. (2006). WHO motor development study: windows of achievement for six gross motor development milestones. *Acta Pediatric, 95* (S450), 86-95. https://doi.org/10.1111/j.1651-2227.2006.tb02379.x

Wu, M., Liang, X., Lu, S., & Wang, Z. (2017). Infant motor and cognitive abilities and subsequent executive function. *Infant Behavior and Development*, *49*, 204–213. https://doi.org/10.1016/j.infbeh.2017.09.005

Appendix A

Normality of Residuals

To check this assumption, we examined the q-q-plots for the best fit model for each dependent variable.

Figure 23

Normality for the Best Fit Model for Total Cortical GM Volume

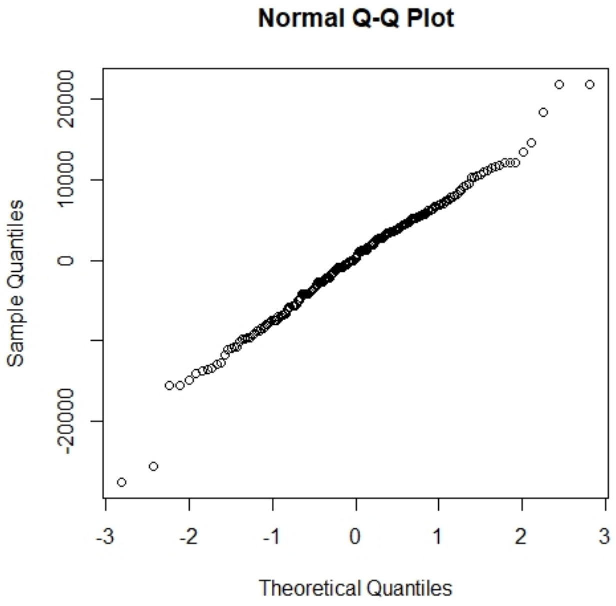


Figure 24

Normality for the Best Fit Model for Average CT

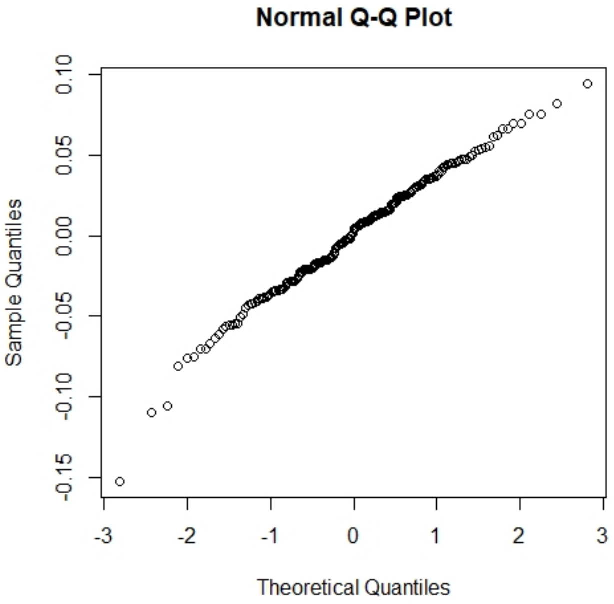


Figure 24

Normality for the Best Fit Model for BSID-II Mental Scale Score

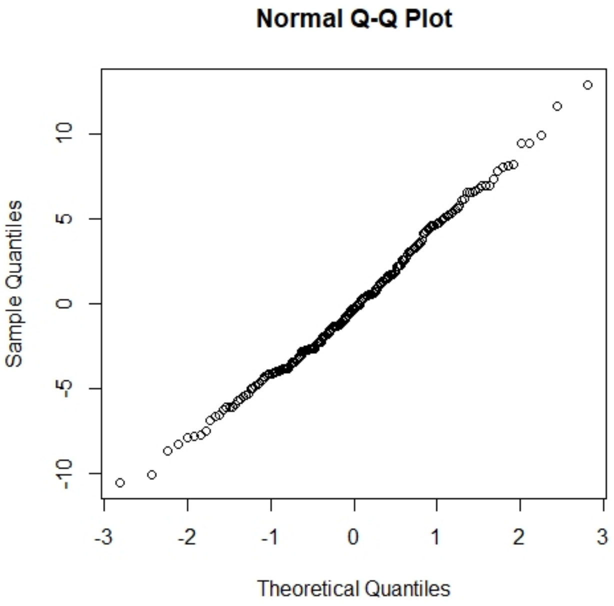
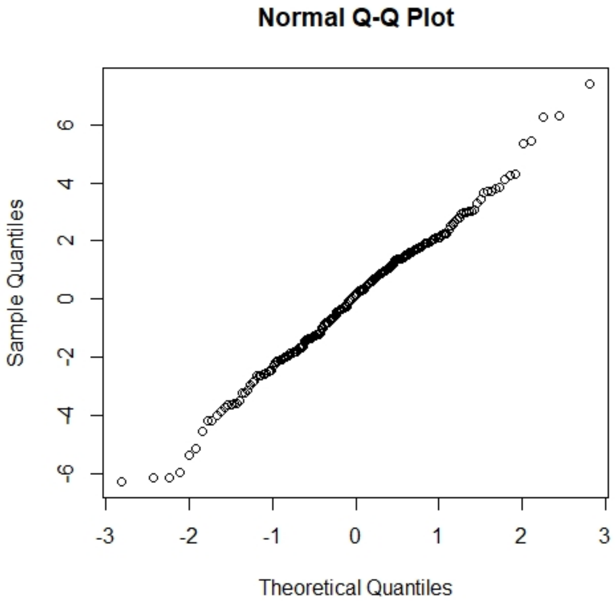


Figure 25

Normality for the Best Fit Model for BSID-II Motor Scale Score



Homoscedasticity

To check this assumption, we examined the plots of the residuals versus the predicted/fitted values for the best fit model for each dependent variable.

Figure 26

Homogeneity of Variance for the Best Fit Model for Total Cortical GM Volume

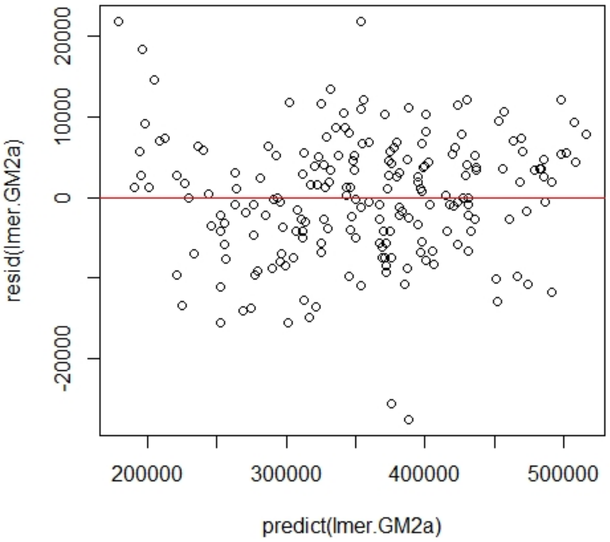


Figure 27

Homogeneity of Variance for the Best Fit Model for Average CT

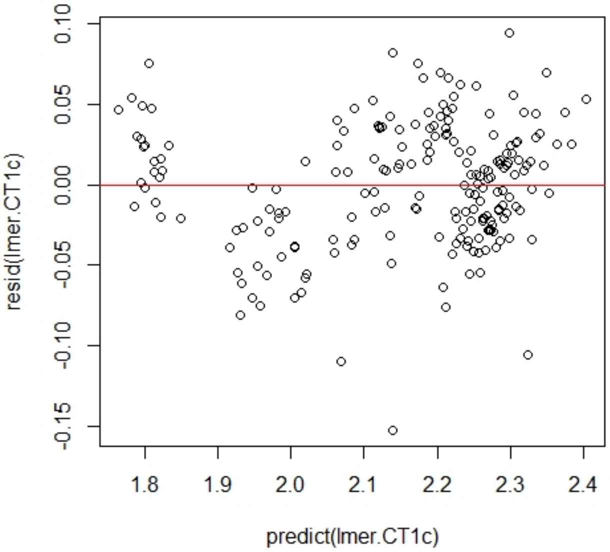


Figure 28

Homogeneity of Variance for the Best Fit Model for BSID-II Mental Scale Score

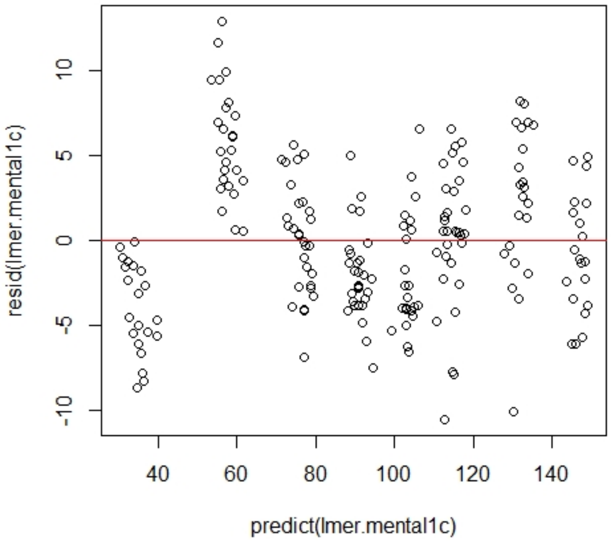
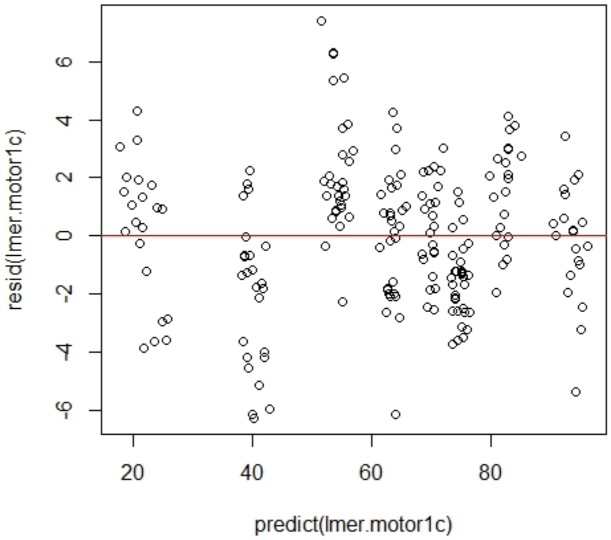


Figure 29

Homogeneity of Variance for the Best Fit Model for BSID-II Motor Scale Score



Appendix B

Sensitivity Analyses

Sensitivity analyses were conducted based on the best fit model used for Hypotheses 1-3. The effect sizes are reported in units of slope.

Specific Aim 1 – Hypothesis 1

Greater Total Cortical GM Volume and Average CT will be associated with better performance on the Bayley Scales of Infant Development-II (BSID-II Mental and Motor Scale Scores), after accounting for age and sex.

BSID-II Mental ~ Total Cortical GM Volume. The study had 80% power to detect effects as small as ß = .00003. However, in our model, the estimate for Total Cortical GM volume was very small (ß = -.00001). We ran the analysis with 70% of power, but the effect size was still greater than the one obtained with our sample. Therefore, we were underpowered to detect the relationship between Total Cortical GM Volume and BSID-II Mental, assuming that there is a relationship between those variables.

BSID-II Motor ~ total cortical GM volume. The study had 80% power to detect effects as small as ß = .00002. However, in our model, the estimate for Total Cortical GM Volume was very small (ß = .000004). We ran the analysis with 70% of power, but the effect size was still greater than the one obtained with our sample. Therefore, we were underpowered to detect the relationship between Total Cortical GM Volume and BSID-II Motor, assuming that there is a relationship between those variables.

BSID-II Mental ~ Average CT. The study had 80% power to detect effects as small as ß = 16.13. In our model, the estimate for Average CT was (ß = -18.441), which indicates that we achieved 80% statistical power to detect the effects of average CT on BSID-II Mental Scale Score.

BSID-II Motor ~ Average CT. The study had 80% power to detect effects as small as ß = 9.555. In our model, the estimate for Average CT was (ß = 10.1178), which indicates that we achieved 80% statistical power to detect the effects of average CT on BSID-II Motor Scale Score.

Specific Aim 1 – Hypothesis 2

Cognitive development (BSID-II Mental Scale Score) will be positively associated with the motor development (BSID-II Motor Scale Score), after accounting for age and sex

BSID-II Mental ~ BSID-II Motor. The study had 80% power to detect effects as small as ß = .338. However, in our model, the estimate for BSID-II Motor Scale Score was smaller (ß = .138). We ran the analysis with 70% of power, but the effect size was still greater than the one obtained with our sample. Therefore, we were underpowered to detect the relationship between BSID-II Mental Scale and Motor Scale Scores.

Specific Aim 2 – Hypothesis 3

Adjusted Household Income will be positively associated with Total Cortical GM Volume, Average CT, and BSID-II Mental Scale Score and Motor Scale Score, after controlling for age and sex.

Total Cortical GM Volume ~ Adjusted Household Income. The study had 80% power to detect effects as small as ß = .190. In our model, the estimate for Adjusted Household Income was (ß = .200), which indicates that we achieved 80% statistical power to detect the effects of Adjusted Household Income on Total Cortical GM Volume.

Average CT ~ Adjusted Household Income. The study had 80% power to detect effects as small as ß = .0000005. However, in our model, the estimate for adjusted household income was smaller (ß = .0000002). We ran the analysis with 70% of power, but the effect size was still greater than the one obtained with our sample. Therefore, we were underpowered to detect the relationship between Adjusted Household Income and Average CT, assuming that there is a relationship between those variables.

BSID-II Mental ~ Adjusted Household Income. The study had 80% power to detect effects as small as ß = .00003. However, in our model, the estimate for Adjusted Household Income was smaller (ß = .00001). We ran the analysis with 70% of power, but the effect size was still greater than the one obtained with our sample. Therefore, we were underpowered to detect the relationship between Adjusted Household Income and BSID-II Mental Scale Score, assuming that there is a relationship between those variables.

BSID-II Motor ~ Adjusted Household Income. The study had 80% power to detect effects as small as ß = .00002. However, in our model, the estimate for Adjusted Household Income was smaller (ß = .00001). We ran the analysis with 70% of power, but the effect size was still greater than the one obtained with our sample. Therefore, we were underpowered to detect the relationship between Adjusted Household Income and BSID-II Motor Scale Score, assuming that there is a relationship between those variables.

Specific Aim 2 – Hypothesis 4

PSI will be negatively associated with Total Cortical GM Volume, Average CT, and BSID-II Mental and Motor Scale Scores, after controlling for age and sex.

Total cortical GM volume ~ PSI. The study had 80% power to detect effects as small as ß = 208.676. However, in our model, the estimate for PSI was smaller (ß = -196.32). We ran the analysis with 70% of power, and effects small as ß = 185.095 could be detected. Therefore, we had 70% statistical power to detect the effects of PSI on Total Cortical GM Volume.

Average CT ~ PSI. The study had 80% power to detect effects as small as ß = .0004. However, in our model, the estimate for PSI was smaller (ß = .0003). We ran the analysis with 70% of power, and effects small as ß = .0003 could be detected. Therefore, we achieved 70% statistical power to detect the effects of PSI on Average CT.

BSID-II Mental ~ PSI. The study had 80% power to detect effects as small as ß = .032. However, in our model, the estimate for PSI was smaller (ß = .0005). We ran the analysis with 70% of power, but the effect size was still greater than the one obtained with our sample. Therefore, we were underpowered to detect the relationship between PSI and BSID-II Mental Scale Score, assuming that there is a relationship between those variables.

BSID-II Motor ~ PSI. The study had 80% power to detect effects as small as ß = .020. However, in our model, the estimate for PSI was smaller (ß = .002). We ran the analysis with 70% of power, but the effect size was still greater than the one obtained with our sample. Therefore, we were underpowered to detect the relationship between PSI and BSID-II Motor Scale Score, assuming that there is a relationship between those variables.

Appendix C

Auburn University Human Research Protection Program

EXEMPTION REVIEW APPLICATION

For information or help completing this form, contact: **THE OFFICE OF RESEARCH COMPLIANCE,**
Location: 115 Ramsay Hall **Phone:** 334-844-5966 **Email:** IRBAdmin@auburn.edu

Submit completed application and supporting material as one attachment to IRBsubmit@auburn.edu.

1. PROJECT IDENTIFICATION Today'sDate June 10, 2020

a. **Project Title** Relationships between motor, cognitive, and language development in infants and young children

b. **Principal Investigator** Melissa Pangelinan Degree(s) Ph.D.
Rank/Title Assistant Professor Department/School Kinesiology
Phone Number 334-744-4142 AU Email mgp0020@auburn.edu

Faculty Principal Investigator (required if PI isa student) ________
Title________ Department/School________
Phone Number________ AU Email ________

Dept Head Mary Rudisill Department/School Kinesiology
Phone Number 334-844-1458 AU Email rudisme@auburn.edu

c. **Project Personnel** (other PI) – Identify all individuals who will be involved with the conduct of the research and include their role on the project. Role may include design, recruitment, consent process, data collection, data analysis, and reporting. Attach a table if needed for additional personnel.

Personnel Name Julia Sassi Degree (s) M.Ed.
Rank/Title Graduate Student Department/School Kinesiology
Role Data analysis and reporting
AU affiliated? ☒ YES ☐ NO If no, name ofhome institution ________
Plan for IRB approval for non-AU affiliated personnel? ________

Personnel Name Davis Dyke Degree (s) M.Ed.
Rank/Title Graduate student Department/School Kinesiology
Role Data analysis and reporting
AU affiliated? ☒ YES ☐ NO If no, name ofhome institution ________
Plan for IRB approval for non-AU affiliated personnel? ________

Personnel Name________ Degree (s) ________
Rank/Title________ Department/School________
Role
AU affiliated? ☐ YES ☐ NO If no, name ofhome institution ________
Plan for IRB approval for non-AU affiliated personnel? ________

d. **Training** – Have all Key Personnel completed CITI human subjects training (including elective modules related to this research) within the last 3 years? YES ☒ NO ☐

The Auburn University Institutional
Review Board has approved this
Document for use from
___06/21/2020________to____--
-------________Protocol # ___20-

page __of __

AU Exemption
Form Version
05.19.2020

Version Date (date document created):________