

Understanding the Association of Breastfeeding and
Food Insecurity on Brain Function in Early Childhood

Deeana Sehr Ijaz

Submitted in partial fulfillment of the
requirements for the degree of
Doctor of Philosophy
under the Executive Committee
of the Graduate School of Arts and Sciences

COLUMBIA UNIVERSITY

2021

© 2021

Deeana Sehr Ijaz

All Rights Reserved

Abstract

Understanding the Association of Breastfeeding and Food Insecurity on Brain Function in Early Childhood

Deeana Sehr Ijaz

Introduction: The present study aims to understand how the absence of food security and breastfeeding in children at one year of age, which can be considered as adverse childhood experiences, may be associated with brain function as measured by the relative and absolute power spectral density of four frequency bands of brain waves (theta, alpha, beta, and gamma) among a sample of infants from low-socioeconomic (SES) backgrounds at age 12 months old.

Methods: A cross-sectional survey was used by the parent study, Baby's First Years (BFY), to collect quantitative data to understand the associations between breastfeeding, food insecurity, and brain function in a sample of 243 low-SES mothers and their infants at age 12 months old. Breastfeeding was measured as ever breastfed, to understand if a mother had ever initiated breastfeeding of their infant, and breastfeeding duration, measured in months. Household food insecurity (HFI) was measured using the U.S. Household Food Security Survey Module Short Form devised by the USDA. Electroencephalography (EEG) data was collected to assess brain function.

Data Analysis: Data was analyzed to determine associations between being ever breastfed, breastfeeding duration, and the presence of HFI and EEG measured relative and absolute theta, alpha, beta, and gamma power in infants at 12 months of age using multiple linear regression (MLR) models based on ordinary least squares (OLS).

Results: 77% (n=187) of mothers reported breastfeeding their child at least one time. The mean breastfeeding duration (including the mothers that never breastfed) was 3.6 months (SD=4.12).

27.6% (n=67) of mothers were found to be food insecure. Ever breastfeeding an infant during the first year of life was found to be associated with higher absolute theta power ($p < 0.05$), and higher relative and absolute alpha power ($p < 0.01$). Breastfeeding duration was not found to be associated with relative and absolute theta, alpha, beta or gamma power. Finally, the presence of food insecurity was not found to be associated with relative and absolute theta, alpha, beta or gamma power.

Discussion: Differences in brain function may be adaptive for children experiencing adversity because of their lower SES, amongst other factors (Ellis et al., 2020). Ever breastfeeding an infant was associated with higher absolute theta power, which was an unexpected finding. However, relative theta power was not associated with ever breastfeeding, and therefore this finding must cautiously be interpreted. Ever breastfeeding an infant was associated with higher relative and absolute alpha power. It is possible that the increases in relative and absolute alpha power within the sample of infants who were ever breastfed are in part due to the emotional connection that breastfeeding elicits and the characteristics of mothers that decide to initiate breastfeeding as compared to those that do not initiate breastfeeding. This research demonstrates significant associations between ever breastfeeding an infant with brain function in a population of infants from diverse, low SES backgrounds. In contextualizing these changes in brain function as plausible adaptations that infants are developing due to their experiences, an opportunity exists to further explore these associations with brain function to understand the skills that low SES infants are developing during the first year of life.

Table of Contents

Table of Contents	i
Acknowledgments	v
Dedication.....	vii
List of Tables	viii
List of Figures.....	x
Abbreviations	xii
Chapter 1: Introduction.....	1
1.1 Purpose of this Study	1
1.2 Rationale for this Study	1
1.3 Background.....	3
1.4 The Development of the Human Brain	4
1.5 Electroencephalography	5
1.6 Statement of the Problem	8
1.7 Aims and Objectives.....	13
1.8 Parent Study: Baby’s First Years	14
1.9 Scope and Limitations	15
Chapter 2: Literature Review	18
2.1 Understanding Nutritional Impacts on Early Childhood Feeding.....	18
2.2 Nutritional Impact During Gestation.....	21
2.2.1 Folic Acid	22
2.2.2 Choline	23
2.2.3 Vitamin B12	23
2.2.4 Vitamin B6	24

2.2.5 Zinc	24
2.2.6 Iron	26
2.2.7 Iodine.....	26
2.3 Nutrition After Birth.....	27
2.3.1 Physiology of Lactation.....	27
2.3.2 Breast Milk Composition	29
2.4 Malnutrition, Brain Growth, and Development in Early Childhood.....	32
2.4.1 Timing of Nutrient Deprivation.....	33
2.4.2 Degree of Nutrient Deficiency	35
2.4.3 Potential for Recovery	36
2.5 Association between Maternal Health Status, Diet, and Early Childhood Intelligence	37
2.5.1 Obesity.....	38
2.5.2 Inflammation	40
2.5.3 Immunity and Gut Microbiome.....	43
2.6 Breastfeeding Attachment and Infant Cognition	45
2.7 Breastfed vs Formula-Fed and Infant Cognition	46
2.8 EEG Findings	52
2.8.1 EEG: Breastfeeding and Formula Feeding	53
2.9 MRI Findings.....	63
2.10 Neuroplasticity, Socioeconomic Disparities, and Adaptive Brain Function.....	73
2.11 Household Food Insecurity.....	74
2.11.1 Identifying Potential Risk Factors	75
2.11.2 Factors Impacting Food Insecurity	76
2.12 Association between Food Insecurity and Breastfeeding.....	78

2.13 Household Food Insecurity and Infant Nutrition.....	78
2.14 Household Food Insecurity and Infant Cognitive Development.....	79
2.15 Household Food Insecurity and Childhood Academic Performance	81
Chapter 3: Methods	83
3.1 Introduction	83
3.2 Research Questions and Hypotheses.....	83
3.3 Study Design	84
3.4 Target Population	85
3.4.1 Baby’s First Years: Sampling and Data Collection.....	85
3.5 Current Study: Association of Breastfeeding and Food Insecurity on Brain Function in Early Childhood.....	89
3.5.1 Ever Breastfeeding and Breastfeeding Duration	89
3.5.2 Household Food Insecurity.....	89
3.5.3 Covariates	93
3.5.4 EEG	95
3.6 Data Analysis Plan	98
3.7 Power Analysis.....	102
Chapter 4: Results.....	103
4.1 Sample characteristics	103
4.2 Descriptive statistics: breastfeeding and household food insecurity.....	106
4.3 Descriptive statistics: infant EEG brain wave frequencies.....	108
4.4 Bivariate descriptive statistics for brain waves and breastfeeding, food insecurity....	110
4.5 Additional bivariate exploration for the household food insecurity and breastfeeding	116

4.6 MLR Results Introduction	120
4.6.1 MLR results for relative and absolute theta power	123
4.6.2 MLR results for relative and absolute alpha power.....	127
4.6.3 MLR results for relative and absolute beta power.....	129
4.6.4 MLR results for relative and absolute gamma power	131
4.7 Interpretation of Findings	133
4.8 Summary of MLR: Significant Main Effects	133
Chapter 5: Discussion.....	136
5.1 Purpose and Main Findings	136
Key Takeaway #1	138
Key Takeaway #2	140
Key Takeaway #3	141
Key Takeaway #4	142
5.2 Additional Findings	144
5.3 Limitations.....	146
5.4 Strengths	148
5.5 Implications	150
References	154
Appendix	184

Acknowledgments

I would like to first and foremost acknowledge with gratitude, my advisor, Dr. Randi Wolf, who has challenged me and supported my development as a researcher during my tenure at Teachers College. I am equally grateful to Drs. Pam Koch and Isobel Contento, who helped me realize my research goals. To Dr. Kim Noble, I am incredibly thankful for your trust in me to engage in your lab and conduct my research utilizing data from the Baby's First Years study and it is through your support that I am realizing the dream of studying nutritional associations with brain function in early childhood. Dr. Sonya Troller-Renfree, thank you for your time, guidance, and knowledge sharing that allowed me to enter this field of study. I am also grateful to Mr. Harold Taylor, my third, fourth, and fifth grade teacher who taught me how to have the mind of an intellectual coupled with the curiosity of a child.

It is through the blessings of my amazing family that I have been able to dedicate the time and resources to pursuing my doctorate degree. My parents, Mujeeb and Sabiha Ijaz have been my constant supporters in each of my educational pursuits, allowing me to feel free to pursue knowledge without constraints and with love. My husband, Muzzamil, moved to NYC with me solely to support my dream and was my confidant throughout my studies that kept me energized in the pursuit of my goal. My daughter Isra, at not even two years of age, has sacrificed and supported me in ways that are beyond her years. My grandmother, Dr. Lubna Ijaz, served as a role model for me and through her life I found the validation that I too can pursue education while balancing my time as a mother. My grandfather, Noor ul Haq Khan instilled in me a gratitude and wonder for science, as he admired all things natural as evidence of God's grace. My siblings, Shazia and Ibrahim, were my forever editors and idea-sounding

boards at each step in my life, especially during my doctorate. My mother-in-law, Kausar Ahmed, was always there to help with Isra to allow me time to complete my work, and I am grateful for that love and support I have found in her.

I am also grateful for my faith and for God's blessings that have brought me to this point in my life. I believe wholeheartedly that it is through prayer that I have been blessed to be able to pursue my doctorate at a world-renowned university amongst brilliant colleagues and amazing advisors. Alhumdolillah (God is great).

Dedication

This work is dedicated to my curious and loving daughter, Isra Sehr, my ever present and constantly supportive husband Muzzamil, my parents Mujeeb and Sabiha who made sure that every dream of mine became a reality, and to my grandparents, Bushra Khan and the late Dr. Mujaddid Ijaz, Dr. Lubna Razia Ijaz, and Noor ul Haq Khan, who showed me the value of education and perseverance and established in me a drive to pursue my doctorate.

List of Tables

Table 1 Literature Review Matrix of EEG and Breastfeeding vs. Formula Feeding Studies .	62
Table 2 Literature Review Matrix of MRI and Breastfeeding vs. Formula Feeding Studies..	70
Table 3 Measurement of Breastfeeding.....	89
Table 4 U.S. Household Food Security Survey (FSS) Module Short Form.....	90
Table 5 Food security status for households	91
Table 6 Covariates.....	93
Table 7 Correlation table for selected numeric predictor variables.....	100
Table 8 Characteristics of Mothers (n=243).....	104
Table 9 Maternal participation in selected social services (n=243)	105
Table 10 Mother's Breastfeeding Behaviors and Household Food Insecurity.....	106
Table 11 A crosstabulation of ever breastfed and breastfeeding duration	107
Table 12 A crosstabulation of household food insecurity (HFI) status and the Household Food Security Survey Raw Score	108
Table 13 Descriptive statistics for infant EEG (n=243)	108
Table 14 Correlation table for dependent and independent variables	111
Table 15 Independent t-tests ever breastfed and relative theta, alpha, gamma and beta power	112
Table 16 Independent t-tests HFI and relative and absolute theta, alpha, gamma and beta power	112
Table 17 Bivariate association of SNAP participation and ever breastfed.....	116
Table 18 Bivariate association of WIC participation and ever breastfed.....	116
Table 19 Bivariate association of SNAP participation and food insecurity	117
Table 20 Bivariate association of WIC participation and food insecurity	117
Table 21 Covariates broken down by ever breastfed	118

Table 22 Covariates broken down by household food insecurity (HFI)	120
Table 23 Relative and absolute theta power MLR results, effect size and standard errors reported.....	124
Table 24 Relative and absolute alpha power MLR model results, effect size and standard errors reported.....	127
Table 25 Relative and absolute beta power MLR model results, effect size and standard errors reported.....	129
Table 26 Relative and absolute gamma power MLR model results, effect size and standard errors reported	131
Table 27 Summary of effect size on household food insecurity, ever breastfed, and breastfeeding duration for relative and absolute theta, alpha, beta, and gamma power.....	133
Table 28 Summary of significant covariate associations for relative and absolute theta, alpha, beta, and gamma power	134

List of Figures

Figure 1 Theoretical model positing that nutritional status is a predictor of infant brain development and function (Prado & Dewey, 2014).....	2
Figure 2 The five bands of human brain waves (delta, theta, alpha, beta, and gamma). Adapted from Ahbang, Suresh, & Mehrotra (2016, p. 19).	6
Figure 3 Consort diagram.....	86
Figure 4 BFY Study Timeline and Current Study Data Collection.....	88
Figure 5 Percentage of household reporting each indicator of food insecurity, by food security status, 2019 (Coleman-Jensen et al., 2019)	91
Figure 6 Electrode Groupings by Region (Troller-Renfree, et al., 2020)	97
Figure 7: Flow chart illustrating the sample used in this study	99
Figure 8 Histograms of relative theta, alpha, beta, and gamma power	109
Figure 9 Histograms of absolute theta, alpha, beta, and gamma power ($\mu\text{V}^2/\text{Hz}$)	109
Figure 10 Boxplots of relative theta, alpha, beta, and gamma power split by whether an infant was ever breastfed or not.....	113
Figure 11 Boxplots of absolute theta, alpha, beta, and gamma power ($\mu\text{V}^2/\text{Hz}$) split by whether an infant was ever breastfed or not.....	113
Figure 12 Scatterplots of relative theta, alpha, beta, and gamma power and breastfeeding duration (months)	114
Figure 13 Scatterplots of absolute theta, alpha, beta, and gamma power ($\mu\text{V}^2/\text{Hz}$) and breastfeeding duration (months).....	114
Figure 14 Box plots of relative theta, alpha, beta, and gamma power and Household Food Insecurity (HFI)	115
Figure 15 Box plots of absolute theta, alpha, beta, and gamma power ($\mu\text{V}^2/\text{Hz}$) and Household Food Insecurity (HFI).....	115

Figure 16 Theta, alpha, beta, and gamma brain waves with corresponding expected directionality for breastfed infants who are food secure	123
Figure 17. A complete correlation matrix of all independent variables and covariates used in study (n=243).....	184

Abbreviations

β	Partial regression coefficient
CI	Confidence interval
CIX	Composite Intelligence Index
DRI	Dietary reference intake
DV	Dependent variable
EEG	Electroencephalography
ERP	Event related potential
ERS	Economic Research Service
FFT	Fast Fourier Transformation
HFI	Household food insecurity
Hz	Cycles per second
IC	Independent components
IDA	Iron deficiency anemia
IQ	Intelligence Quotient
IV	Independent variable
MLR	Multiple linear regression
MRI	Magnetic resonance imaging
NIH	National Institute of Health
NLM	National Library of Medicine
LIHEAP	Low Income Home Energy Assistance Program
PEM	Protein-energy malnutrition
PHQ-8	Patient Health Questionnaire-8
PUFA	Polyunsaturated fatty acid
OLS	Ordinary least squares

p	Probability value associated with inferential test statistic
PDI	Psychomotor Development Index
PSD	Power spectral density
SD	Standard deviation
SE	Standard error
SEM	Structural equation modeling
SES	Socio-economic status
SNAP	Supplemental Nutrition Assistance Program
t	t-test statistic
R ²	R squared (indicating proportion of variance explained).
USDA	United States Department of Agriculture
μV ² /Hz	Micro Volts squared per Hertz
WIC	Women, Infants, & Children
WHO	World Health Organization

Chapter 1: Introduction

Early feeding behaviors and circumstances predict subsequent feeding behaviors in childhood. For example, both duration of breastfeeding and the presence of food insecurity can serve as predictors of nutrition in early childhood (Hanson & Connor, 2014; Perrine et al., 2014; Soldateli et al., 2016). While breastfeeding and household food insecurity have been linked with children's cognitive development, the extent to which these behaviors and circumstances relate to children's brain development in the first year of a child's life is less explored and understood. An opportunity exists to understand the connections between breastfeeding, food insecurity, and brain development in early childhood.

1.1 Purpose of this Study

The overall purpose of the present study is to examine the relationship between nutritional status and brain function in early childhood. More specifically, the purpose is to determine the extent to which being breastfed, duration of breastfeeding, and household food insecurity may be associated with brain function, as measured by electroencephalography (EEG), among infants at 12 months of age participating in a large NIH-funded study, Baby First Years. This chapter presents the rationale, background, methodology, research problem, aims, objectives, and limitations of the study.

1.2 Rationale for this Study

Theoretical and practical reasons drive the need for more research on the relationships between the brain function and nutritional status of infants. The theoretical framework is underpinned by the hypothetical model outlined by the flow diagram in Figure 1.

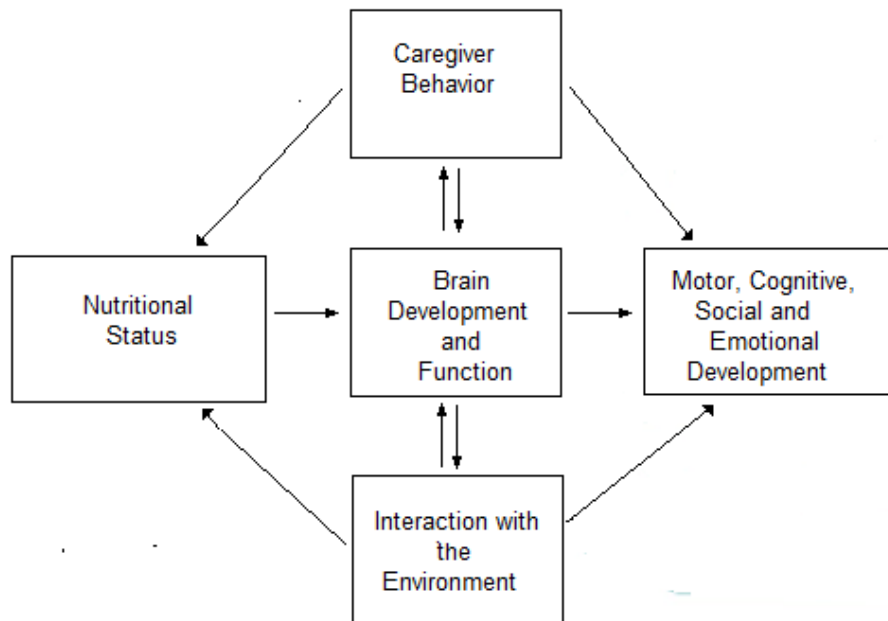


Figure 1 Theoretical model positing that nutritional status is a predictor of infant brain development and function (Prado & Dewey, 2014)

This model illustrates the hypothesis that nutritional status has an impact on the development and functioning of the infant brain, which, in turn has an impact on the motor, cognitive, and social emotional development of the infant. Moreover, the direct relationship between nutritional status and infant brain development and function may be mediated indirectly by at least two pathways. The first pathway develops via caregiver behavior (e.g., the maternal provision of the physical and psychological needs of the infant) and the second pathway develops via interaction with the environment (e.g., the infants’ experiences of visual, auditory, tactile, and other forms of sensory stimulation). This model predicts that high risk infants experiencing poor nutrition, sub-optimal caregiver behavior, and poor environmental stimulation will ultimately perform at lower levels in terms of motor, cognitive, social, and emotional development. In contrast, infants experiencing optimal nutrition, caregiver behavior, and environmental stimulation will ultimately perform at higher levels in terms of motor, cognitive, social, and emotional development.

Empirical evidence is currently available in literature reviews and meta-analyses to support the model depicted in Figure 1. Chatterjee and Saumitra (2016) concluded that

malnutrition during the first two years of life is a major risk factor for poor neurodevelopment, leading to motor, cognitive and speech delay, as well as behavioral problems and learning disabilities. Schwarzenburg et al. (2018) concluded that nutritional status in the first two years of life is a crucial factor in a child's neurodevelopment associated with lifelong mental and physical health. Georgieff et al. (2020) concluded that a better understanding of the impact of nutrition will have a significant impact on improving the neurodevelopment and brain function of infants.

The practical reasons are that more research to improve understanding of the impact of nutrition on infant brain function will have significant implications for public health and social change. About 219 million children, representing about 1% of the 2.2 billion children in the world, experience sub-optimal neural, cognitive, language, and motor development, associated with malnutrition (Sudfeld et al., 2015). About 6.5% of U.S. households with children experience food insecurity, (United States Department of Agriculture, 2019) a risk factor for malnutrition with possible long-term consequences for the education, job potential, mental and physical health of the adult U.S. population (Dauncey, 2009; Wachs et al., 2014; Cusick & Georgieff, 2016). Morris et al. (2008) predicted that the correction of nutritional deficits associated with neurological deficiencies during early childhood may increase the average intelligence quotient of the adult population by 10 points. Prioritizing the provision of optimal nutrition will ensure that infants have an early foundation for optimal neurodevelopment and subsequent long-term health and well-being (Shwarzenberg et al., 2018).

1.3 Background

The rate of development of the human brain does not remain constant over an individual's lifetime. Much of the human brain's ultimate structure, capacity, and function is determined during a critical period in the first 1000 days of life (i.e., between conception and about two years old) when the foundations of good physical and mental health are established

(Cusick & Georgieff, 2016). This critical period is characterized by a high level of phenotypic plasticity, when exogenous factors, including nutrition, medications, pollutants, and environmental interaction, have long-term effects on brain development (Cusick & Georgieff, 2016; Georgieff, Brunette, & Tran, 2015; Fox, Levitt, & Nelson, 2001; Wachs et al., 2014). Early experiences of adversity during this critical period, (e.g., poverty, malnourishment, maltreatment, and exposure to toxic chemicals) may have detrimental effects on brain structure and function related to the physical, social, cognitive, and emotional development of infants, children, and adults (De Oliveira et al., 2020; Child Welfare Information Gateway, 2015; Mackes et al., 2020).

Due to recent advances in EEG, neuroscientists have developed a better understanding of the sensitivity of infant brain function to adverse early experiences (Michel et al., 2015; Pavlakis et al., 2015; Saby & Marshall, 2012); however, many questions remain to be answered regarding how and why specific patterns of infant brain activity are directly or indirectly related to specific early periods of adversity (Braithwaite et al., 2020; Brito et al., 2020; Jones et al., 2020).

1.4 The Development of the Human Brain

The human brain begins to develop prenatally as the neural plate folds inwards to form the neural tube, which is the starting point of the spinal cord and brain. During gestation, neurodevelopment includes the forming of neurons, glial cells, axons, dendrites, and ultimately synapse connections between neurons that allows for signaling between cells (Couperus & Nelson, 2006). Johnson (2003) describes how the first year after birth is characterized by rapid rates of cell division and differentiation in the brain (e.g., the proliferation of neurons, axons and dendrites, and the development of the hippocampus, visual and auditory cortices, language processing areas, and prefrontal cortex) as well as connectedness (i.e., myelination, and synaptogenesis) which form the basis of normal perception and cognition

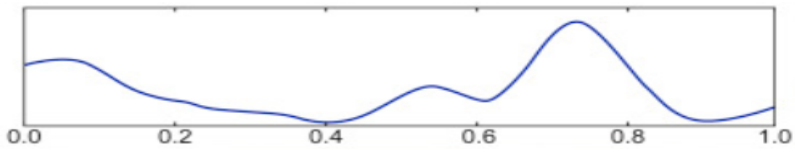
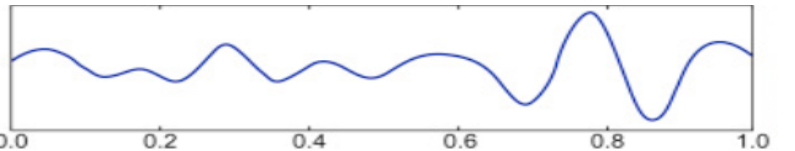
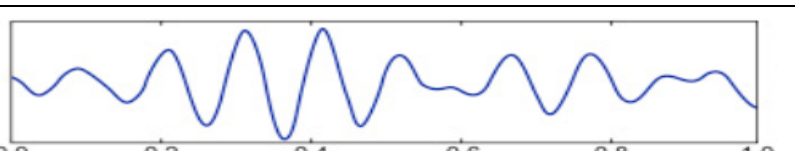
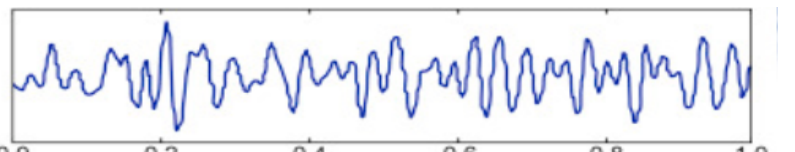
Prado and Dewey (2014) define five key neurodevelopmental processes of consequence during gestation and early childhood that directly impact brain structure and function. All of these developmental processes are directly correlated with nutrient needs during gestation and early childhood as seen in either or both human and animal models. The five processes are neuron proliferation; axon and dendrite growth; synapse formation; pruning, and function; myelination, and apoptosis. Neuron proliferation is the creation of new neurons through cell division, which begins at seven weeks gestation and continues until five months postpartum but occurs subsequently at a much lower frequency. Axons and dendrites are the connectors to neuron cell bodies from other cell bodies. The growth of axons and dendrites starts at 15 weeks into gestation and continues after birth, up until two years of age. Synapses are the connections that form between axons and dendrites and neurons. The process of synapse formation begins around week 23 of gestation and continues through the first year of life. Pruning of synapse connections begins after two years of age and continues into adolescence following an overproduction of synapses in the first two years of life. Myelin is a fatty substance that covers the axons of neurons and helps facilitate speedy cell signaling in the form of nerve impulses. Myelination of axons begins at the time of axon proliferation (as early as 14 weeks gestation) and continues until adulthood; however, the most significant amount of myelination occurs during gestation through two years of age. Apoptosis, otherwise known as programmed cell death, is critical to proper development as more than half of the cells that are produced in the brain die off. This process begins during gestation and continues through adolescence.

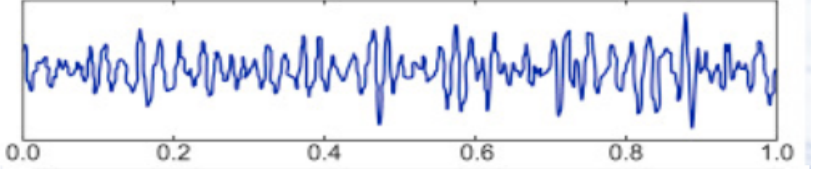
1.5 Electroencephalography

EEG is the ideal methodology with which to examine brain function and development in early childhood, because the measurements are relatively inexpensive and simple to perform non-invasively using an array of electrodes placed on the scalp to record brain activity

(Pavlakakis et al., 2015). EEG measures brain activity in terms of the rhythmic patterns of electrical voltages associated with groups of neurons communicating with each other via synchronized oscillatory activity (Buzsáki, 2006). Analysis of fluctuations in the power or amplitude of brain waves reflects a spectrum of frequency bands, ranging along a continuum from slow and simple Delta waves to fast and complex Gamma waves. The power of a brain wave is measured in terms of voltage, between the peaks of the waveforms. EEG serves as a tool for neurological, cognitive, and behavioral research (Buzsáki, 2006) and for the diagnostic assessment of brain dysfunction (Britton et al., 2016). Figure 2 depicts the five bandwidths of human brain waves (delta, theta, alpha, beta, and gamma) measured in Hz (cycles per second) which play a major role in brain function.

Figure 2 The five bands of human brain waves (delta, theta, alpha, beta, and gamma). Adapted from Ahbang, Suresh, & Mehrotra (2016, p. 19).

Bandwidth	Normal frequency range in adults	Typical electroencephalograph
Delta (δ)	0.5–4 Hz	
Theta (θ)	4–7 Hz	
Alpha (α)	8–12 Hz	
Beta (β)	12–30 Hz	

Bandwidth	Normal frequency range in adults	Typical electroencephalograph
Gamma (γ)	30-100 Hz	

Delta waves with high amplitude arise in the thalamus and are produced during a state of deep dreamless sleep. Between birth and two years old, the human brain functions mainly by means of this slowest of brain-wave cycles (Saby & Marshall, 2010). Delta waves dominate the brain function of infants at birth, explaining why newborn babies do not remain awake for long. At age one, when an infant is awake more often, Delta waves are less predominant (St. Louis & Frey, 2016). For this reason, delta waves will not be examined in this study.

Theta waves reflect activity from the limbic system and hippocampal regions of the brain; however, the scalp distribution of theta rhythm in infants depends on age, reflecting the engagement of different brain networks during growth (Orekhova et al., 2006). A prominent buildup of theta waves develops during periods of light dreamless sleep and drowsiness in infants between 6-12 months old (St. Louis & Frey, 2016). At age one, the infants' brain spends much of its time producing theta brainwave cycles, but theta activity subsequently declines during childhood (Perone et al., 2018). The modulation of theta activity in infants is associated with the development of cognitive skills (Jones et al., 2010) and the regulation of responses (Michel et al., 2015). Braithwaite et al. (2020) found that differences in frontal theta power in six-month old infants, related to different interactions with caregivers, significantly predicted differences in non-verbal cognitive ability. Adversity in early childhood has been linked to increased theta power (Marshall et al., 2004, Troller-Renfree et al., 2020).

Alpha waves are predominantly recorded from the occipital lobes during wakeful relaxation, when the eyes are closed, and the brain is not processing a lot of information (Saby & Marshall, 2010). The highest levels of alpha power are associated with an elevated state of anxiety (Dadashi et al., 2016). By two months, a precursor of the alpha wave (3-4-Hz) has established, increasing to 4 -5 Hz at six months, reaching 5-7 Hz at age 12 months, and finally stabilizing within the normal adult alpha frequency range (8 -12 Hz) by three years (St. Louis & Frey, 2016). Adversity in early childhood has been linked to reduced alpha power (Marshall et al., 2004, Troller-Renfree et al, 2020).

High speed beta waves are produced in the frontal and parietal regions of the brain when a child is conscious, awake, alert, focused, listening, and thinking (Saby & Marshall, 2010). Typical beta activity in the 12-14 Hz range typically emerges between the ages of one and two years (St. Louis & Frey, 2016). A high level of beta power in children reflects cognitive development outcomes (Perone et al., 2018).

Gamma are the fastest and most complex brain waves produced in every part of the brain during periods of concentration, information processing, learning, and problem solving (Saby & Marshall, 2010). High gamma activity in children is positively associated with cognitive developmental outcomes. Children with learning difficulties may have lower-power gamma waves (St. Louis & Frey, 2016). Better memory skill is associated with well-regulated and efficient gamma activity (Perone et al., 2018). Adversity in early childhood has been linked to lower frontal gamma power (Tomalski et al., 2013).

1.6 Statement of the Problem

Among the numerous factors that influence the development, structure, and function of an infant's brain during the first two years of life, three stand out as generating the most profound long-term problems: toxic stress, infant-caregiver attachment, and nutrition (Cusick & Georgieff, 2016). Toxic stress is defined as prolonged activation of the physiological

responses of the body to severe adversity, associated with a lack of nurturance, including poor nutrition and physical abuse. Toxic stress during childhood results in derangement of the neuro-endocrine-immune response system, prolonged cortisol activation, and a risk of changes to brain structure and function, resulting in mood disorders, behavioral dysregulation, and psychosis (Franke, 2014; Dowd, 2017).

Infant-caregiver attachment is the deep emotional connection that an infant develops with his or her primary caregiver, usually the mother. The quality of this attachment is associated with specific patterns and intensity levels of stimulating an infant's sensory system, which directly or indirectly have an impact on brain development, and subsequently contribute to emotionality, cognition, and mental health (Sullivan et al., 2011). Breastfeeding improves the quality of maternal-infant attachment through the production of prolactin and oxytocin associated with lower levels of maternal and infant stress, and enhanced emotional bonding (Liu et al., 2014).

This study focuses on addressing the problem of how nutritional factors, in particular breastfeeding and food insecurity, are related to the functioning of an infant's brain during the first year of life, as observed by EEG. The main reason for focusing on this topic is that more research effort needs to be directed toward achieving a better understanding of the adverse effects of poor nutrition on the neurodevelopment of vulnerable children (De Oliveira et al., 2020; Mackes et al., 2020). An improved understanding of how breastfeeding and food insecurity are related to the functioning of an infants' brain will ensure that public health policies and interventions designed to improve the nutrition-related brain development of infants are underpinned by objective research-based evidence (Shwarzenberg et al., 2018).

The Dietary Reference Intakes (DRIs) developed by the Institute of Medicine (2007) are not underpinned directly by a public health policy that aims to develop healthy brain structure and function in infants. The DRIs for infants are based on the results of evidence-

based research describing the nutrient content of foods consumed by healthy infants with normal growth patterns, including the nutrient content of breast milk. The DRIs for vitamins, minerals, protein, and energy are set at levels that are high enough to satisfy the average nutrient requirements of most healthy infants. It is impossible to define exact DRIs that promote healthy brain development in all infants, because each infant is unique. Infants differ in the amount of nutrients they need, depending on gender, age, body composition, growth rates, physical activity, and many other factors. Infants with medical problems or special needs have different DRIs than healthy infants (Butt et al., 2010).

The DRIs are not designed to promote critically important prenatal development processes in the brain that are dependent on key micronutrients including folic acid, vitamin A, and copper (Couperus & Nelson, 2006). The DRIs were not based on research concluding that the normal development of the postnatal brain may be impacted by deficiencies in protein, long-chain polyunsaturated fatty acids, iron, zinc, iodine, thyroid hormones, and B-vitamins (Innis, 2008; 2014; Prado & Dewey, 2014; Cusick & Georgieff, 2016).

The DRIs take into account that breast milk and formula milk both provide hydration, energy, and nutrients, but they do not take into account the advantage that breast milk naturally contains more of the antibodies, hormones, vitamins, minerals, long-chain fatty acids, and enzymes required by a healthy infant; consequently, breast milk is recommended as the best nutrition for infants (American Academy of Pediatrics, 2012). Several studies have described behavioral and cognitive differences between breast-fed vs. formula-fed infants that may be associated with differences in early brain development. For example, breast-fed infants process speech differently from bottle-fed infants (Ferguson & Molfese, 2007; Pivik et al., 2011); the duration of breastfeeding is associated with differences in infants' responses to emotional body expressions (Krol et al., 2014); breastfed infants develop improved cognitive abilities compared to formula-fed infants (Deoni et al., 2018; Huang et al., 2014; Mackes et al., 2016;

Horta et al., 2015; Luby et al, 2016; Nyardi et al., 2013) and breastfeeding protects against children internalizing behavior problems (Liu et al., 2014).

The 2020-2025 Dietary Guidelines for Americans released by the USDA recommend that for the first six months of life, infants should be fed exclusively human breast milk and at six months of age, infants should be introduced to complimentary, nutrient dense foods (USDA, 2020). These guidelines suggest continuing to feed infants human milk through at least the first year of life, and longer if desired. When human milk is unavailable, they suggest feeding infants iron-fortified infant formula. Finally, they suggest that when infants wean from human milk or infant formula, to transition to a healthy dietary pattern.

In contrast, little is known about how and why breastfeeding has an impact on the structure and function of the infant brain. Only a few researchers have examined the effects of nutrition and associated factors on the EEG spectrum of infants. Various types of early adversity, including lower socioeconomic status (Tomalski et al., 2013), maternal stress (Troller-Renfree et al., 2020), and institutionalization (Marshall et al., 2004) may be associated with differences in the power of different EEG wavebands. Adversity during early childhood has been linked to lower frontal gamma power (Tomalski et al., 2013), increased theta power (Marshall et al., 2004, Troller-Renfree et al, 2020) and reduced alpha power (Marshall et al., 2004, Troller-Renfree et al, 2020). Braithwaite et al. (2020) found that differences in frontal theta power in six-month old infants, related to different interactions with caregivers, significantly predicted differences in non-verbal cognitive ability.

Taboado-Crispi (2018) observed the resting brain EEG spectra of two groups of children between the ages of five and eleven in Barbados sitting in a comfortable armchair, with closed eyes, but not sleeping. Reduced alpha and beta power and increased theta power were observed in the EEG spectra of one group of infants who were diagnosed with protein-energy malnutrition (PEM) compared with that of a matched healthy control group. The PEM

group also contained a higher percentage of EEG abnormalities compared to controls, including frequency of rhythmic background activity, focal abnormality, paroxysmal activity, diffuse slow wave activity, and presence of sharp waves. This study highlighted that EEG technology is a convenient source of measurable and affordable data for assessing the relationships between brain function and nutritional status in early childhood. The implications are that more research is warranted to examine how feeding on breastmilk vs. formula-milk may have an impact on the functioning of the infant brain based on analysis of EEG spectra.

It is possible that the characteristics of the primary caregivers (specifically the mothers) who make the decision to breast-feed or bottle-feed may indirectly shape the neural activity patterns of their infants. Monk et al. (2013) suggested that poor maternal nutrition is a risk factor that may influence infant neurocognitive development. The quality of the mother's diet is a confounding factor because both maternal diet and human milk composition are jointly linked to the neurological development of infants (Innis, 2014).

The poor quality of the diet of mothers is encompassed within the term household food insecurity (HFI) defined as “the lack of physical, social, and economic access to sufficient, safe, and nutritious food to meet the dietary needs and food preferences for an active and healthy life” (Food and Agriculture Organization, 2013, p.1). HFI can be categorized as mild, moderate, or severe, but the longer the exposure to severe HFI the greater the probability that childhood development will be negatively impacted (De Oliveira et al., 2020).

HFI is a stressor which has been found to have significant adverse effects during childhood on the development of academic and social skills, (Hobbs & King, 2018; Johnson & Markowitz, 2018); verbal communication skills (Saha et al., 2010); and motor skills, including control and coordination of fine movement (Milner et al., 2018). A meta-analysis concluded that HFI was most closely associated with abnormal development of vocabulary and math

skills, and marginally associated with abnormal development of reading skills motor development (De Oliveira et al., 2020).

HFI is not only a low-income country problem, but also a common condition in the United States, where household food insecurity affected 13.6 percent of households with children in 2019 (Coleman-Jensen et al., 2020). Historically the rates of food insecurity for U.S. households with children were greatest for single parents as well as African American and Hispanic households with below-poverty income levels (Nord et al., 2011). More recently, the United States Department of Agriculture (2019) reported that in about 0.6% of households with children in the USA, one or more children experienced severe sub-optimal food intake at some time during 2019. At this time, data regarding the impact of the COVID-19 pandemic on food insecurity in the United States has not been released or analyzed by the USDA.

1.7 Aims and Objectives

In the light of the problem described above, the overall aim of this quantitative study is to determine the extent to which being breastfed, duration of breastfeeding, and household food insecurity may be predictors of the relative and absolute power spectral density of four frequency bands of brain waves (theta, alpha, beta, and gamma) as measured by electroencephalography (EEG) among a sample of infants at age 12 months old. The specific objectives are as follows:

1: To understand the relationship between breastfeeding and brain function in infants at 12 months of age.

1.1: To understand how relative and absolute theta, alpha, beta, and gamma waves, as measured by EEG, among infants at age 12 months, are related to whether or not the infants have ever been breastfed.

1.2: To understand how relative and absolute theta, alpha, beta, and gamma, as measured by EEG, among infants at age 12 months, are related to the mother's duration of breastfeeding.

2: To understand how relative and absolute theta, alpha, beta, and gamma, as measured by EEG, among infants at age 12 months, are related to household food insecurity.

The research questions and hypotheses linked to these objectives are presented in Chapter 2.

1.8 Parent Study: Baby's First Years

Baby's First Years (BFY) is an ongoing randomized clinical trial funded by the National Institute of Health (NIH) (R01HD087384-01) and overseen by primary investigators Dr. Katherine Magnuson, PhD and Dr. Kimberly Noble, MD, PhD and supported by a consortium of more than two dozen foundations. BFY is designed to fill a gap in scientific knowledge to understand the impact economic input can have on early childhood development (National Library of Medicine, NCT03593356). One thousand mothers of infants living below the federal poverty line were recruited across four metropolitan areas in the United States shortly after giving birth. Mothers and their infants were randomized to receive a monthly unconditional cash gift of either \$333 (high-cash gift group) or \$20 (low-cash gift group) for the first several years of their child's life. Researchers will evaluate the impact of added income on the children's cognitive, behavioral, and brain development annually for the first several years of life. This study is the first of its kind in that it will be able to demonstrate the causal impacts of unconditional cash gifts on childhood development among low-income families, research that can have a profound impact on policy and practice in the United States. The present study is utilizing data collected for the BFY study within the low-cash gift (control) group only.

1.9 Scope and Limitations

The dependent variables in this study are restricted to child brain function, defined as relative and absolute theta, alpha, beta, and gamma. The independent variables are restricted to the duration of breastfeeding (months); whether the infant has ever been breastfed (yes or no), and the level of food insecurity. Food insecurity is based on the five questions of the six-item U.S. Household Food Security Survey (FSS) Module Short Form, which was included in the Baby's First Years (BFY) Age 1 Survey. The BFY instrument also collected information about other variables which will be used as covariates in the present study, including maternal age, ethnicity/race, mental and physical health, education, substance use (i.e., smoking and drinking behaviors), and economic stress of the mothers. An additional covariate used in this study is epoch count, which represents segments for analysis within theta, alpha, beta, and gamma waves as measured by EEG.

The scope of this study is restricted to a retrospective analysis of data collected for the parent study, BFY, for 243 infants at age one year (who provide the EEG data) and their mothers (who provide the breastfeeding and household food insecurity data). As explained earlier, only infants which were randomized into the low-cash gift group are used. This sample consisted of mothers who gave birth in 12 different hospitals in four different states (NY, LA, NE, MN). External validity is compromised to the extent that this sample is not a nationally representative sample. This is described further in later chapters as the sample is introduced and described.

The main threat to the internal validity of this study is a Type IV error, meaning that the choice of statistical methods to achieve the aims and objectives is incorrect (Tabachnick & Fidell, 2013). Describing the bivariate associations or correlations between brain function, breastfeeding, and household food insecurity are not appropriate statistical methods. In statistical terms, an association implies simply that the distributions of two categorical

variables are related in such a way that the observed distributions are probably not caused by coincidence, with no indication of the strength or direction of the relationship (Agresti, 2013). Correlation analysis simply estimates the extent to which the statistical relationship between two quantitative variables is monotonic or non-monotonic, linear or non-linear, positive or negative, weak or strong, without assuming causation or taking into account the confounding effects of covariates (Ward, 2013; Hung et al.,2017).

We minimize this potential threat by constructing multivariate statistical models that facilitate the prediction of the average value of a dependent variable for any given fixed value of an independent/explanatory variable, after controlling for the confounding effects of other independent/explanatory variables and covariates. The main limitation of predictive models based on a multivariate statistical analysis of cross-sectional data is that prediction does not necessarily imply causation. The analysis of causal relationships requires an experimental design in which the independent variables are antecedents that can be manipulated in order to determine their subsequent effects on the dependent variables (Pearl, 2009). However, for ethical and logistical reasons, it is impossible to conduct an experiment to determine the effects of manipulating the breastfeeding behavior and household food insecurity of groups of mothers on the brain functions of their infants.

The inability to prove causal relationships is not a severe limitation, because an empirical model based on reliably measured variables that accurately and precisely predicts a realistic outcome offers a working hypothesis to underpin future research that may ultimately identify causal relationships (Collier, Sekhon, & Stark, 2010). This study is therefore only a starting point in the research to ultimately determine the extent to which breastfeeding and household food insecurity are the root causes of differences in the brain function of infants at age 12 months, as measured by the spectrum of theta, alpha, beta, and gamma waves, using EEG.

Chapter 2: Literature Review

This chapter will review the relevant literature related to factors associated with infant brain function, specifically breastfeeding and food insecurity.

2.1 Understanding Nutritional Impacts on Early Childhood Feeding

Breastfeeding is widely acknowledged as the most natural and beneficial method for feeding infants because of its association with numerous health benefits for both mother and baby. The World Health Organization recommends that infants worldwide be exclusively breastfed until six months of age to allow for normal growth and then continue as a form of complementary feeding until they reach at least two years old (WHO, 2020). The demonstrated health benefits related to breastfeeding are associated with the combined action of the nutritional aspects and bioactive components found in human milk. Human breast milk contains proteins, lipids, vitamins, minerals, enzymes, hormones, cytokines, and more, that offer countless advantages over infant milk formulas as they are key micronutrients essential to increase immune responses, decrease inflammation, and promote central nervous system development.

The first 12 months of life is one of the most important times for growth and nutrition. There is increasing evidence that early brain development has a long-term influence on childhood and adult health outcomes, intelligence, and aptitude. Recent research has highlighted the importance of breastfeeding as one of the more important elements of health programming (Laouar, 2020). The Centers of Disease Control and Prevention (CDC, 2020), World Health Organization (WHO, 2020), American Academy of Pediatrics (AAP, 2012), and United Nations International Children's Emergency Fund (UNICEF) promote breastfeeding as

a key strategy for improving infant health by implementing policies and promulgating recommendations to meet the Healthy People 2030 Breastfeeding Objectives (Haskins, 2017).

According to the CDC, nearly all infants receive some human breast milk. However, the majority are not exclusively breastfeeding or continue to breastfeed as recommended for the first six months. Only one in four children born in the United States meet these parameters. It has also been found that breastfeeding is less common among women that are considered minorities and those that are qualified to receive benefits through the Special Supplemental Nutrition Program for Women, Infants, and Children program (WIC). The National Immunization Survey (CDC, 2020) data shows that infants born to non-Hispanic Black women (73.7%) are least likely to ever breastfeed when compared with Hispanic infants (84.1%) and Asian infants (90%). In addition, infants eligible for and receiving WIC benefits are less likely to ever be breastfed (77.0%).

Food security within the US continues to be a problem for families with children as well. The United States Department of Agriculture (USDA) reported that over 13.7 million U.S. households were food insecure. Among these households, over 7.2 million included at least one child, with rates appearing even higher among Hispanic and Black non-Hispanic households and those that met the Federal poverty guidelines (USDA, 2019). Children living in households with lower-than-average incomes and impoverished neighborhoods are at risk of higher incidence of food insecurity despite state and federal food assistance programs to the extent that it is considered a major health crisis (Morrissey et al., 2016; Gundersen & Ziliak, 2018).

How does breastfeeding enhance early brain physiology and cognition, and food insecurity potentially impede normal growth and development? A literature review of 17 studies examining the link between breastfeeding and intelligence tests showed that in a random-effects model, breastfed subjects had a higher IQ than non-breast-fed subjects [mean

difference: 3.44 points (95% confidence interval: 2.30; 4.58)] (Horta et al., 2015). Furthermore, a longitudinal study found that infants who were exclusively breastfed until 4 months of age followed by mixed breastfeeding thereafter had significantly higher mean scores for cognition at 12 months, demonstrating that the associations between breastfeeding and cognition may be seen very early in childhood (Choi et al., 2018). Food insecurity and poorer quality diets among younger children have also been associated with decreased academic performance and cognitive development in childhood and adolescence (Jyoti et al., 2005; El Din et al., 2019; Landry et al., 2019).

When examining the infant's brain, we find that an average neonate's brain at birth is about one quarter the size of an average adult brain. However, during the first year of life, it doubles in size (Holland et al., 2014). Numerous MRI studies have demonstrated that neurocognitive development can be positively correlated with infant breastfeeding, including both exclusivity and duration (Schipper et al., 2020; Pang et al., 2020). Various studies attribute these findings to the composition of human milk such as lipid quality, carotenoids, oligosaccharides, and gut microbiome influences, and how they differ when compared to infant milk formulas (Hernell et al., 2016; Zielinska & Kolożyn-Krajewska, 2018; Goehring et al., 2016; Cowan et al., 2020). Compared to the body of literature describing the cognitive development impacts of breastfeeding in childhood and adolescence, far less literature has examined the impacts of breastfeeding on brain development in early childhood. One study found increased overall myelination in children who were exclusively breastfed for three months, as measured by MRI beginning at three months of age, as well as increased cognitive abilities compared to children who were formula-fed (Deoni et al., 2018). Indeed, differences in brain morphology were found to persist until eight years of age. Notably, to our knowledge, there is no literature linking breastfeeding duration to early childhood brain function, as opposed to structure.

Other studies have examined the risk of children exposed to adverse life events in the first years of life. This research has revealed that these children are at a higher risk for neural, behavioral, and psychological conditions (Nelson & Gabard-Durnam, 2020). The studies comparing EEG findings found specifically that early adversity was associated with lower frontal gamma power (Tomalski et al., 2013), increased theta power, and reduced alpha power (Marshall et al., 2004, Hassan et al., 2020). Data suggests that the links between early adversity and brain plasticity during this critical postnatal period (up to 12 months) may in part be accounted for by differences in breastfeeding, food insecurity, and inadequate nutrition (St. John et al., 2017; Inguaggiato et al., 2017, Lauritzen et al., 2016).

The current study evaluates duration and frequency of breastfeeding, level of food insecurity (as measured by the USDA Short Form of the Food Security), and resting brain function as theta, alpha, beta, and gamma waves (as measured by EEG at 12 months) to determine if increased duration and frequency of breastfeeding are associated with early brain development and cognition. Conversely, high food insecurity among infants was evaluated to establish any negative correlations. Study participants are a sub-group from the Baby's First Years (NLM, NCT03593356). The results of this study could provide evidence for further research, through an understanding of the impact of breastfeeding and food security on early childhood brain development. Currently, there is little literature that examines the relationship between breastfeeding, food insecurity and brain function.

2.2 Nutritional Impact During Gestation

Fetal brain development informs neurological development throughout the human lifespan. A maternal diet that meets all nutritional needs is essential during gestation, a time of rapid brain development. Fetal brain development depends upon maternal nutrition to support the integrity of neural stem cell proliferation and differentiation, as well as the normal process

of fetal neural tube closure throughout gestation, leading to subsequent lifelong functions (Zeisel et al., 2018).

Prior to a discussion of the potential role breastfeeding and food insecurity may play in infant brain development and function, it is important to understand how specific nutrients and breastfeeding may impact gestational brain development. Key components to nutritional impact during gestation include a mother's healthy diet and recommended supplementation during pregnancy. The section that follows will discuss the nutritional benefits of breastfeeding on infant health outcomes.

There are a number of consensus nutritional recommendations for pregnant mothers to follow in order to maximize their health and the health of their child. The Academy of Nutrition and Dietetics recommends mothers take 400 mcg folic acid per day as well as a prenatal vitamin. Additionally, they should increase their caloric food intake by 300 calories by ingesting a healthy mix of fruits, vegetables, protein and whole grains. Finally, mothers-to-be should avoid alcohol and cigarettes (Klemm, 2019).

2.2.1 Folic Acid

Folic acid intake during pregnancy is critical for sufficient placental and fetal development. This B vitamin is an essential component in the prenatal diet as it supports early neural tube development. The CDC recommends that women of childbearing age get 400 mcg of folic acid each day to prevent potential birth defects such as anencephaly and spina bifida. If a woman is planning to conceive; it is recommended that she consume 4,000 mcg of folic acid each day for at least one month before conception and then throughout the first three months of pregnancy (Wong et al., 2019). Research has found that supplementation of daily recommended folic acid incorporated into a woman's prenatal care regimen can significantly reduce preterm birth (Liu et al., 2016; Zheng et al., 2016) and improve neurodevelopment in both premature and normal gestation infants (Benton, 2010; Deoni et al., 2018).

2.2.2 Choline

As with folic acid, the nutrient choline (a precursor to acetylcholine) is necessary for early neural tube development and closure but is also essential for neurogenesis in the fetal hippocampus during later gestation and is essential for stem cell proliferation and transmembrane signaling during neurogenesis (Prado & Dewey, 2014). According to research findings by Zeisel et al., (2018) choline has also been found to be associated with enhanced memory performance, as late maternal (third trimester) levels have shown a correlation to improved infant information processing speed (Caudill et al. 2175). It has also been shown to act as a neuroprotective agent suggesting its role in dysregulating certain diseases, improved memory, and influencing mental health throughout life (Bekdash, 2019). Numerous animal studies have demonstrated the effects of choline on inflammatory and immune responses (Garcia et al., 2018; Richard et al., 2017; Lewis et al., 2017). Dellschaft and colleagues (2018) found that supplementation of maternal choline improved the ability of immune cells in their pups to respond ex vivo to mitogens and that higher levels further improved T cell proliferation.

2.2.3 Vitamin B12

Vitamin B12 has been shown to play an important role in brain development, as insufficient intake during pregnancy (especially among vegan mothers) is associated with involuntary muscle movements (Avci et al., 2003), cerebral atrophy (Casella et al., 2005), demyelination of nerve cells (Dror & Allen, 2008) poorer cognitive performance (Veena et al., 2010). Dror and Allen (2008) discovered that prenatal vitamin B12 deficiency leads to delayed myelination or demyelination by alterations in the synthesis of cytokines, growth factors, and oxidative metabolites. Other studies have demonstrated that prenatal vitamin B12 deficiency caused increases in both plasma total plasma homocysteine (tHcy) and methylmalonic acid (MMA) in older children. These markers indicate poorer status among children and were

associated with a decrease in developmental neuropsychological assessments (Kvestad et al., 2017; Coban et al., 2018).

2.2.4 Vitamin B6

Vitamin B6 plays a vital role in infant brain development and when a maternal deficiency is present it impacts neurotransmitter metabolism and signaling pathways related to gamma-aminobutyric acid (GABA), serotonin, dopamine, and glutamate (Almeida et al., 2016). Animal models have shown a correlation between gestational vitamin B6 deficiency and under-connectivity between cerebral cortical association areas. Research by Fernandez et al. (2019) suggests that this is potentially the root cause of some cognitive deficits in neurodevelopmental disorders. Prado and Dewey (2014) determined through a meta-analysis, that prenatal and early postnatal B6 intake resulted in reduced myelination, and dendrite branching in the cerebellum and neocortex. During pregnancy, the DNA methylation framework is being created in the fetal epigenome; therefore, B6 intake could modify DNA methylation and consequently increase the risk of neurological conditions in children. However, in humans, it is not well understood how these fundamental mechanisms control neurological changes. One study by Miyake et al. (2020) found higher maternal B6 intake was inversely related to childhood hyperactivity and low prosocial behaviors, potentially suggesting that childhood behavioral disorders could be reduced with gestational B6 supplementation.

2.2.5 Zinc

Zinc is vital for the normal development and function of cells that regulate the immune system and immune response. Many researchers considered zinc the “gatekeeper of immune function” (Wessels et al., 2017). As with adult zinc deficiency, neonates born to mothers deficient in this mineral will display lower birth weights than other babies born at full term (Daniali et al., 2020; Brion et al., 2020). A recent animal study by QS Medeiros et al. (2019)

showed how zinc-deficient mice infected with *S. flexneri* experienced weight loss, diarrhea, and metabolic changes as a result of inflammatory cell infiltration, epithelial disruption, and increased cytokine production. However, when administered a zinc supplementation, these mice showed reduced intestinal inflammation and stool shedding as well as observed weight gain. Thus, demonstrating a direct correlation between zinc, immunity, and the gut microbiome.

Other studies have focused on maternal zinc deficiency and neurological development among infants and young children. Li and colleagues (2018) determined that zinc deficiency was causally related to neural tube defects (closing) and excessive apoptosis when mice embryos were cultured with the zinc chelator TPEN. These researchers found that within two hours of this process, p53 protein levels in the neural tissue and primary neuroepithelial cells increased. This suggests that increases in p53 protein levels cause neural tube defect and extreme apoptosis and is consistent with findings of current studies that confirm the role of p53 as a regulator of responses to cellular stress and initiator of apoptosis (Felix et al., 2017; Vitillo et al., 2016).

Human studies are limited related to the direct measurement of zinc deficiency and human neurological development. However, as mentioned, animal studies have demonstrated that zinc deficiency can negatively affect cognitive development (memory and learning capacity) by interfering with normal protein function and neural tube development. Many of the current studies related to human zinc deficiency have focused on postnatal observations. Studies by Bhatnagar et al. (2001) and Black et al. (2003) found that zinc deficiency during pregnancy and lactation led to decreased focused attention and worse motor functions in neonates. Overexpression of zinc transporter proteins such as SLC39s/ZIPs and SLC30s/ZnTs (Baltaci et al., 2018; Thingholm et al., 2020) is associated with downregulation of the

autonomic nervous system regulation, as well as cerebellar and hippocampal development (Georgieff et al., 2018).

2.2.6 Iron

Iron is essential to oxygen transport when it binds to hemoglobin and is essential to the survival of all organs of the human body, including the brain (Berg et al., 2002). The underproduction of hemoglobin due to iron deficiency is referred to as iron deficiency anemia (IDA) and is a known risk factor for both short- and long-term cognitive impairment. IDA during pregnancy has been linked to negative maternal-fetal outcomes. Mothers experiencing IDA are more susceptible to infection, reduced working and intellectual capacity, and postpartum depression (de Costa et al., 2016). Neonates born to IDA mothers are at high risk of being delivered preterm and small for gestational age. Despite supplementation, intrapartum IDA has been associated with poor mental and motor development that continues into later childhood, resulting in poor cognition and school achievement (Santos et al., 2018). Various studies indicate that IDA causes neurodevelopmental delays by altering epigenetic regulation (DNA methylation) of the serotonin transporter gene (*SLC6A4*) (Georgieff et al., 2017; Prado & Dewey, 2014; Fumagalli et al., 2018), displayed by decreased later life myelination subcortical white matter and the fimbria of the hippocampus in animal studies (Hu et al., 2016, Lien et al., 2018).

2.2.7 Iodine

Iodine is a mineral that is essential for hormone production (thyroxine-T4 and triiodothyronine-T3) by the thyroid gland. Thyroid hormones regulate essential biochemical reactions that include protein synthesis and enzymatic activity. They are also essential for appropriate brain and skeletal development in the fetus and infant. A study by Miranda and Sousa (2018) reinforces that maternal serum free T4 levels during the first trimester primarily determine infant psychomotor development and can be influenced by iodine intake,

socioeconomic status, and BMI (Laurberg et al., 2016). This hormone is delivered to the brain chiefly through cerebral circulation via the blood-brain barrier (80%) and a much smaller portion is transported through the choroid plexus (Bernal, 2005). The first half of pregnancy appears to be the most critical period of pregnancy with high iodine requirements. Therefore, it is suggested that all women are screened for IDA as part of the first prenatal examination, and maternal vitamins supplemented with iodine be prescribed (Cusick et al., 2016; Benton, 2010; Prado & Dewey, 2014).

2.3 Nutrition After Birth

This section will discuss the physiology of lactation as well as the composition of breastmilk.

2.3.1 Physiology of Lactation

Lactogenesis is the process through which mammary glands develop the ability to secrete milk. A non-lactating female breast volume is primarily composed of collagen and adipose tissues, with a small portion containing mammary glands. During pregnancy, these mammary glands begin to produce total protein, lactose, and immunoglobulin, whereas sodium and chloride concentrations decrease in the glandular fluid (Wambach & Spencer, 2019).

During the last month of pregnancy, the alveoli begin to fill with colostrum that contains high levels of protein and immunoglobulins but less glucose and fat than mature breast milk (Munblit et al., 2016). Only a small amount (3 ounces per 24 hours) of colostrum is secreted during the first 48 to 72 postpartum hours but it supplies ample nutrition for the newborn during these first few days (Lamb et al., 2020).

Prolactin produced by the pituitary gland is principally responsible for the establishment and maintenance of breast milk. This polypeptide hormone is structurally similar to growth hormone and placental lactogen, which appear to have cytokine functions (Al-Chalabi & Alsalman, 2019). By the second month of pregnancy, circulating prolactin levels

begin to increase, ultimately reaching about 10 to 20 times non-pregnant concentrations. This level of prolactin is maintained throughout the third trimester of pregnancy and is elevated enough to initiate milk production. However, high levels of circulating estrogen, progesterone, and other placental hormones inhibit prolactin-mediated milk production at this point until delivery of the fetus and placenta. Once the placenta is delivered, circulating progesterone levels drop and initiate the production of milk (Napso et al., 2018).

The second stage of lactogenesis occurs shortly after childbirth (Kim Y, 2020). The baseline prolactin levels fall sharply but are reestablished for one hour during each feeding to promote the production of additional milk for the next feeding. Progesterone and estrogen also increase slightly during these one-hour spikes in prolactin. Within the female postpartum breast, the mammary glands respond to the suckling of the infant. When the infant feeds at the breast, sensory nerves within the areola initiate a neuroendocrine response resulting in milk secretion from lactocytes lining the alveoli. The posterior pituitary also releases oxytocin upon breast stimulation, which causes the contractile myoepithelial cells in the alveoli to squeeze milk into the lactiferous ducts (Augustine et al., 2017).

Upon stimulation, the breastmilk flows from lactiferous ducts into the lactiferous sinuses. These sinuses (approximately 12–20 arranged around the nipple) are connected to about 4 to 18 openings in the nipple that are referred to as nipple pores. When a baby feeds from the breast, the Montgomery glands within the areola also secrete oil to cleanse the nipple opening and help prevent cracking or chapping of the nipple. By about the third postpartum day, colostrum changes to transitional milk, which is followed by mature milk at approximately ten days postpartum. At this point in breastfeeding, it takes less than one minute from the time an infant begins to feed until milk is flowing. This “let down reflex” is accomplished when oxytocin is released. In addition to prolactin and oxytocin, growth hormone, cortisol, parathyroid hormone, and insulin contribute to lactation, in part by facilitating the transport of

maternal amino acids, fatty acids, glucose, and calcium to breast milk (Mazzocchi et al., 2019, Fields et al., 2017).

The control of milk production is quite efficient. The volume of production remains astonishingly constant at about 800 mL/d but may adjust accordingly to the requirements of the infant by feedback inhibitor of lactation and can directly correlate to the degree of breast (milk) fullness (Żelaźniewicz & Pawłowski, 2019). Breastmilk production is also related to the mother's state of well-being. Diet, stress, and fatigue can adversely affect breastmilk supply. This decrease in milk production is directly affected by higher levels of dopamine and norepinephrine, which inhibit the production of prolactin (Lee & Kelleher, 2016). Increased stress has also been shown to increase circulating levels of glucocorticoids like cortisol within the body, leading to fatigue, weight gain, mood swings, and more (Kominiarek et al., 2018; Caparros-Gonzalez et al., 2019). Among women that are breastfeeding, these higher levels of cortisol are passed through the milk to the child and can result in changed behavioral, cognitive, and physiological outcomes (Pundir et al., 2019; Lester et al., 2018, Pundir et al., 2017)

2.3.2 Breast Milk Composition

Evaluation of human breast milk has shown that this type of milk consists of 87% water, 7% carbohydrates (including 1 to 2.4% oligosaccharides), 4% lipids, and 1% proteins (Mosca, 2017; Boquien, 2018). This unique composition of nutrients and bioactive substances that are produced uniquely by each woman, changes accordingly to meet the needs of her infant. As an individual-specific biofluid, human milk provides not only nutrition but also offers immune protection against potential pathogens (lactoferrin, lysozyme, immunoglobulin A) and inhibits inflammation (cytokine IL-10 and TGF- β) while the infant's systems develop (Andreas et al., 2015; Palmeira & Carneiro-Sampaio, 2016). The actual composition of a mother's milk can be influenced by maternal diet and medical history, as well as the frequency and duration of breastfeeding. Primary protein and lactose levels remain consistent until about six to seven

months, and then gradually decline to lower, but stable levels (Verd et al., 2018), while lipid levels (including over 200 fatty acids) are extremely sensitive to maternal nutritional intake (Innis, 2014).

The 1% of breastmilk that contains proteins includes more than 1000 different types that are responsible for infant growth and neurodevelopment (Beck et al., 2015; Boquien, 2018). These proteins can be separated into two different classes known as casein and whey. Casein proteins are larger and curdle in the stomach making them more difficult to digest, while whey remains in liquid form. Therefore, in early lactation the ratio of whey to caseins is 80/20, making breastmilk more easily digestible. During later lactation, this ratio decreases to approximately 50/50 (Martin et al., 2016; Lönnerdal, 2016). Infant milk formulas tend to have significantly higher ratios of caseins, thus, making them more difficult for young infants to digest. The most abundant free amino acid in human milk is glutamine. This amino acid is nearly twenty times greater in later lactation and lowest during the production of colostrum (Martin et al., 2016, Masum et al., 2020, Lönnerdal, 2016). Glutamine is vital for supplying ketoglutaric acid for the Krebs cycle, potentially serving as a neurotransmitter in the infant brain (Agostoni et al., 2000; Zhang, Z. et al., 2013).

Breast milk lipids are the second most important macronutrients and have been extensively studied. Human milk is rich in linoleic acid and α -linolenic acid which act as precursors of long-chain polyunsaturated fatty acids such as n-6 (such as arachidonic acid) and n-3 (such as eicosapentaenoic and docosahexaenoic acids), which make up the largest proportions within the milk. Breast milk is the only source of these precursors for babies that are exclusively fed, as they are not synthesized by the body (Innis, 2014). These fatty acids are essential for brain development in infants. Research has shown that docosahexaenoic acid (DHA) and arachidonic acid (AA) in particular are important for normal brain functions (Braarud et al., 2018; Martin et al., 2016; Lauritzen et al., 2016), the development of visual and

neural tissues (Destailats et al., 2018), and subsequently motor and cognitive development (Boquien, 2018; Innis, 2014; Zielinska & Kolożyn-Krajewska, 2018; Schipper et al., 2020). Study findings by Braarud (2018) suggest that DHA can be associated with infant problem-solving at 12 months, while other research suggests that higher DHA concentrations during pregnancy and infancy could improve neurodevelopment and potentially prevent autism and behavior disorders (Cardoso et al., 2018). However, all research and reviews recommend that additional studies are necessary to determine direct causality (Lien et al., 2018).

When lipid droplets are secreted by human mammary glands, the glands enclose the droplets resulting in what is known as a milk fat globule membrane (MFGM). The composition of these membranes consists of complex polar lipids such as phospholipids, gangliosides, sphingomyelin, and cholesterol (Claumarchirant et al., 2016). Phospholipids are primarily located in the outer bilayer of the MFGM, while cholesterol and sphingomyelin are largely collected in the lipid rafts (Bhinder et al., 2017). The most important phospholipids in the MFGM include phosphatidylethanolamine, phosphatidylcholine, phosphatidylserine, phosphatidylinositol, and sphingomyelin (Moukarzel et al., 2018). Although MFGMs represent a small percentage of the total lipid content of breast milk, the natural presence of MFGM in human milk could be a factor in observed differences in neurocognitive development when comparing breastfed and formula-fed infants (Schipper et al., 2020). Recent studies of infants fed MFGM milk supplementation (dietary ganglioside) have shown improved neurobehavioral development in preterm babies (Tanaka et al., 2013) and improved cognitive function at six months in healthy term infants (Gurnida et al., 2012).

Carbohydrates in breast milk include oligosaccharides and disaccharide lactose as the main components, as well as glycoconjugates. Oligosaccharides (more than 100 different compounds) are present in large quantities and are extremely varied in their biochemical compositions. Lactose signifies an important source of galactose which is vital in promoting

central nervous system development (Mosca & Gianni, 2017). These oligosaccharides contained within human breast milk serve as prebiotics and enhance the growth of beneficial bacteria (Bifidobacteria and Bacteroides). Furthermore, they regulate numerous infant immune functions (Donovan & Comstock, 2016; Garwolińska et al., 2018, Palmeira & Carneiro-Sampaio, 2016).

Breast milk's unique chemical composition is crucial for supporting neurological development as well as the development of a host of other systems in babies. Breast milk's mix of water, protein, fats and carbohydrates each spur early childhood development and deserve additional study.

2.4 Malnutrition, Brain Growth, and Development in Early Childhood

There is clear evidence that a proper nutritional profile is crucial for seeding a child's neurological development. Mothers must maintain a robust diet during pregnancy to encourage appropriate neurological and hormonal development. Moreover, it's crucial that mothers receive proper screening to reduce the potential for malnourishment. After birth, breastfeeding continues to be an essential pathway for mothers to offer nutrition to their baby in order to encourage brain development.

The importance of lifestyle choices and dietary habits during pre-conception, pregnancy, and breastfeeding, for both the health of the mother and the child, is widely supported by scientific research and published literature. Maternal nutrition (including a varied and well-balanced diet) from pre-conception on, is one of the most important determinants of pregnancy and neonatal outcomes (King, 2016). Current research suggests that reduced intake or lack of specific nutrients (malnutrition) during pregnancy influences the length of gestation, proper placental and fetal growth, neonatal birth weight, and infant development and intelligence (Dhobale et al., 2017, Morrison & Regnault, 2016; Castrogiovanni & Imbesi, 2017). The impact of malnutrition depends on several factors, including the timing of nutrient

deprivation, the degree of nutrient deficiency, and the potential for recovery. The following section will outline some of the brain growth and developmental changes that can occur in the first 1000 days of life (conception to two-years of age) as a result of malnutrition. Human gestation can be divided into two different phases. The first phase (embryonic) begins at conception and continues for eight weeks and includes the establishment of the brain, spinal cord, and peripheral nervous system. The second phase (fetal) continues until birth. It is during this second phase where significant growth and development of the neocortex occurs. The second phase is also marked by vast neurogenesis, neuronal migration, formation of axons and dendrite branching (arborization), and synaptogenesis which continues until the baby is about two years old.

2.4.1 Timing of Nutrient Deprivation

In early brain development of the fetus, newly created neurons morphologically change and migrate from the germ layer to create new connections with other cells. The migration of neurons begins at about 7 weeks gestation and continues into approximately 4-5 months of infancy. This process is vital for the creation of a proper neuronal network, and any disturbances in this development can result in dysfunctional activity of the brain. There are two known major modes of migration with the cerebral cortex, radial migration, and tangential migration (Guerrini & Parrini, 2010). Prenatal exposure to a host of environmental stressor such as alcohol, drugs, and inflammation can disrupt the migration of neurons and cause disorders, as substances that are ingested, inhaled, or created by a woman's body may cross the placenta and lead to unfavorable changes to fetal development (Hwang et al., 2019).

Current scientific evidence suggests that nutrient reduction, deprivation, or imbalance before blastocyte implantation (approximately 6 to 7 days after fertilization) may result in genetic variations in fetal programming such as somatic hypoevolutism at birth (Musumeci et al., 2017; Huang Y et al., 2018), and metabolic (Marciniak et al., 2017; Saad et al., 2016) or

endocrine (Andersen et al., 2017; Jones et al., 2017) dysfunctions in postnatal life. In addition, maternal malnutrition can cause decreased efficacy in the maternal and fetal immune system. This can occur even before conception as maternal malnutrition transfers epigenetic modifications to the fetus (Castrogiovanni et al., 2017; Bourke et al., 2016).

At approximately 15 weeks gestation, fetal axonal and dendrite growth expands, and dendrites begin to develop branching projections that connect cell to cell. Additional development of these neuronal connections in specific areas of the brain continues until about 32-week gestation (Aneesh & Ghugre, 2019). The majority of the studies related to this area of brain development have been conducted with animal subjects. Fauzi (2018) and colleagues conducted research on brain development in rabbit offspring that were deprived of nutrition (50%) during gestation. From previous studies (Ichim et al., 2012, Vieau et al., 2011) these researchers built on the knowledge that central nervous system development requires numerous factors, including growth factors like neurotrophic proteins. Proteins like NGF, BDNF, NT-3 and NT-4, display critical functions related to growth of neuronal cells, specifically in regulating the developmental capacity of neuron cells (Fauzi et al., 2018). This study by Fauzi sought to replicate the results of intrauterine growth restriction (IUGR) seen when a human fetus is subjected to nutritional deficits. The findings of this research showed that a 50% nutritional restriction demonstrated a decrease in dendritic density in the cerebrum and cerebellum of newborn rabbits' brains during pregnancy indicating reduced neural plasticity.

Synaptic formation also begins during gestation (around week 23) and continues throughout life. However, research shows that synaptic density peaks at different times in various areas of the brain. (visual cortex- 4 and 12 months postpartum, prefrontal cortex \geq 15 months postpartum). Synaptic pruning occurs when this peak is followed by decreases in synaptic density. This begins within the first year of birth and continues through adolescence, while synapse overproduction is finalized in the second year of life (Tierney & Nelson, 2009).

Gestational malnutrition can diminish the likelihood of synaptic maturity (Morgan et al., 2020). The effects of gestational malnutrition and synaptic plasticity have been demonstrated in a recent study conducted by DeCapo et al. These researchers focus on the deficit of maternal consumption of protein, carbohydrates, and fats and how this negatively influences offspring outcomes in rodent and large animal models. Their study highlighted that maternal diet as well as her metabolic state (e.g. obesity and diabetes) can influence neurodevelopment. Their extensive literature review showed a direct correlation between ω -6/ ω -3 ratios that are vital to proper brain development and that even slight dietary variations in fatty acids can markedly affect cerebral lipid composition and essential neural function. It was also noted that excessive maternal intake of specific poly-unsaturated fatty acids (PUFA) is related to diminished hippocampal neurogenesis and required synaptic transmission (125).

2.4.2 Degree of Nutrient Deficiency

Mounting scientific and clinical evidence suggests that the fetal environment is crucial to adequate brain development and determines cognitive trajectory beyond childhood. An atypical fetal environment can be the product of factors that should either be absent during critical developmental periods (malnutrition) or when abnormalities or substances (hormone imbalance, lifestyle choices, teratogen exposure) are present that detrimentally affect fetal brain development (Georgieff et al., 2018). When observing required maternal nutrient intake, there is a threshold at which deficiency results in impairment for the fetus. The significance of impairment is related to the level of nutrient deficit and when this deficit occurs. Mild to moderate malnutrition exposure tends to spare adverse neurodevelopment, while moderate to severe malnutrition causes fetal growth restriction of the brain and compromises anticipated development and future cognitive abilities (Miller et al., 2016).

2.4.3 Potential for Recovery

Fetal and infant neurodevelopmental recovery depends on the timing of the insult and experiences beyond that point in time that allow the brain to undertake remodeling (myelin development, vascular remodeling, and synaptic development and pruning) which determines a child's learning and memory abilities. Fortunately, the infant brain displays neuroplasticity that can aid in recovery (Kolb & Gibb, 2011) and allows for the generation of new neurons and glia, as well as establishing new synaptic pathways (Pierre et al., 2017). Additionally, early childhood exposure to enhanced sensory, linguistic, and social interactions has been shown to facilitate recovery (Pineda et al., 2019; Moore et al., 2015).

The exposure-dependent factors that facilitate plastic changes and modify brain activity and responses later in life is referred to as metaplasticity (Kolb & Gibb, 2011; Farashahi et al., 2017). The most significant changes in brain function that affect cognitive processing seem to consistently involve the hippocampus and the cerebellum and prove to be permanently altered (Desky et al., 2019). However, studies have also demonstrated that specific psychosocial factors (maternal education, socioeconomic status, breastfed vs formula feeding, and mother-child interactions), can directly influence early childhood cognitive development including reasoning, attention, visuospatial functions, verbal fluency, and intelligence attainment when compared to children of equal age and siblings that were adequately nourished. (Islam et al., 2017; Wade et al., 2018; de Souza et al., 2011; Nassar et al., 2012). The rate of recovery has also been demonstrated to be slower in the prefrontal cortex and the parietal lobe maintain a slower rate of improvement even when proper nutrition is provided. It appears to predominantly affect visual and executive functions (parietal and frontal) and the language areas (temporal) of the brain (Barra et al., 2019).

2.5 Association between Maternal Health Status, Diet, and Early Childhood Intelligence

A mother's health and diet may be associated with early childhood intelligence. Intelligence, not an innate and immutable factor, is often described using assessments that yield numeric scores. There are several risk factors within a mother that can be associated with reduced scores on tests of early childhood cognitive abilities, including obesity, malnutrition and gestational inflammation. Breastfeeding interacts with each of these dimensions in unique ways, and it is crucial for researchers to study each of these factors when considering ways to improve maternal health and bolster early childhood intelligence.

Neurodevelopment among infants and young children includes multiple behavioral areas such as sensory, mental, motor, and socioemotional. It is imperative to recognize that these behaviors are a direct manifestation of brain activity. Therefore, recognizing normal infant brain development and how nutrition and inflammation play a role in influencing this development and function are critical for evaluating future cognition and academic performance. A child's brain is particularly susceptible to early life exposures (positive and negative) and because of this plasticity, specific attention must be dedicated to the factors that support proper brain development. Studies have shown that a child's brain demonstrates the potential for recovery from these early exposures, but the majority of the evidence suggests vulnerability outweighs plasticity and normal development through sources such as proper nutrition is significantly more effective than attempting to reestablish the neurodevelopmental trajectory following specific deficiencies.

The brain is composed of discrete regions such as the cerebellum, hippocampus, cortex, and striatum, and processes such as myelination and neurotransmitters release and reuptake. All of these demonstrate various developmental trajectories that begin, peak, and end at different times. When exposed to nutritional deficits, vulnerability and the region's

requirements for specific nutrients will depend on the timing of the event. This principally occurs from the time of conception, throughout childhood, and to the end of brain development. The process of brain development is especially vulnerable during times of rapid brain growth and differentiation that is witnessed during infancy and early childhood and include regions such as the auditory, visual, and motor cortices, the limbic system including the hippocampus (memory), and the cerebellum including the frontal cortex that is responsible for later functions such as high-level thinking, working memory, and executive function. This particular area of the cerebellum displays differentiation in early infancy and continues through young adulthood, thus it is highly vulnerable beginning in early infancy.

Brain-wide, highly metabolic processes evolve rapidly during infancy and include myelination, synaptogenesis, and the dopamine neurotransmitter system. Nutrients that support this metabolic process include protein, glucose, iron, selenium, zinc, and iodine. The integration of the nutrients occurs through signaling cascades and can influence the rate of protein synthesis and actin polymerization in neurons, which are associated with neuronal functional capability and dendritic complexity. Therefore, any nutritional deficiencies can demonstrate profound negative consequences in the young brain.

2.5.1 Obesity

It is well documented that adequate maternal weight gain during pregnancy is a contributing factor to positive fetal outcomes. However, it has also been found that pre-pregnancy body mass index (BMI) and excessive gestational weight gain can inversely be associated with infant cognition and childhood intelligence assessment. A study by Huang and associates (2014) discovered that maternal obesity ($BMI \geq 30\text{kg/m}^2$) was independently associated with a 1.3 to 3.6-fold increase for the risk of infant cognitive impairment and childhood intellectual disabilities and that excessive gestational weight gain among these women accelerated this association. The results of this research also support previous findings

from other studies by Tanda et al. (2013) and Noble & Kanoski et al (2016) that suggest that fetal exposure to obesogenic diets are associated with neurodevelopmental changes (particularly hippocampal-dependent memory) that persist beyond weaning and introduction of a healthy diet.

Berger and colleagues found that breastfeeding frequency and maternal weight (obesity) had a particular bearing on infant cognition (learning and memory) when measuring 2'-fucosyllactose (2'FL) levels at 24 months of age (2020). Fifty mother-infant pairs were recruited for this study based on pre-pregnancy BMI values. As a requirement of the study, the mother-infant pairs attended three visits. At 1-month, historical health-related information (maternal age, infant sex, and infant birth weight) was collected, mothers and infants were weighed, breast milk was collected and analyzed, and questionnaires related to breastfeeding frequency were completed. At 6 months, mothers completed the same questionnaires, breast milk was collected and analyzed, and the mothers and infants were weighed. At 24 months, maternal and infant weight was measured, and the Bayley Scales of Infant Development (Third Edition, Bayley-III) was administered to evaluate the developmental functioning of cognitive, language, and motor skills.

The percentages of mothers participating in this study were categorized into three groups: normal weight (34%), overweight (36%), and obese (30.0%) and were based on their pre-pregnancy BMI values. It was found that infant weights at 1, 6, and 24 months were not different between the groups (pre-pregnancy BMI) but changes in individual oligosaccharides were observed in that DSLNT (disialyl-LNT), LNH (lacto-N-hexaose), and FLNH (fucosyl-LNH) levels decreased between 1 and 6 months while 2'FL and LSTb (sialyl-LNT b) were similar between 1 month and 6 months. It was also determined that maternal pre-pregnancy BMI was an independent predictor of infant cognitive development, as it predicted lower infant cognitive development scores, but was not associated with breast milk feeding frequency at 1

and 6 months, or any of the nineteen measured oligosaccharides, including 2'FL levels measured at 1 and 6 months. These findings support previous studies that have observed that women with higher pre-pregnancy weights (BMI \geq 25 kg/m²) were more likely to have a child with lower intelligence test scores at 4 to 14 years of age (Adane et al., 2016; Van Lieshout et al., 2011; Casas et al., 2017).

Increased maternal BMI can influence the presence of fatty acid content in colostrum and circulating hormone levels in breastmilk. Research conducted by de la Garza Puentes et al (2019) found that breastfeeding women that were obese (BMI > 30) presented with elevated colostrum saturated fatty acids and n6 to n3 ratios, as well as decreased levels of DHA, AHA, and MUFA that influenced excessive infant weight gain and decreased cognition when measured at 6 month and 18 months, respectively. It is thought that certain adverse neurodevelopmental effects can also be attributed to impairment of the brain-derived neurotrophic factor (BDNF) gene that regulates canonical nerve growth factor in the brain and is primarily responsible for the regulation of neurogenesis (Edlow, 2017; Noble & Kanoski, 2016). Studies such as one conducted by Prince et al. (2017) have demonstrated maternal obesity alters the level of brain derived BDNF signaling in the placenta causing decreased placental BDNF protein levels. Other studies have linked decreased BDNF levels to juvenile deficits in memory and spatial learning that have continued into adulthood (Tozuka et al. 242) when examining rodent offspring.

2.5.2 Inflammation

Obesity in the non-pregnant female can result in complications related to the dysregulation of inflammatory and immune responses. Pregnancy stimulates inflammation and causes changes within the immune system. The combination of elevated maternal BMI, pregnancy, and these inflammatory and immune changes can cause multiple fetal complications throughout the pregnancy and beyond (Schmatz et al., 2010). Studies conducted

by Edlow (2017) and Sanders et al. (2014) have shown a direct correlation between elevated maternal BMI, pro-inflammatory cytokine concentration levels, and activation of pro-inflammatory placental pathways. The presence of placental inflammation can result in fetal growth restriction (FGR) from placental dysfunction, resulting in small for gestational age infants (Sharps et al., 2020). These observed changes in placental function have been designated as risk factors for poor neurodevelopment. The placenta acts as both a barrier to maternally derived bioactive substances (cortisol) critical for fetal neurodevelopment, and as a source of neuroactive steroids and neurotrophins that are vital to regulating neurogenesis and apoptosis (Mestan et al., 2009).

Animal studies have shown that exposure to gestational inflammation increases cytokine expression in the placenta and the fetal membranes, resulting in impairments in axonal processes, enhanced microglial and astrocyte activation, and macrophage infiltration in the fetal brain (Offenbacher et al., 2005). The increase in pro-inflammatory cytokines can directly affect the fetal brain, as well as increase the permeability of the fetal blood-brain barrier, allowing for increased leukocyte infiltration into the neural compartment (Ghiani et al., 2011). Other animal models have shown that prenatal inflammation exposure results in numerous cognitive deficits, including spatial learning, working memory, and cued associative learning in rodents (Hodyl et al., 2017).

Numerous nutrients contained in human breast milk and certain milk-based infant formulas (oligosaccharides, fatty acids, proteins, and hormones) can have a direct effect on infant brain development and neurodevelopmental trajectories. These levels of these components at specific periods of development can have varied effects on current performance (Goehring et al., 2016; Asgarshirazi et al., 2017) and future health (Vieira Borba et al., 2018, Anderson et al., 2016), and cognitive abilities (Hansen-Pupp et al., 2011, Berger et al., 2020).

Research designed by Goehring and associates (2016) was conducted as a randomized, double-blind study at 28 sites in the United States to evaluate biomarkers of immune function in 317 exclusively formula-fed infants that were enrolled at 5 days old and followed until four months old. These infants were randomly assigned to three groups that were fed slightly different variations of infant formula, all of which contained 2.4 g total oligosaccharides/L. The control group contained galactooligosaccharides (GOS) only and the experimental formulas included GOS + 0.2 or 1.0 g 2'-FL/L. The data from these groups were compared to a group of breastfed infants (n=107) of the same age range.

In this study, lacto-N-fucopentaose II (LNF-II), a major human milk oligosaccharide, was assessed as a representation of the total concentrations of oligosaccharides present in human milk. This marker was chosen as elevated levels of LNF-II in maternal milk (2 weeks postpartum) were linked to fewer respiratory problems in infants by the age of 6 and 12 weeks. The use of 2'-FL was chosen because it is one of the most abundant components in breast milk (Bode 383S) and at the time of this study was not included in infant formula. These researchers believed that 2'-FL could play a key role in breast milk's protective effects, so to test this hypothesis, they evaluated the infants fed the various formulas containing 2'-FL. They focused the majority of the study on differences between the breastfed and control (formula-fed) groups. At six week of age, blood samples were drawn from each study participant to determine plasma cytokine concentrations (IL-1 α , IL-1 β , IFN- γ , IL-6, IL-1ra [anti-inflammatory], and TNF- α).

Results from these laboratory studies revealed that circulating plasma concentrations of inflammatory cytokines IL-1a, IL-1b, IL-6, and TNF-a and anti-inflammatory IL-1ra were significantly elevated in the control formula-fed group compared to those in the breastfed group, while the other two formula groups had results equal to the breastfed group. Among all groups, there were no significant differences in plasma cytokines IFN-a2, IFN-g, IL-10, IP-10,

or RANTES. The control formula-fed group had significantly lower levels of circulating T lymphocytes than those in the breastfed group. Measured phytohemagglutinin-activated PBMCs, did not display significant differences between the control formula-fed and breastfed groups (percentage distribution of cells in the G0/1, S, and G2/M phases or in the mean proliferative indexes).

From this information, it was determined that infants fed formulas that were fortified with 2'-FL displayed cytokine levels that were between those found with the breastfed and control formula-fed infants yet were closer to those exhibited in breastfed participants. It was found that greater doses of 2'-FL (1 g/L) in experimental infant formula were not shown to have a greater effect on cytokine levels than the lower dose of 2'-FL (0.2 g/L) when compared to breastfed infants. However, they did discover that fortifying infant formula with 2'-FL helped modify innate and adaptive immune profiles to levels closer to the breastfed reference group.

2.5.3 Immunity and Gut Microbiome

Numerous studies have shown that initial gut bacterial colonization is partially established through the infant's diet. Full gut colonization allows for a symbiotic relationship between colonizing bacteria and lymphoid and epithelial tissues (Walker, 2013). The resulting innate and adaptive immunologic relationship collectively defends the body against harmful pathogens (Cowan et al., 2020; Carlson et al., 2018; Parsons et al., 2020). In the mature intestine, this is an important component of immune response when exposed to benign bacteria and harmful antigens (Brennan et al., 2019). Surprisingly, the process of complete gut colonization can be achieved during early infancy and breastfeeding can contribute significantly to this accomplishment (Cerdo et al., 2019; Guaraldi & Guglielmo, 2012). Human breast milk offers a constant source of probiotics that promote infant gut microbiota development. The major genus is *Bifidobacterium*, which impedes the establishment of

Enterobacteria and fungi, and *Lactobacillus*, which promotes lactose fermentation, by producing an acidic environment to suppress pathogenic microorganism growth (Aloisio et al., 2018; Ward et al., 2017; La Doare et al., 2018).

Additional studies have established a microbiome-gut-brain axis and that this ecosystem of microorganisms is recognized as a regulator of brain and behavior (Cowan et al., 2020). Specific periods in which a change in the microbiota coincide with instances of rapid development within other systems, particularly the brain. It has been well established that critical periods in infant growth that exhibit heightened neuroplasticity and the brain's responsiveness to specific environmental influences (La Doare et al., 2018; Guaraldi & Guglielmo, 2012; Brennan et al., 2019). Studies examining the ongoing communication between the gut, the brain, the HPA axis, suggest that numerous postnatal factors can influence infant gut microbiome and correlate with cognitive development. Some studies suggest evidence that these bodily systems influence one another and theorize potential (physical and mental) health implications with initial disruptions in these systems during infancy (Brennan et al., 2019; Clarke et al., 2014).

Other studies connect the health of the infant gut microbiome as a direct causality of inflammation and that the postnatal period is vital for immune system maturation of infants (Anderson et al., 2016, Groer et al., 2014). Breastfeeding influences the infant's immune system as compounds within the milk provide a healthy gut microbiota colonization. The advantage of breastfeeding is that it can directly influence immune homeostasis by providing antimicrobial factors that protect against pathogen invasion and provide protective bacteria leading to optimal gut function (Yatsunenko et al., 2012). The result is that breastfeeding can improve antigen transference and provide epithelial inflammatory response factors (TGF- β , sCD14). Breast milk also stimulates proper antigen-specific long-term immune responses (Krebs et al., 2017; Goehring et al., 2016). A study by Asgarshirazi (2017) has shown that gut

microbiota plays an important role in the development of immunologic functions of the infants and breastfeeding provides a great advantage over milk formulas. Another study by De Palma (2012) confirmed these findings by demonstrating that specific bacterial colonization patterns during the first 4 months of infancy can influence the risk of developing celiac disease in later life and that breastfeeding could have a protective role in this disorder. A final study of interest is a large prospective observational study conducted by Jiang and colleagues (2014) to directly measure the association of biomarkers of inflammation (6 months) on motor and cognitive function (12 and 24 months). Within their study cohort, fever and inflammation showed a strong correlation with substantially lower scores on cognitive, language, and motor skills tests.

2.6 Breastfeeding Attachment and Infant Cognition

Breastfeeding has been found to be associated with enhanced maternal sensitivity and greater attachment between the mother and her child (Tharner et al., 2012). Research findings have shown that mothers who breastfeed tend to touch their infants more, are more responsive to feeding needs, and display more eye-to-eye contact with infants during feeding (Pearson et al., 2011; Jansen et al., 2008). The prospective longitudinal study by Tharner et al. (2012) observed 675 mother–infant pairs, to determine if increased duration of exclusive breastfeeding correlated with attachment quality and disorganization (assessed with Strange Situation Procedure), and maternal sensitivity (assessed using Ainsworth’s sensitivity scales) among 14-month-old infants. The findings of this study showed that a longer duration of exclusive breastfeeding was related to more maternal sensitive responsiveness, greater attachment security, and less attachment disorganization.

Brain imaging offers evidence for the positive influence of breastfeeding on the mother–infant connection. Functional MRI studies have discovered that mothers who exclusively breastfeed displayed superior brain activation in various limbic brain regions when they heard their infant’s cry (Musser et al., 2012). This suggests larger engagement of

emotional brain systems within mothers that breastfeed when compared to those that feed their infants by bottle (Kim et al., 2011). This is additionally supported by a study conducted by Britton and colleagues. Their research data displayed that increased maternal sensitivity when the infant reached 3 months could substantially predict the duration of breastfeeding for the first year.

A study conducted by Krol and colleagues (2015) looked at the differences in how the duration of exclusively breastfed (EBF) infants reacted to displayed images of fearful and happy body expressions. Each 8-month-old infant was shown these images (6 of each) in a random, non-repeating order while brain responses were measured by electro-cortical responses to body expressions to determine neural processing of emotional signals. The study cohorts were divided in two groups based on duration of exclusive breastfeeding (low EBF: $M = 102.66$, high EBF: $M = 198.43$ days). The results of the EEG records showed that the infants within the high EBF group exhibited more significant attention allocation to displayed happy stimuli whereas the low EBF infants showed a more significant allocation of attention to displayed fearful stimuli. These findings suggest that the duration of exclusive breastfeeding positively correlates to differences in the neural processing of displayed emotional body images in 8-month-old infants. Additionally, animal models show similar results. Research by Liu et al. has demonstrated that breastfed primates developed greater white matter when compared to those that had been bottle-fed and raised in a nursery setting. Thus, different feeding methods may elicit different developmental progress (Liu Z et al., 2019).

2.7 Breastfed vs Formula-Fed and Infant Cognition

There are numerous reasons why a woman or parents may or may not choose to breastfeed. The current literature shows that these reasons may be related to maternal age, education, or health (Ogbo et al., 2017), socioeconomic status (Gonzalez et al., 2018), marital status, culture, ethnicity (McKinney et al., 2016), family history, and family or significant

other's support (Donath & Amir, 2013). The following explores some of the reasons that influence a mother's choice to breastfeed, as well as factors that may affect duration.

Parents effectively have three options to feed newborns: breast milk, formula or a combination of the two. However, for new parents, breastfeeding may be impossible due to the need to return to work. Despite the health benefits, literature available, and encouragement by medical professionals, breastfeeding initiation rates in the United States remain lower than desired. According to statistics from 2017, the CDC estimates that of those infants born in the US during that year, 84% were started on breast milk but only 58% were still breastfeeding at 6 months. Even more concerning is that nearly 20% of these infants were given supplemental formula within the first two days of life (Smith et al., 2006).

To be successful in breastfeeding, initiation should begin within the 24 hours of birth. The process of putting the newborn to the breast stimulates the production of hormones that in turn stimulates milk production. However, the choice to breastfeed starts much sooner than that for most women. Research has shown that most women and their partners make this decision before conception or during the first trimester of the pregnancy. The results of many self-reported studies show that for most women, this choice has been influenced by the known benefits of breastfeeding, its naturalness, and the emotional bonding with the infant that comes from this type of intimate contact and nurturing (Chabrol et al., 2004; Briggs et al., 2020). In studies by Arora et al. (2000), Hunegnaw et al. (2018), and Maharlouei et al. (2018) women reported that they chose not to breastfeed because of quality of support (spouse, family, medical staff), the mother's perception of the father's views on breastfeeding, uncertainty of the quality or quantity of milk, previous failure with breastfeeding, and a need to return to work. Other women state that they may have been encouraged to initiate breastfeeding or extend the duration if more information was available or provided to them, and if they had more support (Bresnahan et al., 2020; Demontigny et al., 2018). Recent clinical research by Gray et al. (2020)

showed that study participants who had early feeding assistance by a trained lactation consultant before the administration of any infant formula were more likely to experience successful exclusive breastfeeding (80%) than those women who had a feeding assisted by a non-lactation nurse (40%).

However, women who fear that they will not be able to successfully breastfeed may deeply internalize fear and anxiety of failure. If a new mother fails to meet breastfeeding recommendations, they may feel inadequate, increasing their risk for depression (Borra et al., 2015).

Maternal health is always of great concern when choosing a method of feeding a newborn. Many of the concerns can be related to pre-existing conditions (Kaul et al., 2019) that would make breastfeeding inadvisable and can be both physical and mental in nature. Pre-existing medical conditions can cause a woman to produce not enough milk or none entirely (breast reduction or mastectomy). While other women who are diagnosed with metabolic disorders such as diabetes may have difficulty producing breast milk (Anderson, 2018). Medication that a woman may have withdrawn during pregnancy because of its potential or known adverse effects during pregnancy, should be resumed upon delivery to reduce health risks to the mother. Therefore, once resuming these medications, she would be advised not to breastfeed (Kronenfeld et al., 2018). Currently, many medications are not suggested to be used during pregnancy and lactation, simply because not enough is known about the potential teratogenicity to the fetus (Talabi et al., 2020).

Communicable diseases and substance use/abuse are of concern as well when considering breastfeeding. As part of the global efforts to eradicate new HIV infections in children, mothers living with HIV are advised to choose formula-feeding over breastfeeding (Ajibola et al., 2018, Dong et al., 2020). However, there remain concerns for mothers who cannot obtain or afford commercially infant formulas, adequate supplies of clean drinking

water, and do not have free and universal access to antiretroviral therapy (Alverenga et al., 2019). However, women living in developed countries are see far greater benefits for combination therapies, living longer with the infection, and emerging views among patients and providers may be changing (Etowa et al., 2020, Tuthill et al., 2019). For other women and parents, the preference to formula-feed their infant is made based on lifestyle choices. Those who use tobacco may choose to formula-feed their child as a precaution to minimize exposure to tobacco smoke or vapor (Miranda et al., 2020). For mothers who are currently using illicit drugs or are receiving medication-assisted treatment for drug abuse (opioids, heroin), current guidelines suggest that they abstain from any breastfeeding (Cleveland, 2016).

Numerous studies throughout the last decades have demonstrated the health benefits of exclusive breastfeeding (Allen & Hector, 2005; Cushing et al., 1998; Salone et al., 2013; Belfield & Kelly, 2012). More recent studies have shown the importance of the nutritional components contained within breast milk that cannot be duplicated even with modern versions of infant formulas. This nutritional content is particularly important when comparing the cognitive development of those infants exclusively fed formula to those that are exclusively fed breast milk (Toro-Campos et al., 2020) These findings point to the importance of breastfeeding within the first six months of an infant's life and how it can determine future intelligence (Horta et al., 2015; Huang et al., 2018; Sabri et al., 2020; Quigley et al., 2012, Bernard et al., 2013).

Despite these known benefits, the number of mothers that choose exclusive breastfeeding for the recommended first six months remains low worldwide (WHO, 2020). Lenehan et al. (2020) explored the effects of short-term breastfeeding (2 months) on long-term intelligence scores (5 years old). This study compared the results of two separate groups that included 1) only children who had been predominantly breastfed at 2 months (n = 288) and 2) children who had never been breastfed at 2 months (n = 254) and was determined through a

questionnaire administered to mothers at 2 months post-enrollment. The neurodevelopmental assessment of these participants was conducted at 4.8 to 5.5 years of age by using the Kaufman Brief Intelligence Test II (KBIT-II).

Analysis of the data showed that KBIT-II composite cognitive scores of breastfed infants were significantly higher (2.47 points higher) at 5 years of age. Similar findings were also evident in the KBIT-II verbal (1.88 points higher) and non-verbal (1.68 points higher) scores. From these results, these researchers determined that predominantly breastfed infants have a greater advantage of achieving cognitive scores, even when breastfed for a short duration in early infancy. These findings confirm the results that were also discovered by Pang and colleagues (2020). These researchers also evaluated two child cohorts that included children that were either breastfed (n=73) or formula-fed (n=296). However, they conducted neurodevelopmental assessments between 6 and 54 months using the Bayley Scales of Infant and Toddler Development (Third Edition) at 2 years of age, and the Kaufman Brief Intelligence Test (Second Edition) at 4.5 years. The results of these assessments were similar to those found in the research conducted by Lenehan, showing that those exclusively fed breast milk (directly from the breast) scored higher on several memory tasks when compared to bottle-fed breast milk participants, that included deferred imitation tasks at 6 months and relational binding tasks at 6 and 54 months.

Bellando et al. (2020) compared the effects of infant feeding (breast or formula) on childhood cognition and language skills. This longitudinal study of infants from ages 3 to 60 months that were either breastfed (n=174), milk-based formula-fed (n=169), or soy protein-based formula-fed (n=161). These study participants were followed for six years in which all formula-fed children remained on the same formula for a minimum of 12 months and all breastfeeding mothers were encouraged to continue until the child reached one year of age. Mothers who changed their child's feeding method were removed from the study. By year five,

341 participants remained in the study. Parents selected the method of feeding their child, so it was not a randomized control trial. Several methods were used to determine cognitive development and language skills including the Wechsler Abbreviated Scale of Intelligence (WASI), the Preschool Language Scale-3 (PLS-3), the Bayley Scales of Infant Development—2nd Edition (BSID-2), and the Reynolds Intellectual Assessment Scales (RIAS).

The data from this study showed that the Mental Development Index scores from the BSID-2 were within the average range and did not differ significantly between the three different feeding type groups. However, significant differences were observed with the Psychomotor Development Index (PDI) scores between the three different feeding groups at three months of age. The breastfed and milk formula-fed infants displayed higher scores than soy formula-fed infants. There were significant variations in the Composite Intelligence Index (CIX) of the Reynolds Intellectual Assessment Scale (RIAS) between the three feeding groups at 48 months. The results of these evaluations showed that the breastfed children had higher scores than children in either of the formula-fed groups, with no difference detected between these two cohorts. A significant difference was discovered with the Verbal Intelligence Index (VIX) at 48 and 60 months, with breastfed children displaying the highest scores, but no differences in the Nonverbal Intelligence Index (NIX) between feeding groups at 48 or 60 months were detected. At ages 36 and 48 months the breastfed children had significantly higher total scores on the Preschool Language Scale-3 (PLS-3) than children that were fed formula.

In addition, variations were discovered in auditory comprehension and expressive communication at later ages (24, 36, 48, and 60 months), with breastfed children scoring significantly higher than any of those participants that were formula-fed. The summary of the results showed that all children within the three groups scored within normal limits for all assessments. Breastfed children performed higher on most of the tests, but this information does not indicate that formula feeding is clinically detrimental with respect to cognitive

function and language development skills because of the relatively small magnitude of the difference. Additionally, as a correlational study, there are undoubtedly potential confounders that were not measured in this study. These findings support the earlier finding of Choi et al. (2018) in that examinations at 6 and 12 months provided information supporting exclusive breastfeeding up to 4 months of age may enhance the effects of infant development within their first year of life.

While there are significant challenges to breastfeeding ranging from socio-economic and epidemiological to cultural and emotional, it is a crucial method of promoting early childhood brain development. Formula-fed children consistently perform somewhat worse on most cognitive tests. While the magnitude of these differences may vary somewhat study by study, there is clear and pervasive evidence that breastfeeding improves cognitive development for infants.

2.8 EEG Findings

Research related to identifying early neural predictors of cognitive function in infancy could allow for future mapping of the neuro developmental pathways that emphasize individual differences in learning ability, education performance, and IQ. Individual differences in cognitive function during childhood can forecast long-term outcomes, particularly those associated with cognitive delays related to developmental risk factors such as preterm birth, small for gestational age, and poor nutrition (Jones et al., 2020, Pivik et al., 2011). Some studies have used EEG as a measurement of brain function to determine if there is any difference in infant neurodevelopment between those subjects that were exclusively breastfed and those that were fed formula. The use of event-related potential waveforms is particularly beneficial when studying infants, as they provide a non-invasive means for recording brain processes that cannot be discovered by the use of behavioral assessment alone.

EEG signals can be decomposed into oscillations occurring in different frequency bands. While there is no literature to describe differences in neural development concerning nutrition, several studies have suggested that various types of early adversity, including lower socioeconomic status (SES), (Tomalski et al., 2013), maternal stress (Troller-Renfree et al., 2020), and early institutionalization (Marshall et al., 2004) may be associated with differences in infant EEG signals. Specifically, early adversity has been related to lower frontal gamma power (Tomalski), increased theta power (Marshall, Troller-Renfree), and reduced alpha power (Marshall, Troller-Renfree). One possibility is that the links between early adversity and brain function may in part be accounted for by differences in breastfeeding, food insecurity, and nutrition.

2.8.1 EEG: Breastfeeding and Formula Feeding

As mentioned previously, human milk contains polyunsaturated fatty acids (PUFAs) that have been identified for their nutritional benefits and potential long-term brain and cognitive development benefits among infants. A study conducted by Ferguson et al. (2007), investigated the impact of breast-feeding when compared to a PUFA-enriched milk formula among infant subjects tested at 6 months of age. These researchers utilized event-related potential (ERP) waveforms and a variety of behaviors to evaluate the two groups (breastfed vs formula fed). ERP waveforms are measured using the same methodology as EEG, the difference being that ERPs are the waveforms that are measured following a particular stimulating event. Resting EEG, in contrast, are the waveforms measured when the subject is in a resting state and there is no stimulating event. Upon evaluation of their findings, Ferguson and colleagues determined that regardless of the presence of PUFA-enriched feedings among the two groups, a review of the ERP waveforms detected noticeable differences in the ERP recordings. After controlling for several factors between the two groups, it was found that only the ERPs recorded from the breastfed group varied throughout their recorded periods (700 msec) and were demonstrated

over both left and right hemispheres and all infants generated responses to stimuli across all electrode regions (frontal, temporal, posterior-temporal, central, parietal, and occipital). Formula-fed infants demonstrated changes in just the left hemisphere electrode sites and were limited to more posterior regions (temporal, parietal, and occipital). The differences detected in this study within brain responses in the breastfed group could indicate an advantage for infants who are breastfed with respect to linguistic and cognitive development in childhood.

Pivik and colleagues (2011) used a similar approach to Ferguson in that they observed event-related potential (ERP) responses to speech sounds among six-month-old infants who were fed breast milk, a milk-based formula, or a soy formula. These researchers analyzed infant ERP responses (waveforms) to speech stimuli to address the question as to whether diet-related differences in ERP measures of speech stimuli discrimination and processing were observed when infant intake was limited to exclusive breast milk, milk formula, or soy formula feedings. They found that significant group differences were present. There was a general absence of differences between formula-fed groups, and all groups demonstrated significantly greater response amplitudes to the infrequent syllables across all EEG sites at 3 months and frontally at 6 months. However, differences remained significant at temporal sites at six months only among those breastfed infants.

Jing et al. (2010) found similar findings when examining infants that were divided into similar cohorts. They observed differences in the development of brain electrical activity during infancy when comparing infants who are exclusively breastfed with those who were fed either a milk-based or soy-based formula (no significant difference between milk and soy). They determined that the observed variations in EEG activity reflected diet-related influences on brain structure development and function that could potentially elicit different neurodevelopmental trajectories, as well as cognitive and brain function development.

Cantiani et al. (2019) and Jones et al. (2020) chose to research macroscopic brain oscillations on EEG recordings of infants. Cantiani chose EEG oscillations, as research has previously demonstrated that neural oscillations at rest in the gamma frequency band (25–45 Hz) are correlated with neurodevelopmental pathways and potentially determine differences in future intellect (Cantiani et al., 2019). One key area of neuroscientific research shows that neurons within the human brain produce intricate displays of oscillatory activity characterized as rhythmic, periodic shifts from high to low states of excitability. At the point of neural ensembles, macroscopic oscillations can be observed on an EEG as a result of copious synchronized neuronal activity. This activity has been theorized to contribute to the growth and development of cortical networks.

By the time a child reaches the age of two, they typically possess the ability to speak between 150-250 words, can understand many more, and are starting to form rough statements and sentences. These early language milestones are predominantly inhibited by brain development and potentially by exposures related to childhood situations (environment, nutrition, and health) (Rudolph & Leonard, 2016; Flensburg-Madsen et al., 2019). Cantiani and colleagues (2019) looked specifically at high-frequency neuronal oscillations in the gamma frequency range (> 25 Hz). Research has shown that gamma range oscillations correlate to the establishment of specific synchronization of distributed neural responses (Uhlhaas et al., 2010), and gamma power could represent synchronization throughout extensive cortical regions. Neural resources accountable for language are dispersed throughout the brain. Therefore, the coordination of gamma frequency oscillations in distinct brain regions could be critical for language achievement (Veit et al., 2017).

When reactions to specific stimuli elicit expanded power within the gamma frequency range, the response has been associated with different cognitive processes such as memory, attention, perceptual learning, object recognition, and language skills (Ou & Law, 2018; Ortiz-

Mantilla et al., 2016; Houweling et al., 2020). Increased gamma frequency synchronization of neural ensembles has also been determined to be essential for higher cognitive processes and perception during early childhood development (Gupta et al., 2020). The study by Cantiani (2019) aimed to discover (hypothesis 1) if an interrelation exists between brain growth and development features such as gamma frequency oscillatory activity, Structural Equation Modeling (SEM), and language acquisition, by comparing gamma power in infants (6 months) and specific language outcomes in the same children at 24 months. They also investigated whether (hypothesis 2) SES during zero to six months had an effect on gamma power at 6 months and if (hypothesis 3) gamma power changed the SES findings of language outcomes. The researchers stated that they believed that this was the only known study designed to explicitly examine the hypothesized direction of association connections between oscillatory gamma power at 6 months and language outcome at 24 months, and SES using a specified framework.

Eighty-four infants born to parents holding positions from unskilled workers to white-collar professionals were recruited for this study. Parents were asked to complete the supplied Language Development Survey (Rescorla et al., 2016) by identifying each word on the checklist that their child spontaneously uttered. Four-minute baseline EEG recordings were gathered by using a 60 scalp electrode net while a study assistant blew bubbles to gain the infants' attention. All baseline EEGs were collected when study participants were six months old (± 15 days). The parental SES was collected for both parents when the children were six months old and ranged from 10 to 90. The SES scores of 10 corresponded to unskilled workers, 50 corresponded to sales workers, and 90 corresponded to professional positions. Scores ≤ 60 were determined to be low to middle income, while scores ≥ 61 were considered to be in a high-income range. Expressive language was once again determined by using the same parent-completed Language Development Survey at 24 months of age.

The data from this study concluded that an interrelation exists between brain growth and development features such as gamma frequency oscillatory activity, Structural Equation Modeling (SEM), and language acquisition. The data also supported previous research that showed gamma oscillator activity related to neural processes supports the growth of the brain and cognitive development and are essential for ideal linguistic development. However, researchers did note some variation in findings that included evaluation of infants at six months instead of using older (16–36 months) or younger (< four days), showing that later language development is associated with gamma power and that the cohort age (6 months) correlation with later language outcomes seems to related central and parietal regions exclusively. They also discovered left-lateralized relationships between gamma power at 6 months and language outcome. Therefore, these findings were expected based on the knowledge that language is connected to specialized brain systems found in the left cerebral hemisphere. Any disturbances in this lateralization would result in language impairments.

Hypothesis 2 (SES during zero to six months affected gamma power at 6 months) was confirmed; additionally, parental SES was associated with significant differences in the frontal, parietal, and central brain regions. These findings repeat and support previous studies related to this question. However, Cantiani and colleagues (2019) found that their SES data distribution was slightly skewed toward the professional end, or higher income level. The final hypothesis (gamma power was related to SES findings of language outcomes) looked for a potential link between SES and behavioral outcomes in language acquisition during infancy. Their data revealed that there was a significant, though indirect, effect between SES and MLU score related to left central gamma power. This finding suggests that SES was linked to more positive gamma power at six months of age and that this correlation affected the use and arrangement of words at twenty-four months. However, these researchers did recognize that

their study did have one specific limitation. They chose to use language outcomes that had been assessed solely by parental reporting methods.

Jones and colleagues (2020) also researched macroscopic brain oscillations on EEG recordings of infants. This study was designed to distinguish early neural predictors of cognition in infant study subjects to determine the neurodevelopmental pathways that emphasize intellectual differences among young children. These researchers identified a need to progress beyond observation behavioral studies and advance newly-available infant-friendly methods to directly measure infant brain activity. Therefore, they chose to measure the brain activity of 106 twelve-month-old infants that were grouped into three distinct cohorts to analyze dynamic changes in theta power (3–6 Hz) measured by EEG (128-channel Geodesic sensor nets) data recordings when study participants were exposed to an “ecologically valid stimuli”.

Within the three cohorts, the first (cohort 1) consisted of a large cross-sectional group of typically developing 12-month-old infants. The data gathered from this group were analyzed to determine that the dynamic semi-naturalistic video viewed by these infants produced measurable increases in theta power. It was also verified that changes observed in theta power with the first presentation could predict observations with repeated viewing of the same stimulus, thus demonstrating an association with infant learning and memory. A smaller subset of this cohort was further evaluated by observing for potential theta power changes related to concurrent cognitive skills. These infants were shown videos specifically containing women talking and toys moving. After viewing once, they were exposed to a 10-minute video of separate static stimuli and then shown the initial video a second time. It was observed that these video stimuli produced gradual increases in frontal theta and determined that with repeated exposure to the same stimuli these theta changes could be predicted.

The second and third cohorts included 12-month-old infants at low or high familial risk for autism that was independently studied and followed longitudinally. Cohort 2 was evaluated at 12 and 24 months, while cohort three was evaluated through 7 years of age. In the third cohort, Jones and colleagues investigated whether dynamic changes in frontal theta power could predict later intelligence when these children underwent subsequent cognitive assessment (Mullen Scales of Early Learning, Mullen 1) at 2, 3, and 7 years of age to determine an increased risk for cognitive delay by administering the Wechsler Abbreviated Intelligence Scale (WASI).

The infants were evaluated for change in theta power while watching two sets of videos. Each set consisted of two one-minute videos that were repeated twice during each session. One video was socially oriented, and the other was considered non-social. The primary outcome consisted of the percentage of change in theta power demonstrated between the first and second halves of the first presentation of each video “frontal theta during second half-frontal theta during first half/frontal theta during first half”. This process was designed to account for the possibility that the second presentation would be skewed by familiarity. They then observed EEG findings for associations with current cognitive skills by examining the percentage of change in posterior theta power, scalp high alpha power, and the proportion of clean attended segments (a substitute for a behavioral measure of focused attention). This information can offer evidence of whether similar outcomes could be gathered from the exclusive measuring of behavior as seen in other recent studies by Braithwaite et al. (2020) and Begus et al. (2020).

The results of this study led Jones and colleagues to determine that when infants viewed selected videos, it stimulated an increase in theta power that can predict ensuing changes in EEG responses when that specific video is repeatedly viewed by the infant. EEG and cognitive data from participants in cohort 2 showed that frontal theta change in 12-month-old high-risk infants correlated with greater nonverbal and verbal skills at 24 months, while larger changes

in frontal theta for cohort 3 was related to higher nonverbal cognitive skills at 36 months throughout this group (regardless of risk). However, nonverbal cognitive skills were not related to change in posterior theta power, clean attended segments, and were weakly associated with scalp alpha power at 3 and 7 years of age. When seven years old, this same cohort was evaluated for IQ. Researchers discovered a substantial overall connection between 12-month frontal theta and 7-year IQ scores that did not vary significantly by risk group (low or high), but WASI total scores were not correlated with observed changes in posterior theta power, scalp alpha power, and clean attended segments. In three separate cohorts, they demonstrated that individual differences in frontal theta percentages during the viewing of these videos were associated with variations in nonverbal and verbal cognitive skills at 12 months, and again at 2, 3, and 7 years of age. These results illustrate that among 12-month-old infants, task-dependent changes of frontal theta power is strongly correlated with individual differences in present and later cognitive development. Their study represents a breakthrough approach to identify a predictive biomarker for childhood intelligence.

Additional research conducted by Krol and colleagues (2015) used a similar approach to invoke brain changes among infants, but included the variable of duration that the child was exclusively breastfed at the time of the study to determine if exclusive breastfeeding demonstrates a promotion of healthy brain development and cognition, as measured by EEG recordings. Oxytocin (released with infant suckling) is one component of breast milk that has been shown to elicit numerous social processes and behaviors related to relationship and infant-mother bonding (UvnäsMoberg et al., 2020; Newton et al., 2018). Additional research using oxytocin-containing nasal spray has demonstrated effects (yet not completely understood) on the assessment of positive emotional expressions by adult study subjects (Pavarini et al., 2019; Hovey et al., 2020).

Relying on these previous study results in adults, these researchers displayed different static images to 8-month-old infants. These static images consisted of black and white pictures of happy and fearful body expressions to determine if infant brain activity corresponded to positive and negative content, as infants by this age have typically developed an ability to distinguish and differentiate between another person's positive and negative emotional expressions (e.g. smile vs frown or fearful) (Matsunaga et al., 2020). The 28 infant participants were shown these pictures after an alert tone to gather attention to the image. Alerting sounds were varied throughout the session and abstract screensavers were displayed between desired images. The images were shown in a randomized order (upright and inverted) without the same image or position being displayed back-to-back, while EEG responses were recorded as with similar research studies (Missana et al., 2014) during a time window of 700–800 ms (27 electrode elastic cap) to measure the negative central component in their event-related brain potential.

The data from this study by Krol et al. (2015) showed that of the 28 infant participants, 14 were breastfed at least one time per day (equal to a meal). The analysis of EEG recordings (averaged right frontocentral (F4 and C4) late negative central component) produced a highly significant emotion (high exclusive breastfeeding) when images were displayed in the upright position. Additional analyses showed that the low exclusive breastfed group infants ($M = 102.66$ days) displayed higher (more negative) late Nc responses to fearful body images when compared to happy images, suggesting a more significant allocation of attention to displayed fearful stimuli.

In contrast, high exclusively breastfed infants ($M = 198.43$ days) exhibited more significant late Nc responses to happy body images and greater positive late Nc responses to fearful images, exhibiting more significant attention allocated to displayed happy stimuli. Upon further assessment of these interactions, it was revealed that group differences (low vs

high) in emotional processing were seen specifically by late Nc responses to happiness, as no group averages differed significantly when explored for fear. Ultimately, the study revealed that the duration of exclusive breastfeeding positively correlates to differences in the neural processing of displayed emotional body images in 8-month-old infants.

Table 1 Literature Review Matrix of EEG and Breastfeeding vs. Formula Feeding Studies

Author, Date and Study Design	Aims	Subjects	Methodology and Exposure	Results and Conclusion
Jing et al., 2010 Cohort study	Compare effects of infant diets on development of brain electrical activity during infancy.	40 full-term infants either breastfed (BF) or fed milk formula (MF) or soy formula (SF) through the first 6 months	Scalp EEG signals (124 sites) recorded from the same infants during quiet wakefulness (resting) at 3, 6, 9, and 12 months. Exposure: BF, MF, and SF	Significant diet-related differences were present across frequency bands and included effects that were time- [peaks in 0.1–3 Hz at 6 (MF,SF) and 9 months (BF); 3–6 Hz at 6 months (MF, SFNBF); increases in 6–9 Hz from 3 to 6 months (MFNBF) and from 6 to 9 months (MFNSF)] and gender-related (9–12 Hz and 12–30 Hz: at 9 months BFNMF, SF boys, and MFNSF girls). The development of brain electrical activity during infancy differs between those who are BF compared with those MF or SF but is generally similar for FF groups. These variations in EEG activity reflect diet-related influences on the development of brain structure and function that could put infants on different neurodevelopmental trajectories along which cognitive and brain function development.
Krol et al., 2014 Cohort study	Examined whether and how duration of EBF impacts neural processing of emotional signals by measuring electro-cortical responses to body expressions.	28 infants, 8 months old	Different static images displayed in random order consisting of black and white pictures of happy (6) and fearful (6) body expressions and were shown. Abstract screensavers were displayed between desired images, while EEG responses were recorded during a time window of 700–800 ms to measure negative central component in event-related brain potential. Exposure: EBF	Infants with high EBF experience show a significantly greater neural sensitivity to happy body expressions than those with low EBF experience. Analyses showed neural bias toward happiness or fearfulness differs as a function of the duration of EBF. Longer BF duration is associated with a happy bias, and shorter BF duration is associated with a fear bias. Findings suggest that breastfeeding experience can shape the way in which infants respond to emotional signals.
Pivik et al., 2011 Longitudinal study	Study brain responses (ERPs) to speech sounds for infants who were either BF or formula-fed	351 infants	Infants were grouped according to method of feeding: BF (n=75), MF (n=88), and SF (n=76). Data was gathered at study visits 3 and 6 months for responses of ERPs to speech sounds (two syllables presented in an	Two syllables presented in an oddball paradigm elicited a late positive wave (P350) from temporal and frontal brain regions involved in language processes. All groups showed significantly greater response amplitudes to the infrequent syllable across sites at 3 months and frontally at 6 months, but

	(MF or SF) during the first 6 months of life.		oddball paradigm). ERP responses were determined from EEG activity (bandpass 0.1–100 Hz, sampling rate 250 Hz) using 124 channel electrode nets. Exposure: BF, MF, and SF	significant discrimination at temporal sites was only observed at 6 months in BF infants. Decreases in response amplitudes from 3 to 6 months were greater for the frequently presented syllable, most prominent in BF infants, and greater in females than males. Results indicate greater syllable discrimination in BF than FF infants. Feeding method and background factor differences between BF & FF infants may also contribute to observed differences.
--	---	--	--	---

2.9 MRI Findings

MRI’s are another effective tool for measuring brain growth and structural development among infants. They can be used to measure both grey and white matter growth in terms of volume as well as location. They can also be used to measure other predictors of white and grey matter development. MRIs are a key methodology utilized to better understand the impact of breastfeeding on infant brain development.

The benefits of breast milk for infant brain function have been displayed by MRI study findings among infants and beyond with lasting effects among school-aged children. Many of the current studies are related to the evaluation of gray matter or white matter development, while few look at either or both among infants. Identified research by Luby et al. (2016) and Ou et al. (2018) chose to investigate the impact of breastfeeding versus formula feeding on structural brain development (gray matter) and cognition among infants and young children.

Luby and colleagues conducted a longitudinal study to determine how breastfeeding may influence intelligence through evaluation of the whole brain and subcortical brain volume (as separate mediators). As part of their research, they identified a gap in the current literature and established a study outcome to address this gap by testing the hypothesis that “the relationship between breastfeeding and IQ would be mediated by the effect of breastfeeding on structural brain development and, in turn, the effect of brain on IQ. Within this study, 211 child participants (ages 3 to 6 years old) were recruited for evaluation by MRI scanning during three

sessions throughout 16 years (2008 to 2014). These sessions were conducted to determine subcortical gray volume across the three scans to test for any effects on long-term volumetric brain structure related to breastfeeding. Of these participants, the final sample included findings related to 148 children who had data that were complete and high quality in all of the variables of concern.

The MRI scans were conducted, and structural images were obtained as part of a longer session and encompassed the gathering of functional connectivity and task-based data. During these scans, cerebral white matter volume and total cortical and subcortical gray matter volumes were acquired, while whole brain volume was determined as the sum of all three of these measures. In addition to the MRI scans, the child participants were evaluated for intelligence. The Kaufman Brief Intelligence Test (KBIT) or the Wechsler Abbreviated Scale of Intelligence (WASI) was used for assessing verbal and nonverbal intelligence during school age. Children 10 to 15 years old were evaluated by using the KBIT and children 8 to 11 years old were evaluated by using the WASI.

From the data gathered these researchers aimed to gain information related to two hypotheses including 1) “breastfed children would have significantly higher IQ scores compared with non-breastfed children” and 2) “breastfed children would have significantly larger whole brain volumes (WBV) compared with non-breastfed [children].” The findings from this study showed that cortical white matter volume results indicated that children that were breastfed did not display large WMV and therefore, it was determined not to be a significant predictor of a child’s white matter volume. When measuring total grey volume, breastfed child participants had more significant total gray matter volume than did non-breastfed participants, as displayed by a substantial and additional percentage of the variance in total gray matter volume.

When calculating whole brain volume, the child's sex and age were significant predictors of WBV and that breastfeeding was associated with greater WBV as well. These researchers also found that subcortical gray matter volume (SGMV) was the most significant finding when evaluating the effects in WBV and total gray matter volume and that SGMV facilitated the correlation between breastfeeding and higher intelligence scores. The final determination of this study was that the data demonstrated an indirect association between breastfeeding and IQ through the expansion of gray matter volume, particularly the subcortical gray matter even when controlling for maternal education and the child's age and sex.

A smaller study (42 eight-year-old children) was conducted by Ou et al. (2016) to determine whether being breastfed or receiving cow's milk formula feeding has an influence on the development of grey matter structures. The breastfed participants were fed breast milk exclusively for a minimum of 8 months (average, 12.6 months), and milk formula-fed participants received the same type of cow's milk formula for at least 8 months after birth. All child participants underwent one MRI examination that included a structural scan and an fMRI study. These same participants were administered the Reynolds Intellectual Assessment Scales (RIAS) test, to measure verbal, nonverbal, and composite IQ, and the Clinical Evaluation of Language Fundamentals (CELF-4) test, to measure expressive, receptive, and overall language skills.

In contrast to the research findings by Luby et al. and Zhang, Y et al., Ou found no difference in total brain gray matter volume when comparing MRI findings of the breastfed (n=22) and cow's milk formula (n=20) groups. However, MRI scans revealed that breastfed participants had greater regional gray matter volume in multiple brain regions, explicitly in the left and right parietal and left temporal lobes, and one region in the left superior parietal lobe and one region in the left inferior temporal lobe displayed significantly greater gray matter volume than those participants that were predominantly milk-based formula-fed (716).

When assessed by fMRI showed that breastfed participants displayed significantly more widespread activation than milk-based formula-fed participants. Significant findings were observed in the right frontal and left and right temporal lobes when evaluating perception tasks and in the left temporal/occipital lobes when evaluating language tasks. Though these findings are different from those seen with Luby et al. and Knickmeyer et al. (2008), they support earlier findings from a study by Wilke et al. (2003) and are supported by more recent findings by Zhang et al., in that whole-brain gray matter volume was directly related to the age of their participants (older vs younger children), yet gray matter volume in several distinct brain areas (deep grey matter structures) was decidedly related to cognitive functions (Wilke et al., 2003; Zhang et al., 2019). This information is also conveyed by Ou in that diet (breastfeeding vs formula feeding) may influence brain maturation, showing a greater effect on deep gray matter during infancy, as these areas of the brain develop earlier than cortical regions that develop more during later childhood (Ou et al., 2016; Aubert-Broche et al., 2013, Makropoulos et al., 2016; Mills et al., 2016).

Other major studies are related to the research of white matter development during early childhood. In contrast to grey matter volume development that occurs predominantly during infancy and then decreases during childhood and adolescence, white matter volume increases can be observed across infancy, early childhood, and adolescence (Aubert-Broche et al., 2013, Makropoulos et al., 2016; Mills et al., 2016). Two identified studies used MRI scans to determine if breastfed children display a higher level of cognitive skills as a result of early nutrition (breastmilk) that impacts early trajectories of myelination and differences in white matter tracts.

Deoni et al. (2018) focused on the nutritional needs of the infant, particularly how specific micro- and macro-nutrients, long-chain polyunsaturated fatty acids (DHA and ARA) (Braarud et al., 2018; Martin et al., 2016; Lauritzen et al., 2016), phospholipids

(phosphatidylcholine and sphingomyelin), neurotrophic factors (Kim et al., 2020), and hormones (Kinney & Volpe, 2018) contained within breastmilk are essential for myelination. Though many milk-based infant formulas attempt to replicate these needs, they cannot provide the different compositions of human milk from colostrum through mature milk. These researchers believe that the differences in the nutritional composition of breast milk and infant formula could explain some observed disparities in cognitive function between breastfed and formula-fed infants.

Participants included in this study were chosen from a large and ongoing longitudinal study known as the Brown University Assessment of Myelination and Behavior Across Maturation (BAMBAM) study (Deoni et al., 2012) that includes more than 500 children that are between 0 and 5 years of age. The children in this study were grouped according to how they were fed. Researchers split participants into two groups; the first were exclusively formula-fed (n=88) and the second were exclusively (at least 90 days) breastfed (n=62). The formula-fed infants were then divided into three groups based on the specific formula that was used (group 1= 21, group 2=28, group 3=39).

MRI scans were obtained throughout this study and included a total of 231 scans with breastfed children and 221 with formula-fed children. Along with MR imaging, general cognitive ability and skills were assessed using the Mullen Scales of Early Learning (Mullen 1) in each child that was under 5 years and 8 months of age (within 7 days of scanning) and for older children, the Wechsler Intelligence Scale for Children, 5th Edition (WISC-V) was used. To detect specific nutritional values of the identified (groups 1-3) formulas, each was analyzed for their content of phospholipids (Phosphatidylinositol, Phosphatidylethanolamine, Phosphatidylcholine, Phosphatidylserine, and Sphingomyelin), Alpha-lactalbumin, Beta-lactoglobulin, ARA, DHA, folic acid, phosphorus, calcium, sodium, copper, potassium, magnesium, and vitamin B12.

Throughout this study, researchers found differential patterns of development in all investigated brain regions. However, breastfed participants qualitatively displayed sustained, rapid development between 500 and 750 days of age and an overall increase in myelin by age two, that persisted throughout their childhood. The formula-fed participants showed increased myelin before age one, but a slower initial rate of development between ages 1 and 2 and did not reach the same extent of myelin development as the breastfed participants.

The data displayed significant differences throughout most brain regions examined (parietal and cerebellar white matter, splenium of the corpus callosum) and in nearly all Gompertz model parameters (frontal, temporal, and occipital white matter, and the body and genu of the corpus callosum). These researchers noted that the child participants who received formula compositions with higher levels of DHA, ARA, choline, and sphingolipids (formulas #2 and #3) indicated higher levels of myelin development. Children fed formula #1 (lowest concentration of DHA, ARA, and sphingomyelin, but the highest concentration of iron and vitamin B12) exhibited slower and reduced myelin development. The analyses of this study focused on the importance of known neuro-associated nutrients. Though some infant formulas come closer than others, none contain the necessary nutrients to achieve the myelin trajectory of those infants that are breastfed.

The findings of this study are important, in that, previous studies (Dean et al., 2015) related to the relationships between myelin water fraction maturation and cognitive development demonstrate a strong correlation between changes in myelin water fraction and measurements of gross motor skills, visual reception, and receptive language, while the connection between myelin water fraction and fine motor skills and expressive language were found to evolve.

An additional study by Bauer and colleagues (2020) used diffusion tensor imaging to evaluate the major white matter tracts and volumetric measurements of the corpus callosum in

4 to 8-year-old children. The focus of this study was to determine 1) if breastfeeding duration is positively associated with total white matter and fractional anisotropy scores, and volumes of specific subsections of the corpus callosum and 2) if feeding methods (breast or formula-fed) influence longitudinally running tracts that link the temporal and parietal areas to the frontal lobe demonstrate substantial changes in fractional anisotropy and volume(s).

Sixteen children were ultimately selected for corpus callosum analysis. Before any MRI scans, children were categorized into three groups based on the primary form of feeding, exclusively breastfed (n=7, mean duration=9.9 months), exclusively formula-fed (n=2), or both breast and formula-fed (n=7). The data from these MR images showed that breastfeeding duration did not demonstrate a significant correlation with total corpus callosum volume or any sub-sections (anterior, anterior-central, central, posterior-central, posterior). The scans also demonstrated that there was no significant difference in total corpus callosum volume when comparing the type of primary feeding methods. There was no demonstrated correlation between breastfeeding and total white matter volume or grey matter volume, and no significant difference was seen when compared to scans of those children that were exclusively formula-fed.

However, breastfeeding duration had a positive correlation with both and weighted fractional anisotropy scores in the left angular bundle and significantly higher center fractional anisotropy scores for the left superior longitudinal fasciculus. Although neither of the study hypotheses was supported, these researchers found that their results suggest a highly specific, left-lateralized association that is related to infant feeding methods. The results did support and expand on some of the findings of Deoni and colleagues in that they found the left superior longitudinal fasciculus (specifically the temporal portion) results but also discovered differences in this tract (using water fraction measures) when comparing a younger cohort of children who were exclusively breastfed compared to those participants that received any

formula-feeding and in previous studies that have been associated with higher neurocognitive performances (Can et al., 2013; Lebel et al.; 2018, Qiu et al., 2015; Krogsrud et al.; 2016, Genc et al., 2017; O'Muirheartaigh et al., 2014; Liu et al., 2016).

The existing literature is mixed on whether breastfeeding promotes grey matter development in terms of volume. However, there is strong evidence that breastfeeding changes the locations where grey matter is clustered; these breastfed formations are associated with more mature neurological development. White matter and other predictors of white matter growth have been positively associated with breastfeeding. Additionally, small, highly specialized parts of the brain may be supported by breastfeeding. More research using MRIs is needed to develop a better consensus around the relationship between breastfeeding and grey and white matter development.

Table 2 Literature Review Matrix of MRI and Breastfeeding vs. Formula Feeding Studies

Author, Date, and Study Design	Aims	Subjects	Methodology and Exposure	Results and Conclusion
Deoni et al., 2018 Longitudinal study	To address how differences in the nutritional composition of breast milk and infant formula could explain observed disparities in cognitive function between these two types (feeding) of infants.	150 children	Children were grouped according to whether they were exclusively given infant formula-fed (EFF) (n=88) or exclusively (at least 90 days) breastfed (EBF) (n=62). The ff infants were then divided into three groups based on the specific formula that was used (group 1= 21, group 2=28, group 3=39). Mri scans were obtained, children are scanned and cognitive assessments at 6-month increments from time of recruitment until 2 years of age, and yearly thereafter. The mullen scales of early learning (mullen 1) in children under 5 years and 8 months and the wechsler intelligence scale for children, 5th edition (wisc-v) with older children. Exposure: EBF, EFF	Results reveal significantly greater overall myelination in breastfed children accompanied by increased general, verbal, and non-verbal cognitive abilities compared to children who were exclusively formula-fed. These differences were found to persist into childhood even with groups matched for important socioeconomic and demographic factors. They also find significant developmental differences depending on formula composition received and that, in particular, long-chain fatty acids, iron, choline, sphingomyelin and folic acid are significantly associated with early myelination trajectories. These results add to the consensus that prolonged and exclusive breastfeeding plays an important role in early neurodevelopment and childhood cognitive outcomes.
Isaac, et al., 2010	Investigate whether breast milk mediates	50 Adolescents	Data was gathered from a randomized feeding trial to calculate the percentage	In the total group, %EBM correlated significantly with verbal intelligence quotient (VIQ); in

Retrospective cohort study	cognitive effects by affecting brain growth.		of expressed maternal breast milk (%EBM) in the infant diet of 50 adolescents. MRI scans were obtained (mean age 15 y 9 mo), allowing volumes of total brain (TBV) and white and gray matter (WMV, GMV) to be calculated. Exposure: EBM	boys, with all IQ scores, TBV and WMV. VIQ was, in turn, correlated with WMV and, in boys only, additionally with TBV. No significant relationships were seen in girls or with gray matter. These data support the hypothesis that breast milk promotes brain development, particularly white matter growth. The selective effect in males accords with animal and human evidence regarding gender effects of early diet.
Kafouri et al., 2012 Retrospective cohort study	Evaluate association between duration of EBF and structure of cortical regions implicated in general intelligence.	571 adolescents aged 12–18 years	Hierarchical linear modelling was used to assess whether breastfeeding (BF) was considered an important predictor of cortical thickness when other predictors are considered. Target cortical regions were identified using a meta-analysis of functional neuroimaging studies of cognitive abilities relevant for general intelligence. Exposure: BF	Data showed duration of EBF was associated with cortical thickness in the superior and inferior parietal lobules, and this study replicated the association between BF and general intelligence. This study showed that BF is associated with variations in the thickness of the parietal cortex in a community-based sample of adolescents and replicated previous findings that displayed an association of breastfeeding duration with full scale and performance IQ.
Bauer et al., 2020 Retrospective cohort study	Determine if BF duration is positively associated with total white matter (TWM) and fractional anisotropy scores (FAS), and volumes of specific sub-sections of the corpus callosum and if feeding methods influence longitudinally running tracts that link the temporal and parietal areas to the frontal lobe demonstrate substantial changes in FAS and volume(s)	16 4 to 8-year-olds	This study used diffusion tensor imaging to evaluate the major white matter tracts and volumetric measurements of the corpus callosum. Before any MRI scans, children were categorized into three groups based on the primary form of feeding, exclusively breastfed (n=7, mean duration=9.9 months), exclusively formula-fed (FF) (n=2), or both breast and formula-fed (n=7). Exposure: EBF, EFF, both BF and FF	Data MR images showed that BF duration did not demonstrate a significant correlation with total corpus callosum volume (CCV) or any sub-sections (anterior, anterior-central, central, posterior-central, posterior). Scans also demonstrated that there was no significant difference in total CCV when comparing primary feeding methods. There was no demonstrated correlation between BF and TWM volume or GM volume, and no significant difference was seen when compared to scans of those children that were EFF. BF duration had a positive correlation with both and weighted FAS in the left angular bundle and significantly higher center FAS for the left superior longitudinal fasciculus. Neither of the study hypotheses was supported. Results suggest a highly specific, left-lateralized association that is related to infant feeding methods. The results support and expand findings of other studies that they found the left superior longitudinal fasciculus (specifically the temporal portion) results but also discovered differences in this tract (using water fraction measures) when comparing a younger cohort of children who were EBF

				compared to those participants that received any FF and in previous studies that have been associated with higher neurocognitive performances.
Ou et al., 2016 Cohort study	Evaluate brain gray matter (GM) structure and function in children who were predominantly BF or cow's milk FF as infants.	42 healthy 8-year-old children	Forty-two healthy children (BF: n= 22, FF: n=20) were studied by using structural MR imaging (3D T1-weighted imaging) and blood oxygen level-dependent fMRI (while performing tasks involving visual perception and language functions). Children were administered standardized tests evaluating intelligence (Reynolds Intellectual Assessment Scales) and language skills (Clinical Evaluation of Language Fundamentals). Exposure: BF, FF	Total brain GMV did not differ between BF & FF groups. However, BF children had significantly higher regional GMV measured by voxel-based morphometry in the left inferior temporal lobe and left superior parietal lobe compared with FF children. BF children showed significantly more brain activation in the right frontal and left/right temporal lobes on fMRI when processing the perception task and in the left temporal/occipital lobe when processing the visual language task than FF children. The imaging findings were associated with significantly better performance for BF than FF children on both tasks. Findings indicate greater regional grey matter development and better regional grey matter function in BF than FF children at 8 years of age and suggested that infant diets may have long-term influences on brain development in children.

The above-described literature demonstrates the positive impacts of breastfeeding on brain development in early childhood as measured by EEG and MRI, specifically when compared to formula feeding. The present study is unique in that the large sample size is derived from four large metropolitan areas and all participants have incomes below the federal poverty line. Based on the literature above describing the impact of low-SES factors and brain development in early childhood, one possibility exists that the links between early adversity and brain function may in part be accounted for by differences in breastfeeding approach. Finally, the current study will be the only one of its kind to evaluate the impact of breastfeeding on four frequency bands of brain waves (theta, alpha, beta, and gamma) as measured by electroencephalography (EEG).

2.10 Neuroplasticity, Socioeconomic Disparities, and Adaptive Brain Function

The socioeconomic status (SES) of a child is shaped by a variety of factors, including family income, parental occupation, and education. This chapter has previously discussed the patterns of associations between being from a lower SES as a child and outcomes including brain function and structure (Noble & Giebler, 2020). This section will review literature that suggests that the differences seen in brain function associated with SES can be considered *adaptive* rather than *deficits* due to our understanding of how neuroplasticity is influenced by experience. New research suggests that the adaptations in brain function in children who have had adverse experiences may in fact be contextually appropriate adaptations. These adaptations could be phenotypically perceived as “skills” that may support a child who is experiencing adversity (Ellis et al., 2020). This framing of differences in brain function as adaptations allows us to recognize the resiliency of a child’s brain to overcome adversity and develop the skills necessary to thrive within their environment. This area of study offers an alternative perspective to the way in which differences in brain function are perceived with respect to behavior, achievement, and other characteristics.

For example, in a study which measured ERPs while children were asked to selectively pay attention to a story being played in one ear while ignoring another story being played in the other ear found that children from low SES backgrounds demonstrated less evidence of neural suppression irrelevant to the audio stimuli when compared to their peers from higher SES backgrounds (Stevens et al., 2009). In the deficit framework, it could be perceived that the children from higher SES backgrounds had an advantage of skill over their peers, while the adaptive framework allows us to consider that the children from lower SES backgrounds may have developed this skill as a mechanism of vigilance that is more supportive of their real-life experiences. Similarly, another study has demonstrated that children with a history of physical abuse are more capable at detecting cues of anger (Shackman et al., 2007). This adaptation

though comes at the expense of poorer attentional control and increased brain activity in the presence of anger. The adaptive framework allows for the consideration that these children, who may suffer with respect to their attention in an academic setting, which could result in lower academic performance, have adapted in order to have the skills to navigate the realities of their environment which prioritizes safety over educational experience. Finally, the ability to understand differences in brain function as adaptations rather than deficits allows scientists to prioritize the identification of adaptive brain function that may allow children to improve their academic experiences. For example, children from low SES backgrounds are more likely to prefer spatial problem-solving skills over verbal strategies in arithmetic, in contrast with their peers from higher SES backgrounds (Demir et al., 2015). Additional research has similarly found differences in brain connectivity and structure with respect to SES and other aspects of a child's environment, in relation to cognitive performance (Ellwood-Lowe et al., 2020; Leonard et al., 2019). This body of literature offers an opportunity for future exploration to consider how children from different backgrounds with adaptive differences in brain function can be better served with respect to alternative teaching strategies and curricula (Ellis et al., 2020).

2.11 Household Food Insecurity

Household food insecurity is a crisis impacting millions of Americans; it disproportionately affects Black and Hispanic households as well as families living below the poverty line. Low educational attainment, being a renter or an immigrant are all additional risk factors for food insecurity. There are, however, a number of government programs, notably the Supplemental Nutrition Assistance Program (SNAP) and the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC), which help alleviate food insecurity for families.

The United States Department of Agriculture (USDA) utilizes the description of food insecurity as defined by Anderson 1990 — “*Food insecurity is the limited or uncertain availability of nutritionally adequate and safe foods or limited or uncertain ability to acquire acceptable foods in socially acceptable ways.*” The USDA Short Form (U.S. Household Food Security Survey Module 2) uses six items to determine household food security and is scored according to a set scale that allows for consistent responses. According to the current USDA statistics (2019), over 35 million people are living in food-insecure households. Among these households, over 5 million included at least one child, with rates appearing even higher among Hispanic and Black non-Hispanic households and those that met the Federal poverty guidelines (USDA, 2019). These at-risk children are of concern, as reduced access to adequate, nutritious food sources has been shown to increase a child’s risk of delayed or decreased cognitive development and lower academic performance (Landry et al., 2019; Fram et al., 2015; Koleilat et al., 2016; Hanson & Connor, 2014).

2.11.1 Identifying Potential Risk Factors

Hunger and undernutrition can arise as a result of food insecurity, depending on the severity and duration. Food insecurity may also cause the onset or exacerbate other conditions such as emotional stress, which is important to consider as socio-emotional functioning develops within the first years of life. A study conducted by Leitz (2018) identified specific factors that contribute to food insecurity in the United States. It was stated by Leitz, that it is well known that the majority of food-insecure households are associated with low income, poor education, unemployment, or disability among young single parents who predominantly live in urban areas, specifically among ethnic minorities with a greater number of children living in the household. Other research suggests that households that are comprised of non-citizens, as well as renters, are also prone to food insecurity (Bartfeld & Men, 2017).

Additional studies are concerned with how food insecurity can affect infant nutritional needs and neurological development at a vulnerable age, as high food insecurity is associated with poorer diet quality and quantity, which may result in malnutrition which in turn has been associated with impaired brain development leading to cognitive deficits and poor academic achievement. However, according to a review conducted by Hanson and Conner (2014), their primary conclusions were that food insecurity is not consistently linked to poor diet quality in children but showed less fruit consumption, the amount of sugar consumption showed no association with food insecurity, and food insecurity among adults consisted of fewer vegetables, fruit, and dairy items that individuals reported as food secure, with lower intake of vitamin A and B6, calcium, magnesium, and zinc.

2.11.2 Factors Impacting Food Insecurity

Several risk groups are associated with food insecurity. From literature, we find that younger people, certain minorities (African American or Hispanic), income marital status (single mothers), and educational attainment (low levels) increase an individual's or family's risk of food insecurity (Bartfeld & Men, 2017). Health status has been shown to directly affect food insecurity. According to Coleman-Jensen and Nord (2009), poor mental health, disability, and chronic physical health conditions not only increase the likelihood of being food-insecure but are also associated with more severe levels of food insecurity among households experiencing food hardship. In addition, research by Palar et al. (2016) identifies data showing that drug abuse, specifically injection drug use, and food insecurity are exceedingly prevalent among individuals living in the United States with HIV-hepatitis C virus co-infection (5).

Several federal programs are available to individuals and families that are experiencing food insecurity. SNAP is the largest nutrition program in the U.S., is strongly associated with improved food security and positive health outcomes from the prenatal period through early childhood and into adulthood. A study by Ratcliffe et al. (2011) found that 15% of all U.S.

households and 40% of near-poor households were food insecure in 2009. Results suggest that receipt of SNAP benefits reduce the likelihood of being food insecure by roughly 30% and reduce the likelihood of being very food insecure by 20%. Other studies over the past ten years have shown that household food insecurity doubled among families with recently arriving immigrant mothers and their US-born children and child food insecurity remained these families remains alarmingly high (Lessa & Rocha, 2012; McClain et al., 2019), potentially due to fear of deportation (Bovell-Ammon et al., 2019). A study by Ettinger de Cuba and colleagues (2019) shows that among groups whose SNAP benefits were reduced or eliminated, the odds that these children and households experience food insecurity was significantly increased when compared to other groups with consistent SNAP participation. Reduction in benefits is associated with greater odds of fair or poor caregiver (1.43 times higher) and child health (1.22 times higher) (Ettinger de Cuba et al., 2019). These findings support a correlation between socioeconomic status, food insecurity, and cognitive development from the prenatal period through adulthood, suggesting that increasing nutrition increases health, food security, and cognitive development.

Another federal program is WIC, this assistance program is part of the Food and Nutrition Service of the United States Department of Agriculture and was created to promote proper healthcare and nutrition among low-income pregnant women, breastfeeding women, and children under the age of five. According to the CDC (2020), WIC counselors are trained to encourage breastfeeding among women that are currently pregnant and seeking help through this program. It has also been shown that a large disparity exists among women that are considered minorities and those that are qualified to receive benefits through the WIC program. These disparities are critical to minority populations within the United States as the National Immunization Survey (CDC, 2020) data shows that infants born to non-Hispanic Black women (73.7%) are less likely to ever breastfeed when compared with Hispanic infants (84.1%) and

Asian infants (90%). Unfortunately, data also shows that infants currently eligible for and receiving WIC benefits are less likely to ever be breastfed (77.0%).

2.12 Association between Food Insecurity and Breastfeeding

Research has shown that giving women access to educational sources and support helps promote the likelihood and duration of breastfeeding. However, providing formula through programs like WIC does not improve breastfeeding initiation (CDC, 2020). Education and maternal confidence in the ability to provide sufficient breastmilk are important factors regarding maternal choices related to breastmilk versus formula (Wallenborn et al., 2017). Recent studies have found no association between breastfeeding duration and household food insecurity, regardless of family income (Wong et al., 2019). However, research by Melchior et al. (2009) found that food insecurity among families with young children tends to be more frequent when the mother of the household experiences a mental health condition. These findings have been additionally supported by more recent research findings (Wu et al., 2018; Johnson et al., 2018). In addition, food insecurity predicted elevated rates of behavioral problems among children as maternal mental health issues can lead to less responsive caregiving and fewer early childhood stimulation opportunities in the home (Shankar et al., 2017; Fram et al., 2015).

2.13 Household Food Insecurity and Infant Nutrition

A study by Landry et al. (2019) emphasizes that household food insecurity (HFI) is adversely related to both the physical and mental wellbeing of children of any age. These researchers examined a specific relationship between self-reported HFI and dietary quality within low-income households with children. However, unlike other studies, this study chose to have the children (n=598, mean age of 9.2 years old, 64% Hispanic, and 55% female) living in these low-income households complete a self-reported questionnaire that included a modified version of the 5-item Child Food Security Assessment (CFSA). The data collected

from this questionnaire showed that when assessing dietary quality (Health Eating Index-2015), children experiencing food insecurity had less access to greens and beans, seafood and plant protein, and more access to added sugar when compared to children living in houses that are determined to be food secure. Similar study findings have been reported by other researchers in the past and have been outlined by authors such as Hanson and Conner (2014). However, many of these studies utilized questionnaires and interview answers that were provided by the parents, guardians, or others related to these at-risk children (Koleilat & Whaley, 2016; Fram et al., 2015).

2.14 Household Food Insecurity and Infant Cognitive Development

There has been an abundance of systematic reviews and meta-analyses in the past few years related to the subject of food insecurity and infant cognitive development. de Oliveira et al. (2020) conducted a systematic review and meta-analysis to investigate the association between household food insecurity and early cognitive development among children under 5 years old. The research studies in this literature review were conducted in various countries (both high and low income) and showed that household food insecurity was associated with developmental risk (cognitive/vocabulary and cognitive/math) and was specifically associated with poor early cognitive development in children under the age of five. Household food insecurity was also identified as marginally correlated with cognitive/school readiness and reading, and motor development, as demonstrated by poor math and vocabulary skills even when studies were conducted in countries considered to be high and low to middle income. These findings are consistent with previous reviews focusing on food insecurity and cognitive development of children that are considered at risk (Shankar et al., 2017, Marshall et al., 2004; Tomalski et al., 2013).

A review conducted by Noble & Geibler (2020) looked at recently published literature directly correlating socioeconomic inequality with brain structure and function among young

children. In addition, they reviewed recent research assessing specific experiential mechanisms that may be responsible for such connections including home language, environment, and family stressors. The same variables have been identified as adversities by others (Nelson & Gabard-Durnam, 2020). Some results of this review included findings such as an association between socioeconomic disadvantages and increased psychopathology and poorer neurocognitive performance in younger children as demonstrated by reduced overall gray matter volume and gray matter density. They concluded that research related to the mechanisms connecting socioeconomic disparities to neurodevelopmental outcomes are favorable for future identification of preventive and interventional actions.

One of the most recent studies related to this topic has investigated the potential risk factors of food insecurity among young children and how these factors can influence how a child's brain develops and they mature. In a study by El Din and associates (2019), 655 infants ranging from 3 to 24 months of age were assessed to determine if external factors such as low income increased a child's risk of having a below-average cognitive composite score. A study-specific questionnaire was designed for the assessment of socio-demographics then infant and maternal dietary practices were evaluated at physical examinations. Cognitive development was assessed through the Bayley Scales of Infant and Toddler Development (Bayley-III) and was administered consistent with the infant's age-specific start point. The results from this investigation showed that the risk of having lower cognitive composite scores was substantially correlated with the infant's paternal income. Infants belonging to lower to middle-income families demonstrated a risk that was 1.64 times higher than those in upper to middle-income families. Thus, demonstrating that lower income was a significant risk factor for food insecurity and can influence childhood cognitive development.

2.15 Household Food Insecurity and Childhood Academic Performance

Food insecurity not only demonstrates adverse changes in early cognitive development but continues to display ongoing effects throughout school-aged children. Research related to the topic of academic performance has shown that food insecurity during critical years of neurocognitive development can have a lasting effect even when children are no longer experiencing food insecurity later in life. Alaimo et al. (2001) investigated the associations between food insufficiency and cognitive and academic outcomes among two cohorts of children ages 6 to 11 (n=3286) and 12 to 16 years (n=2063). The data for this assessment was collected from the Third National Health and Nutrition Examination Survey (NHANES III). The children were determined as food-insufficient if the family member responding to the survey reported that “his or her family sometimes or often did not get enough food to eat.” Cognitive functioning of the children was assessed using 2 subtests of the Wechsler Intelligence Scale for Children–Revised (WISC–R) (Block Design and Digit Span), while academic performance assessed by using the reading and arithmetic subtests of the Wide Range Achievement Test-Revised (WRAT–R) .

The results of this investigation provided evidence that there is an association between food insufficiency and academic performance in school-aged children. They found that in both age cohorts that WRAT and WISC scores were approximately 1.3 to 2.5 points lower and that these children were more than twice as likely to have repeated a grade (40% of food-insufficient teenagers) and missed nearly twice as many days of school when compared to food-sufficient children. This information supports previous findings from research conducted by Jyoti and colleagues (2005). This earlier study also found that among their prospective sample of approximately 21,000 children that were enrolled in kindergarten and followed through third grade, food insecurity was a significant predictor of poor developmental trajectories and that evidence of self-reported food insecurity is linked to specific developmental consequences.

As described in this section, it is known that food insecurity is negatively linked to academic performance and cognitive development in adolescents (Alaimo et al., 2001; de Oliveira et al., 2020; Jyoti et al., 2005). Self-reported-food insecurity has also been shown to be significantly associated with poorer quality diets in adolescents (Landry et al., 2019). Poor feeding behaviors have been shown to be negatively associated with cognition, memory, and attention in adolescents (Reichelt, 2016). This evidence suggests that food insecurity is negatively associated with both cognition and diet quality in adolescents, but the literature stops short of measuring the impacts of food insecurity on brain development in early childhood. The current study aims to fill this gap by evaluating the impact of breastfeeding on four frequency bands of brain waves (theta, alpha, beta, and gamma) as measured by electroencephalography (EEG).

Chapter 3: Methods

3.1 Introduction

The overall purpose of this study is to examine the relationships between brain function and nutritional status in early childhood. More specifically, we aim to determine the extent to which being breastfed, duration of breastfeeding, and household food insecurity may be associated with the relative and absolute power spectral density of four frequency bands of brain waves (theta, alpha, beta, and gamma) as measured by electroencephalography (EEG) among 243 mothers and their infants at age 12 months old participating in the control group of the Baby's First Years study. This chapter presents the research questions and hypotheses, and describes and justifies the study design, target population, instrumentation, and procedures used to collect and retrospectively analyze the cross-sectional survey data.

3.2 Research Questions and Hypotheses

Little information is available regarding the extent to which breastfeeding, and household food insecurity is associated with increases or decreases in brain function. Whether the relative and absolute power spectral densities of the theta, alpha, beta, and gamma waves are associated with breastfeeding and household food insecurity is currently unknown.

Research Question 1: To what extent is breastfeeding related to the brain function of infants at 12 months of age?

Hypothesis 1.1: Whether an infant has ever been breastfed is associated with the relative and absolute power spectral densities of theta (decreased), alpha (increased), beta (increased), and gamma (increased) waves, as measured by EEG, among infants at age 12 months, after controlling for covariates.

Hypothesis 1.2: A mothers' duration of breastfeeding is associated with the relative and absolute power spectral densities of theta (decreased), alpha (increased), beta (increased), and gamma (increased) waves, as measured by EEG, among infants at age 12 months, after controlling for covariates.

Research Question 2: To what extent is household food insecurity related to the brain function of infants at 12 months of age?

Hypothesis 2: Household food insecurity is associated with the relative and absolute power spectral densities of theta (increased), alpha (decreased), beta (decreased), and gamma (decreased) waves, as measured by EEG, among infants at age 12 months, after controlling for covariates.

3.3 Study Design

The study design is defined as non-experimental, or observational, because the extent to which breastfeeding, and household food insecurity are related to the brain function of infants at age 12 months was investigated without intervention or manipulation of the participants by the researcher. A cross-sectional survey is used to collect quantitative data to understand the relationships between breastfeeding, food insecurity, and brain function in a sample of 243 mothers and their infants at age 12 months old. The current study is also defined as analytical/inferential because it involves multivariate statistical analysis of secondary data to examine the relationships between more than two naturally occurring variables collected in a cross-sectional survey (Hair et al., 2010; Tabachnick & Fidell, 2013).

The limitation of an observational study design is that cross-sectional survey data cannot establish causal relationships between naturally occurring variables, because there is no causation without manipulation (Bollen & Pearl, 2013; Collier et al, 2010; Taq, 2011). Per Hung et al., "there must be a convincing body of evidence to take the next step on the path to inferring that one variable causes the other" (Hung et al., 2017, p. 904). Therefore, using an

observational study design, it is not possible for the researcher to prove definitively if nutrition (specifically breastfeeding and food insecurity) has a direct or indirect effect on brain development in early childhood.

Observational studies do not involve the random allocation of participants into control vs. experimental groups, nor do they evaluate the effects on specified outcomes of manipulating one or more potential causal factors (Concato et al., 2000; Guyatt et al., 2008). Nevertheless, observational research designs involving the inferential analysis of relationships between naturally occurring variables are relevant in behavioral nutrition research. An observational design was the only practicable method of studying the impact of nutrition on brain development because an experimental design was not feasible for ethical and logistical reasons (i.e., it was unethical and practically impossible to experimentally investigate the outcomes on brain development of manipulating the nutrition of the participants). Furthermore, observational designs often help to generate significant evidence to support the testing of hypotheses using experimental designs, leading ultimately to the establishment of causal relationships (Mann, 2003; Thompson et al., 2005).

3.4 Target Population

3.4.1 Baby's First Years: Sampling and Data Collection

The sampling and data collection procedures were performed by investigators participating in the BFY study. This study is a large, multi-center, NIH-funded randomized clinical trial (NLM, NCT03593356). The purpose of the BFY project was to fill gaps in scientific knowledge about the role of economic resources in early childhood development. The sampling procedure is outlined in Figure 3 using a Consort diagram.

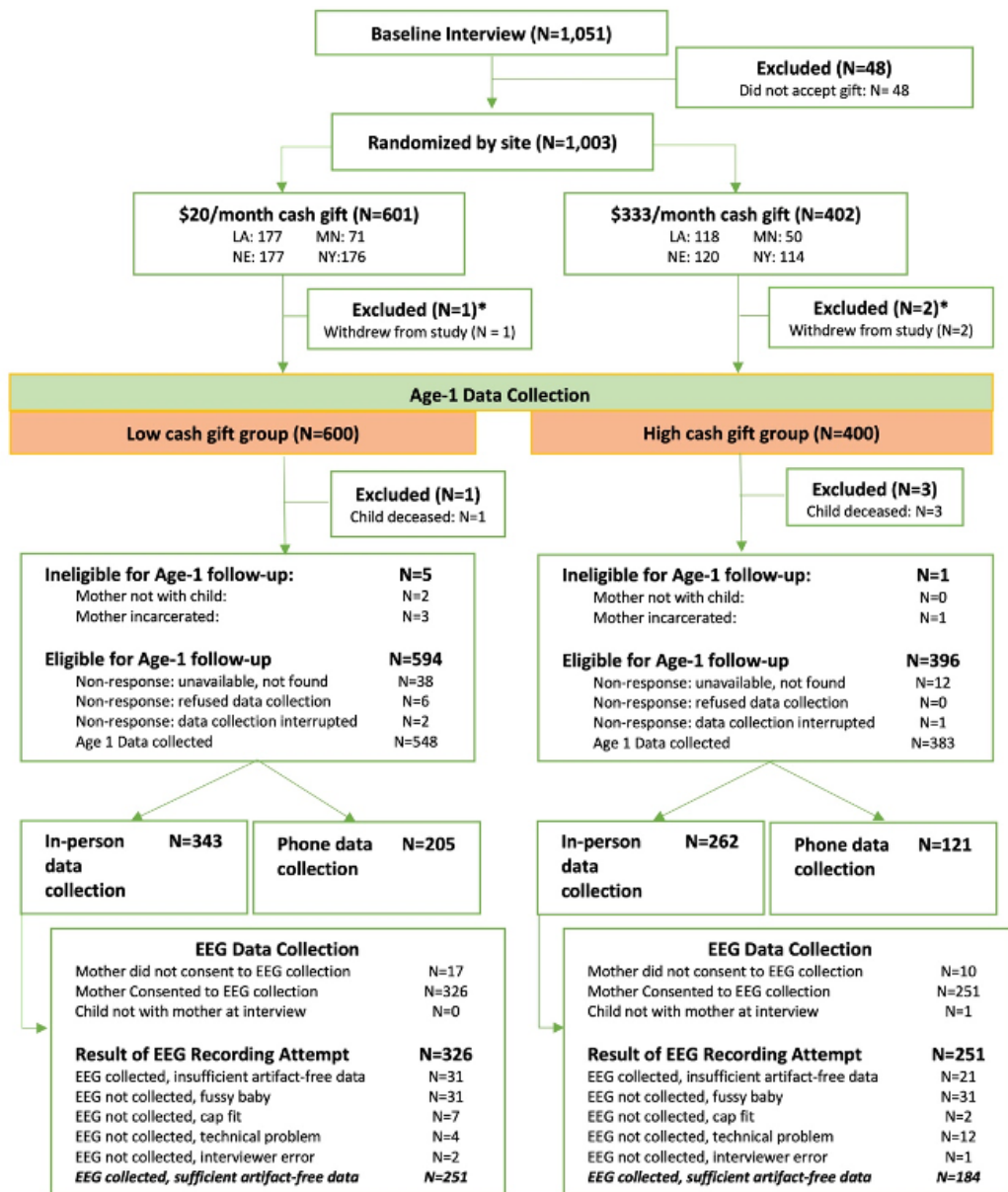


Figure 3 Consort diagram

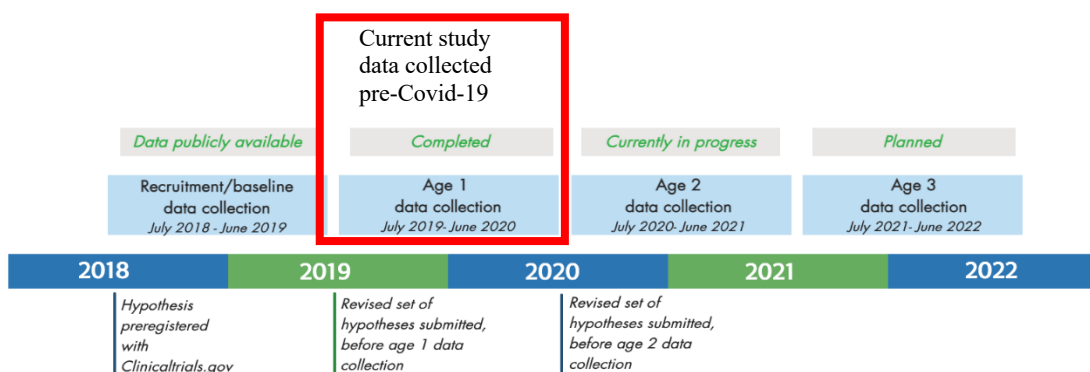
In the BFY Parent study, a total of 13,482 mothers were assessed for eligibility shortly after giving birth at 12 hospitals across four metropolitan areas with a baseline interview using the following criteria: (1) of legal age for informed consent (age 18 or older in NY, MN and LA; 19 or older in NE owing to its higher age of consent); (2) household income below the federal poverty threshold in the calendar year prior to the interview, counting the newborn; (3) infant not requiring admittance to the intensive care unit; (4) residence in the state of recruitment; (5) mother reports that she is not likely to move to a different state or country in the next 12 months;

(6) infant is discharged in the custody of the mother; (7) mother is English or Spanish speaking. A total of 1051 mothers were recruited between May 2018 and June 2019, meaning that they were judged to be eligible based on the information provided in the baseline screening interview, and they consented to participate.

The mothers were randomly assigned following recruitment to two groups which were well-balanced in terms of their baseline characteristics. A sample of 1,003 mothers and infants were assigned at random within each metropolitan area into either an experimental group or a control group. The division of the sample was 40/60, stratified by the four sites, as opposed to 50/50 in order to reduce total study costs. The sample was distributed by site as follows: 121 mother-infant pairs in MN; 295 in LA, 295 in NE and 289 in NY. The high-cash gift group (400 or 40% of 1000 mothers) were allocated to receive unconditional cash gifts of \$333 per month for 40 months. The low-cash gift group (600, or 60% of 1000 mothers) were allocated to receive a nominal gift of \$20 per month for 40 months. Because this money was given in the form of a gift, it was not considered to be taxable income. The Baby's First Years research team advocated for legislation within each of the four states in order to ensure that study participants would not lose access to social services as a result of their increase in income from the cash gift. The sample for the current study includes 243 mothers and infants in the control group only. Data collection began in July 2019 and is currently ongoing as of August 2021.

In order to understand the longitudinal effects of economic resources in early childhood cognitive and behavioral development, the differences between the high-cash and low-cash gift groups are assessed when the infants are one, two, three, and four years old. The five data collection points are referred to as: "Baseline", "Age 1", "Age 2", "Age 3, and "Age 4." The data collection point used in the current study is "Age 1". No data from the baseline, Age 2, Age 3, or Age 4 collection points are used in this study.

The parent study collected data related to brain development, child cognition, language, memory, self-regulation, and socio-emotional development. For the current study, only data related to food security, breastfeeding, and brain development, were used to answer the study aims. Figure 4 visually depicts the parent study’s data collection timeline and highlights the time period during which (July 2019 – June 2020) survey data and EEG data was intended to be collected. EEG data and survey data were collected during in person visits with trained researchers up until March 2020 when the first lockdown of the COVID-19 pandemic began in New York. Thus, data for this study was collected in advance of that lockdown in March 2020. A total of 605 mother and infant pairs completed pre-pandemic age-one visits, a total of 577 mothers consented to EEG data collection (95% consent rate). A total of 142 infants did not contribute a usable EEG recording for reasons including excessive artifact during recording (N=52), poor cap fit (N=9), infant fussiness (N=62), technical problems (N=16), and interviewer error (N=3). Ultimately, 435 infants provided usable data for analysis (75% of participants who consented to EEG collection).



Source: <https://www.babysfirstyears.com/data-collection-1>

Figure 4 BFY Study Timeline and Current Study Data Collection

3.5 Current Study: Association of Breastfeeding and Food Insecurity on Brain Function in Early Childhood

3.5.1 Ever Breastfeeding and Breastfeeding Duration

This study focuses on two constructs as independent variables: maternal breastfeeding behaviors and household food insecurity. The Baby’s First Years (BFY) Age 1 Survey includes the items in Table 3 as measurements of whether the infants have been breastfed (yes or no) and the duration of breastfeeding (months) as measured at age 1. The reliability of the self-reported answers about infant feeding is reported to be moderately high among mothers of infants up to 35 months old. In a convenience sample of 41 mothers (35 non-Hispanic white mothers, 5 Hispanic white mothers, and 1 Black) of infants between the ages of 19 and 35 months were interviewed and surveyed between 2012 and 2014. A weighted Cohen’s κ for breastfeeding duration at 12 months was 0.76 (95% CI: 0.58, 0.95) within this sample. It was found that the questions about the timing of breastfeeding were accurate to within about one month (O’Sullivan et al., 2017).

Table 3 Measurement of Breastfeeding

Variable	Question	Measures
Ever breastfed	Did you ever breastfeed?	0 = No 1 = Yes
Duration of breastfeeding	In what month(s) did you breastfeed [CHILDNAME]?	Time (Months)

3.5.2 Household Food Insecurity

Household food insecurity is measured with five of the six questions included on U.S. Household Food Security Survey (FSS) Module Short Form devised by the USDA (available at <https://www.ers.usda.gov/media/8282/short2012.pdf>). This abbreviated question set is a subset of a larger 18-item survey also administered by the USDA. A limitation of this shorter

tool is that it is not sensitive to severe ranges of both adult and child food insecurity where greater adult and child hunger occur (USDA, *Guide 2000*).

The parent study, *Baby’s First Years*, inadvertently eliminated the following question: “In the last 12 months, were you ever hungry but didn't eat because there wasn't enough money for food?”. Table 4 displays the questions used in this instrument to elicit information regarding five aspects of food security. With respect to food insecurity, a clear limitation of this study is the inability to detect very low food insecurity, as defined as the USDA, due to the elimination of one of the six items of this tool.

Table 4 U.S. Household Food Security Survey (FSS) Module Short Form

Question	Response
The food that we bought just didn’t last, and we didn’t have money to get more.	Often true= 1 Sometimes true=1 Never true=0
I/we couldn’t afford to eat balanced meals.	Often true= 1 Sometimes true=1 Never true=0
In the last 12 months, did you ever eat less than you felt you should because there wasn't enough money for food?	Yes =1 No =0
In the last 12 months, did you or other adults in your household ever cut the size of your meals or skip meals because there wasn't enough money for food?	Yes =1 No =0
If they responded “Yes” to the previous question, then they were also asked: “How often did this happen.” If they answer “No” to the previous question, then this question was skipped.	Almost every month =1 Some months but not every month =1 Only 1 or 2 months =0

Note: Parent study utilized a modified version where one question was omitted.

In advance of these questions, the interviewer qualified the questions by indicating, “For these statements, please tell me whether the statement was often true, sometimes true, or never true for you or your household in the last 12 months—that is, since last [current month].” This tool is designed to allow researchers to assign food security status to households. For questions with the responses of “often true,” “sometimes true,” or “never true,” “often true” and “sometimes true” were assigned the value of 1 as an affirmative response and “never true” the value of 0.

For questions with a “yes” or “no” answer choice, “yes” was coded as a 1 as an affirmative response and “no” as a 0. Finally, “almost every month” and “some months but not every month” were coded as an affirmative response with a value of 1 and “only 1 or 2 months” was coded as a 0. Participants could receive a raw score between a 0 and a 5. For the purpose of this dissertation, food security status was dichotomized where scores of 0-1 were given a 0 (food secure) and scores of 2-5 were coded as 1 (food insecure). Table 5 illustrates food security status designation.

Table 5 Food security status for households

Food security status	Raw score
Food secure	0-1
Food insecure	2-5

Note: Adapted from USDA, Guide 2000

The dichotomization of the HFI variable was done due to the accidental elimination of one question from the U.S. Household FSS Module short form in age 1 data collection by the parent study, Baby’s First Years. Figure 5, from the USDA Economic Research Service (ERS) (2019) illustrates the percentage of households reporting each indicator of food insecurity by food security status.

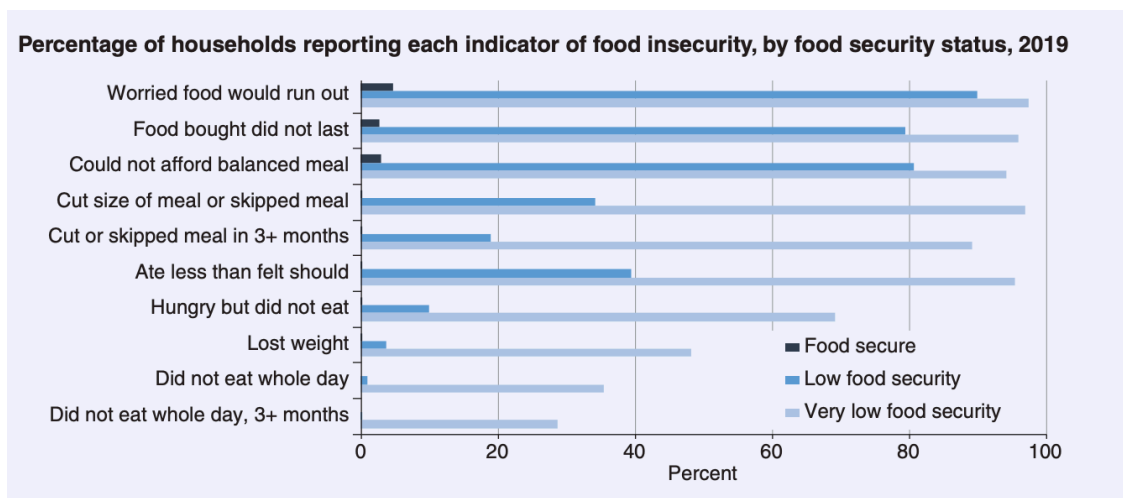


Figure 5 Percentage of household reporting each indicator of food insecurity, by food security status, 2019 (Coleman-Jensen et al., 2019)

This figure illustrates that no food secure households in 2019 affirmed that “In the last 12 months, were you ever hungry but didn't eat because there wasn't enough money for food?”. Therefore, the omission of this question only limits the ability to discern a distinction between those with low food security and very low food security, which are scored as 2-4 affirmations and 5-6 affirmations to the U.S. Household FSS Module Short Form, respectively. For this reason, the HFI variable was dichotomized to allow for the detection of any level of food insecurity.

Cronbach’s alpha for the five-item version of this instrument was 0.84 for the sample used in this dissertation. This internal consistency measure of reliability is greater than the minimally recommended value of 0.70 for Cronbach’s alpha.

The six-item U.S. Household FSS module has been validated as a food insecurity screener by Blumberg et al., 1999, where the shorter module was found to correctly classify food insecurity 97.7% of 44,647 households participating in the 1995 Current Population Survey’s food security module whose food security was measured using an 18-item scale. In addition, a study conducted in the Caribbean within a diverse population of Black and Asian participants validated the six-item U.S. Household Food Security Survey (FSS) Module Short Form in a sample of 531 participants in 286 households (Gulliford et al., 2004). The test-retest correlation coefficients were adequate (Spearman’s rho = 0.52 to 0.79) and the internal consistency reliability was excellent (Cronbach's alpha = 0.87). This instrument is also reported to identify food insecure households with a high level of sensitivity (i.e., an accurate true positive rate) and with a high level of specificity (i.e., an accurate true negative rate). Total scores for food security were associated with race/ethnicity and socioeconomic status of the respondents as expected, providing some predictive validity evidence. Moreover, food security was associated with reduced consumption of green vegetables after controlling for income and education.

In all cases, the ordinal variables were transformed to binary variables as follows. A mother's reported substance use of both alcohol ("Never in the last year" vs. those that did), smoking habits ("Never in the last year" vs. those that did) and physical health ("Poor" and "Fair" vs "Good," "Very Good" and "Excellent") were dichotomized. Financial stress was also dichotomized from its original ordinal coding (mothers who reported being in the never, very rarely, and rarely categories were coded as 0, where any financial stress was coded as a 1).

Specifically, the covariates are the following variables: maternal race/ethnicity, age, mental health, physical health, education, substance use (i.e., behaviors of using either alcohol or cigarettes), an index of economic stress, services support, and epoch count. Most of these are measured on a nominal or ordinal scale. The only interval scale variable is for mental health, which is measured with items extracted from the Patient Health Questionnaire and a cutoff score of 10 was used (PHQ-8; Kroenke & Spitzer, 2002). Within the subgroup of 243 mothers, the PHQ-8 shows good reliability with a Cronbach's alpha of 0.82. This estimate is similar to Shin et al. (2019), who reported a Cronbach's alpha of 0.89 for the PHQ-8. Shin et al. (2019) also report evidence about convergent validity for the PHQ-8. As expected, the PHQ-8 is strongly correlated with the Hamilton depression rating scale (Spearman correlation= 0.62).

The BFY instrument also includes items extracted from the Global Health Tool (Idler & Beryamini, 1997) to measure maternal physical health of the mothers, and items extracted from the instrument devised by Kling, Liebman and Katz (2007) to measure maternal substance abuse, specifically alcohol and smoking cigarettes. The investigators also collected state and local administration data regarding parental employment, current utilization of public benefits such as Medicaid and Supplemental Nutrition Assistance Programs (SNAP), and any involvement in child protective services. Finally, epoch count was also included as a covariate, which is the number of segments the EEG data was spliced into for analysis. A higher epoch count indicates more data for analysis purposes. This range is variable depending on the length

of data initially available for analysis and cleaning, which is dependent upon the real-life conditions of an infant tolerating an EEG cap for a period of around 5 minutes. Within developmental EEG data collection, these segments are often between 1-2 seconds long as infant EEG data often contains “noise” resulting from movement, eye blinks, or other sources.

3.5.4 EEG

The sampling and data collection procedures for EEG were performed by investigators participating in “The Baby’s First Years” (BFY) study. EEG data was collected in order to assess functional brain activity of a sample of 243 infants at age one year old using a mobile, in-home EEG system across all four sites. This system was previously evaluated for utility, cultural appropriateness and feasibility (Troller-Renfree et al., 2021). Interviewers were trained using the findings of this pilot to collect EEG data in-home. EEG was recorded using a 20-channel Neuroelectronics cap with an Enobio 20 amplifier (Neuroelectronics, Barcelona, Spain). The sampling rate was 500 Hz and a DRL/CMS reference configuration placed near the mastoid bone was used for reference. Following the placing of the Neuroelectronics cap, infants were seated on their mother’s laps in a dim room in front of a soundless video of infant toys. EEG data was collected for approximately five minutes per infant and up to seven minutes in order to ensure approximately five minutes of EEG data without infant movement or fussing.

For the parent study, Baby’s First Years, there were 577 mothers who consented to EEG data collection out of the 605 participants who were able to complete their age 1 visits before the pandemic and COVID-19 lockdowns were enforced, which halted in-person data collection for the remaining 395 mother and infants within both the treatment and control group. Of the 577 infants who participated in EEG data collections, 142 infants did not contribute usable data due to technical problems, infant fussiness, and interview error. 435 infants did contribute usable data for analysis. Of these 435 infants, 251 infants were of the control group from which the sample for this study is derived.

EEG data was cleaned and prepared for analysis by researchers at Teachers College, Columbia University. EEG data was prepared for analysis using the EEGLAB toolbox, the miniMADE pipeline, and MATLAB scripts that allows for processing of the data to ultimately derive relative and absolute power (Debnath et al., 2020; Delorme & Makeig, 2004; The MathWorks). This researcher did not participate in the preparation of EEG data for analysis, but an explanation of the process follows (Troller-Renfree et al., 2020). Data were high-pass filtered at 0.3 Hz and low-pass filtered at 50 Hz. Data were segmented into epochs of 1 s with 50% overlap between epochs. In developmental research, it is important to review EEG data to remove ocular artifacts from eye movement and other generic noise in order to have a cleaned dataset for analysis (Debnath et al., 2019). Data was then cleaned to ensure that artifacts outside of brain function activity were removed from analysis. Ocular artifacts were identified and removed by applying a voltage threshold rejection ($\pm 250 \mu\text{V}$) to four frontal channels (FP1, FP2) and if both frontal electrodes exceeded the voltage threshold of $\pm 250 \mu\text{V}$ in an epoch, that epoch was removed from further processing and analysis. Additional artifacts were identified in epochs using three criteria: a voltage threshold as described above ($\pm 250 \mu\text{V}$), a flat channel threshold where the range of activity was less than $1 \mu\text{V}$ for at least 50% of that epoch, and a jump channel threshold which was identified as a $>50 \mu\text{V}$ increase from sample to sample. Data were then re-referenced to an average of T7 and T8 (corresponding to electrodes above the temples) in order to express voltage at the EEG scalp channels with respect to a new reference. Epochs that contained fewer than 16 artifact-free electrodes and participants who had less than 20 artifact-free epochs were excluded from analysis. Finally, a Fast Fourier Transformation (FFT) with a 1-second Hanning window was applied to the epoched data. The FFT is used to estimate the averaged power spectral density, which is a single number summarizing the contribution of a given frequency band to the relative and absolute power of the signal, expressed in $\mu\text{V}^2/\text{Hz}$ (Vallat, 2018, Tomalski et al., 2013).

Absolute power spectral densities were computed as interval level measures of four frequency bands: theta (3-5Hz), alpha (6-9 Hz), beta (13-19 Hz) and two gamma frequency ranges (21-30 Hz, 31-45 Hz). Average absolute power is computed for each hemisphere across electrodes in five electrode groups as is visually defined below in Figure 6. Each frequency band is then averaged across all included electrodes, a process which creates whole-brain measurements of theta, alpha, beta, low-gamma, and high-gamma power. Finally, whole-brain relative power is calculated by dividing absolute power of a single frequency band, such as alpha, by the total absolute power of all the frequency bands (theta, alpha, beta, low-gamma, and high-gamma power). Developmental literature frequently utilizes relative power as a measurement of brain function and as such relative power values are used in this dissertation (Vanderwert et al., 2016). Power is reflective of the number of neurons firing synchronously within a given frequency band (i.e. 3-5 Hz for theta) (Perone et al., 2018). EEG analysis code can be found at <https://github.com/ChildDevLab>.

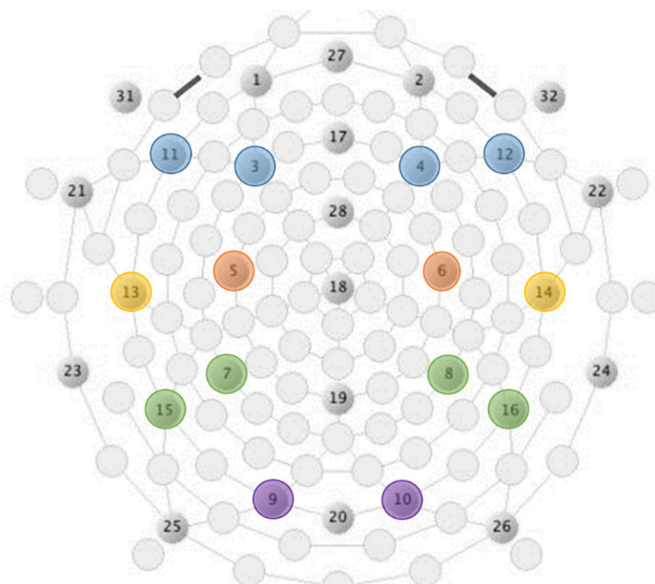


Figure 6 Electrode Groupings by Region (Troller-Renfree, et al., 2020)

The reliability and validity of quantitative EEG involving the measurement of power spectral densities of brain waves was assessed by Thatcher in a review of hundreds of peer-reviewed articles (2010). The results of a literature review indicated that quantitative EEG

exhibits high levels of split-half and test–retest reliability (90%) over many days and weeks in adolescent and adult EEG studies, since older subjects are needed in order to correlate findings with other neuropsychological tests. Quantitative EEG also exhibits high levels of predictive validity, indicated by replicable correlations with other neurological measures and accurate predictions of outcomes on other neuropsychological tests. The content validity of quantitative EEG has been established by correlations with independent measures such as MRI and neuropsychological tests related to various clinical disorders. In contrast, non-quantitative or qualitative EEG, based on simple visual examinations of the EEG signal traces has almost zero predictive validity and a very low level of interrater agreement.

3.6 Data Analysis Plan

The cross-sectional data from this study is being analyzed to determine if there are associations between breastfeeding and EEG measured theta, alpha, beta, and gamma relative and absolute power, and if there are associations between food insecurity and EEG measured theta, alpha, beta, and gamma relative and absolute power in one year-old children.

Figure 7 illustrates details about the final sample used in this dissertation. Of the 486 cases for which data was retrieved, 16 cases were missing values for all DV measures. Of these 470 cases, 200 subjects were discarded since they participated in the treatment group - leaving 270 cases in total. Nineteen cases with fewer than 20 artifact-free epochs were then dropped, leading to 251 cases. Finally, since missingness in the independent variables and covariates was limited, listwise deletion was used as a missing data strategy. Complete case analysis led to only 3.2% (n=8) of the observations not being used in the final model (See Figure 7 to see which variables had missing data). 243 mother and infant pairs were included in the regression models for relative and absolute theta, alpha, beta, and gamma power at the end of chapter 4.

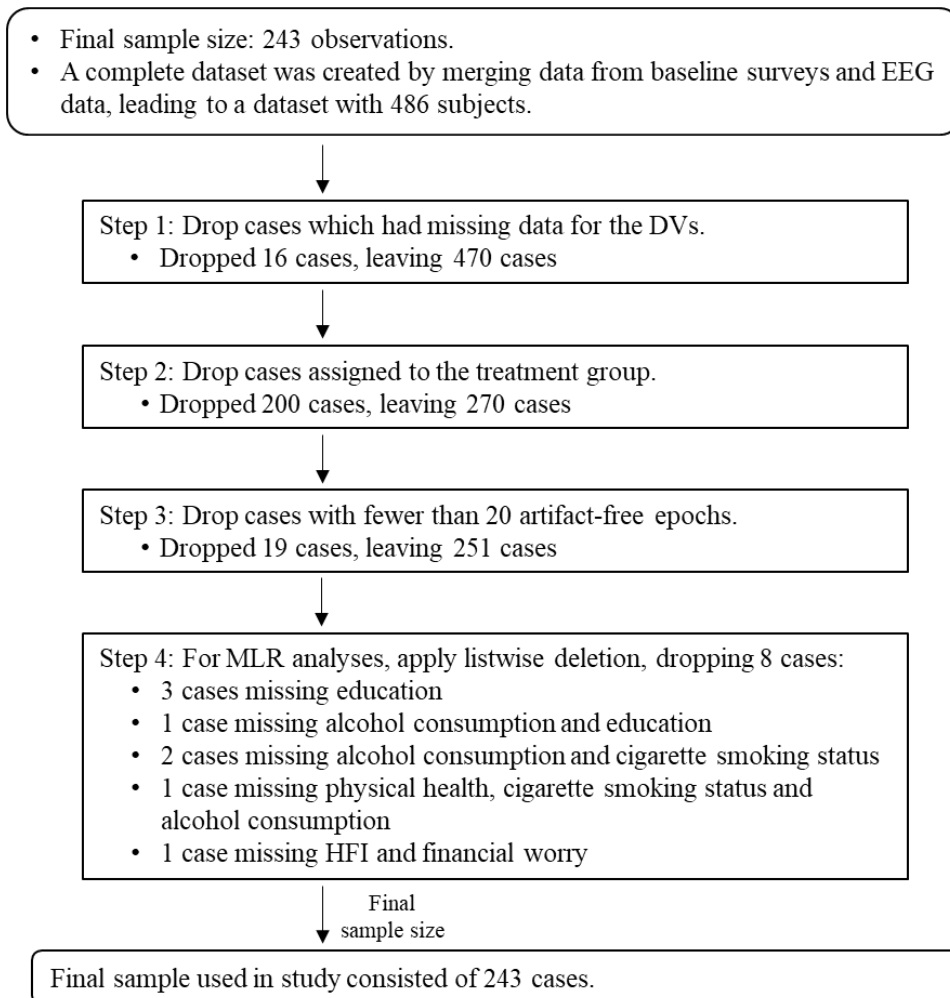


Figure 7: Flow chart illustrating the sample used in this study

Multiple linear regression (MLR) models based on ordinary least squares (OLS) estimation are used to test the research hypotheses. The rationale for using MLR is that this modeling method has for many years been widely applied in medical research (Cleophas & Linderman, 2018). MLR is commonly used to facilitate the prediction of interval level dependent variables, which are usually clinical, biochemical, or physiological outcomes (e.g., the four frequency bands of the EEG signal used to measure Child Brain Function) based on the values of two more independent variables measured at the interval, binary, nominal, or ordinal level which are usually the hypothesized causes of the outcomes (e.g. Duration of Breastfeeding, Ever Breastfed, and Household Food Insecurity).

MLR is underpinned by a generalized predictive model defined by the equation:

$$Y_i = \beta_0 + \beta_1 X_1 + \dots + \beta_k X_k + \varepsilon_i$$

Where Y_i is the observed value of the dependent variable for person i ; β_0 is a constant or baseline value; and $\beta_1, \beta_2, \dots, \beta_k$ are the partial regression (β) coefficients for k independent (X) variables (Rawlings et al, 2013). The standard assumptions of a MLR model are assessed. Namely, these assumptions are: (a) the residuals (i.e., the differences between the predicted and measured values of the dependent variable) should be normally distributed and not skewed; (b) the mean of the residual distribution should be around zero (c) multicollinearity is not extreme (i.e., the independent variables should not relate to each other); and (d) there must be homoskedasticity (i.e., the error variance must be equal across the independent variables and the covariates). If these strict assumptions are violated, then the results of MLR are misleading, and another method of testing the hypotheses is necessary (Rawlings et al, 2013).

Multicollinearity is assessed via a correlation matrix as seen in Table 7 (note: there is a complete correlation matrix which includes all independent variables and covariates in the Appendix).

Table 7 Correlation table for selected numeric predictor variables

	1	2	3	4	5	6	7	8	9	10
1. Ever BF	1.00									
2. BF duration	0.48	1.00								
3. HFI	0.03	0.04	1.00							
4. Age	-0.01	0.05	-0.04	1.00						
5. Depression	-0.13	-0.07	0.39	-0.05	1.00					
6. Physical Health	0.01	-0.04	-0.25	-0.06	-0.34	1.00				
7. Education	0.11	0.03	-0.11	0.03	0.05	0.14	1.00			
8. Smoking status	-0.26	-0.15	0.08	0.09	0.21	-0.17	0.00	1.00		
9. Alcohol status	-0.08	-0.13	0.03	-0.05	0.07	0.02	0.05	0.19	1.00	
10. Financial hardship	-0.04	-0.02	0.36	-0.04	0.24	-0.09	0.01	0.12	0.07	1.00

Note: All ordinal variables were dichotomized as described above. Bolded numbers indicated correlations greater than 0.30 in absolute value.

Multicollinearity is only a problem if the bivariate correlation coefficients between pairs of independent variables are > 0.8 (Yoo et al., 2014). Since this assumption can be checked prior to fitting the regression models, a correlation table with all the independent variables and selected covariates is shown (note that even among the covariates not shown, like maternal race, collinearity is not a problem). As the correlation matrix shows, there is clearly not a collinearity problem in the data. The highest correlations are for *ever breastfed* and *breastfeeding duration* ($r=0.48$), *HFI* and *maternal depression* ($r=0.39$) and *HFI* and *financial hardship* ($r=0.37$). Food insecurity (*HFI*) is associated with both increased levels of maternal depression (*PHQ8*) and experiencing financial difficulties.

Note the high correlation between *ever breastfed* and *breastfeeding duration* is sensible since they are merely different operationalization of a similar construct. Given the importance of these two variables in the current research, adding both variables to the same regression model is avoided since their large correlation would introduce a moderate degree of multicollinearity. Since multicollinearity undermines statistical power, it is better to estimate separate models for each operationalization of breastfeeding behaviors. The remaining assumptions are assessed as each model was estimated. Residual normality is checked visually with a QQ plot, while the homoskedasticity assumption is assessed with partial residual plots. The assumptions only violated for the models which had (both relative and absolute) gamma power as a DV.

Specifically, the error distribution had significant skew and was not normally distributed. There was an additional problem that the homoscedasticity assumption was violated. Partial residual plots showed that the error variance correlated with predicted values of *Y*. Although OLS estimators are still unbiased in the presence of heteroscedasticity, the standard errors of the regression coefficients can become both biased and inconsistent (Midi, Rana & Imon, 2009). A direct consequence of this bias in the standard errors is that the t-

statistic itself (which is beta divided by the standard error) is itself biased – becoming either too liberal or too conservative in making statistical significance decisions depending on the context. A common solution to a violation of the homoscedastic assumption is using robust standard errors (Midi, Rana & Imon, 2009). Robust regression also helps overcome violations of the normality assumptions. Robust regression was therefore used for the set of models estimated for Gama. Specifically, Huber-white standard errors, which are also called heteroscedastic-consistent standard errors, were used for the subset of models where Gama was specified as the DV. The lack of violation for all other models based on the other DVs is not a surprise. Histograms of all DV measures were approximately normal in shape (see below in chapter 4). When the DV is normally distributed, the standard assumptions of OLS regression are typically not problematic. That was the case here. Other than the models with gamma as a DV, the QQ-plots showed the sample quantiles followed the theoretical quantiles along the 45-degree diagonal in the test for normality. The residual distribution was also revealed to have relatively constant variance across all the predicted values of *Y*.

3.7 Power Analysis

Power analysis was conducted with G*Power software (Faul et al., 2009) using the following assumed parameters: Small effect size ($R^2 = .10$); conventional level of statistical significance ($\alpha = .05$); a high level of statistical power ($1 - \beta = .80$); with a maximum of eleven predictors. The recommended total sample size = 179. As Faul et al. (2009) observe, this sample size recommendation applies to testing both main and interaction effects. In comparison, the expected sample size is 243 infants at age one year (and their mothers). The expected sample size is therefore large enough to provide a high level of statistical power to test the hypotheses across all four brain waves effectively using the proposed data analysis plan.

Chapter 4: Results

This chapter starts by describing the study's sample of 243 mothers. Descriptive statistics are introduced showing the frequency distributions (counts and percentages) for categorical variables and quantitative (mean, standard deviation (SD), minimum and maximum) information for numeric variables. Tables 8 through 12 show descriptive information for all categorical and numeric variables. After describing the sample's characteristics, descriptive information for the four dependent variables is presented in Table 13. These univariate descriptive statistics are followed by exploratory bivariate descriptive procedures (e.g., procedures which compare two variables, like comparing ever breastfed and relative alpha power). This chapter concludes with reporting all relevant multiple linear regression output. The missing data strategy employed in this dissertation is listwise deletion given the small missingness percentage across all variables. This led to a final sample size of 243 being used in the regression analyses. All data included in this chapter was collected during the age 1 survey visits for the parent study, Baby's First Years.

4.1 Sample characteristics

Inclusion criteria for the BFY study were that the women were at least 18 years old, their infants were born without complications, they were residents of the state of recruitment and were not likely to move in the next 12 months, their infants were discharged into their custody, and that that they were either English or Spanish speaking. Table 8 highlights characteristics of the 243 mothers within this study.

Table 8 Characteristics of Mothers (n=243)

Characteristic	Category	Frequency		Mean	SD
		Count	Percentage		
Maternal Age	--	--	--	26.99	6.08
Maternal Education	--	--	--	11.97	3.03
Maternal Race/ Ethnicity	White	34	14.0	--	--
	Black/African American	88	36.2	--	--
	Hispanic, Latina, Spanish	99	40.7	--	--
	Other	10	4.1	--	--
	Multiracial	12	4.9	--	--
Maternal mental health	Depressed (10 < PHQ8)	32	13.2	--	--
	Not depressed (10 > PHQ8)	211	86.8	--	--
Maternal physical health	Excellent	58	23.8	--	--
	Very good	47	19.3	--	--
	Good	87	35.8	--	--
	Fair	43	17.7	--	--
	Poor	8	3.3	--	--
Maternal substance use - smoking	Every day	24	9.8	--	--
	Several times a week	16	6.6	--	--
	Several times a month	9	3.7	--	--
	Less than once a month	4	1.7	--	--
	Never in the last year	190	78.2	--	--
Maternal substance use-alcohol	Every day	1	0.4	--	--
	Several times a week	0	0.0	--	--
	Several times a month	18	7.4	--	--
	Less than once a month	80	32.9	--	--
	Never in the last year	144	59.3	--	--
Index of Economic Stress	All the time	58	23.8	--	--
	Very frequently	41	16.9	--	--
	Occasionally	58	23.9	--	--
	Rarely	37	15.2	--	--
	Very rarely	21	8.6	--	--
Site	Never	28	11.5	--	--
	Louisiana	66	27.2%	--	--
	Minnesota	34	14.0%	--	--
	Nebraska	73	30.0%	--	--
Count of Support Service Received	New York	70	28.8%	--	--
	--	--	--	2.97	1.62

By design, the principal investigators who collected the BFY data sampled women living below the poverty line. The background of mothers in the sample of 243 mothers is consistent with this intent. For example, Table 8 shows that mothers completed 12.0 years of education (SD=3.1) on average, which is equal to the 12 years it would take most to complete

high school without attending any post-secondary education. Many mothers also reported worrying about financial stress. Approximately one-fourth (23.8%) of the sample reported worrying “All the time” about their financial wellbeing. The average age of mothers included in the sample for this study was 26.9 years (SD=6.08) and most of the mothers were self-described as either Black (n=88, 36.2%) or Hispanic (n=99, 40.7%), while approximately 14.0% identified as White and the rest were either other (4.1%) or multiracial (4.9%). The participants are evenly distributed across three states (LA, MN, NY), with relatively fewer mothers living in MN (only 14.0%). Another background variable that correlates with socioeconomic status is the reported count of federal programs (e.g., Head Start, Medicaid, or WIC, full list of government programs that were asked about described in chapter three and shown in Table 9) that a mother reported receiving or participating in. On average, mothers reported participating in 2.97 of the federal programs asked about, with substantial variation (SD=1.62). Table 9 describes in further detail maternal participation in social services.

Table 9 Maternal participation in selected social services (n=243)

Social service	Frequency	
	N	Percentage
SNAP ^a	160	65.8%
Free or reduced childcare	49	20.2%
Early Head Start	20	8.2%
Head Start	15	6.2%
WIC ^b	173	71.2%
Unemployment insurance	1	0.4%
Cash assistance	35	14.4%
Medicaid	172	70.8%
Housing assistance	61	25.1%
LIHEAP ^c	27	11.1%
Other	9	3.7%
None	14	5.8%

^a Supplement Nutrition Assistance Program
^b Women, Infants, & Children
^c Low Income Home Energy Assistance Program

Table 9 shows maternal participation in various social surveys that the BFY survey asked about. Most mothers (94.2%) participated in at least one social service provided by the government. Specifically, most mothers reported participating in SNAP (65.8%), WIC (71.2%)

and Medicaid (70.8%). A minority reported benefiting from free or reduced childcare (20.2%) or receiving cash (14.4%) or housing assistance (25.1%). Only a small proportion of mothers indicated their child participated in Early Head Start (8.2%) or Head Start (6.2%).

Information about maternal physical and mental health was also collected. Approximately 13.2% of the mothers were rated as depressed based on a cutoff score of 10 for the PHQ-8 inventory (as reported in the methods chapter, the PHQ-8 demonstrated internal consistency reliability). Maternal substance use was minimal for most mothers, with a clear majority reporting not smoking (78.2%) and 156 of 251 mothers (59.3%) reporting that they had not drunk alcohol within the past year. When asked to rate their physical health, most mothers reported being healthy – only eight (3.3%) and 43 (17.7%) rated their health as “Poor” and “Fair” respectively. The majority (78.9%) indicated their health was either “Good” (35.8%), “Very good” (19.3%), or “Excellent” (23.8%).

4.2 Descriptive statistics: breastfeeding and household food insecurity

Table 10 shows that 77.0% (n=187) of mothers reported breastfeeding their child at least one time. The mean breastfeeding duration (including the mothers that never breastfed) was 3.6 months (SD=4.1). As compared to the mean of 3.6 months, the variability here is notable in how large it is (SD=4.1).

Table 10 Mother’s Breastfeeding Behaviors and Household Food Insecurity

Characteristic	Category	Frequency		Mean	SD
		Count (n=243)	Percentage		
Breastfeed	Ever breastfed	187	77.0	--	--
	Not breastfed	56	23.0		
Duration of breastfeeding (months)				3.60	4.12
HFI ^a	Food insecurity	67	27.6		
	Food security	176	72.4		

^a Household food insecurity

As expected, these two variables have a strong relationship, as seen in Table 11.

Table 11 A crosstabulation of ever breastfed and breastfeeding duration

Breastfeeding duration	Ever breastfed (n=187)	Never breastfed (n=56)
0 months	12	56
1 month	33	0
2 months	26	0
3 months	32	0
4 months	14	0
5 months	14	0
6 months	9	0
7 months	6	0
8 months	9	0
9 months	0	0
10 months	4	0
11 months	3	0
12 months	7	0
12+ months	18	0

The two variables have a Pearson’s correlation of 0.48, and an interesting pattern emerges in Table 11 when cross tabulating these variables. Although 12 mothers reported breastfeeding their child at least one time, they never breastfed their child continuously for one entire month. Based on the review of literature described in chapter two, there is insufficient evidence to suggest that a time frame of breastfeeding for less than one month should affect brain development.

The other key independent variable is household food insecurity (HFI), which was dichotomized as shown in Table 12. 27.6% (n=67) of the mothers were rated as experiencing food insecurity based on responses to an adapted version of the U.S. Household FSS Module Short Form.

Table 12 A crosstabulation of household food insecurity (HFI) status and the Household Food Security Survey Raw Score

Raw Score	Food security (n=176)	Food insecure (n=67)
0	133	0
1	43	0
2	0	19
3	0	12
4	0	16
5	0	20

Note: raw scores of 0 and 1 were defined as food secure and scores between 2-5 were defined as food insecure.

4.3 Descriptive statistics: infant EEG brain wave frequencies

There are eight dependent variables in this dissertation, all of which relate to brain wave frequencies (relative and absolute power theta, alpha, beta and gamma). The scale of these variables is $\mu V^2/Hz$ (although relative power is a proportion as described in Chapter 3). Table 13 shows the scale of the relative power are typically very small numbers.

Table 13 Descriptive statistics for infant EEG (n=243)

Variables	Mean	SD	Min	Max
Relative theta power	0.569	0.090	0.365	0.793
Relative alpha power	0.268	0.036	0.155	0.367
Relative beta power	0.104	0.041	0.022	0.219
Relative gamma power	0.058	0.034	0.006	0.188
Absolute theta power	1.472	0.297	0.457	2.169
Absolute alpha power	0.797	0.264	0.153	1.454
Absolute beta power	0.357	0.197	0.022	1.007
Absolute gamma power	0.211	0.150	0.006	0.737
Epoch Count	323.9	189.8	0.000	823

Note: Absolute theta, alpha, beta and gamma power measured in $\mu V^2/Hz$, relative theta, alpha, beta and gamma power are ratios.

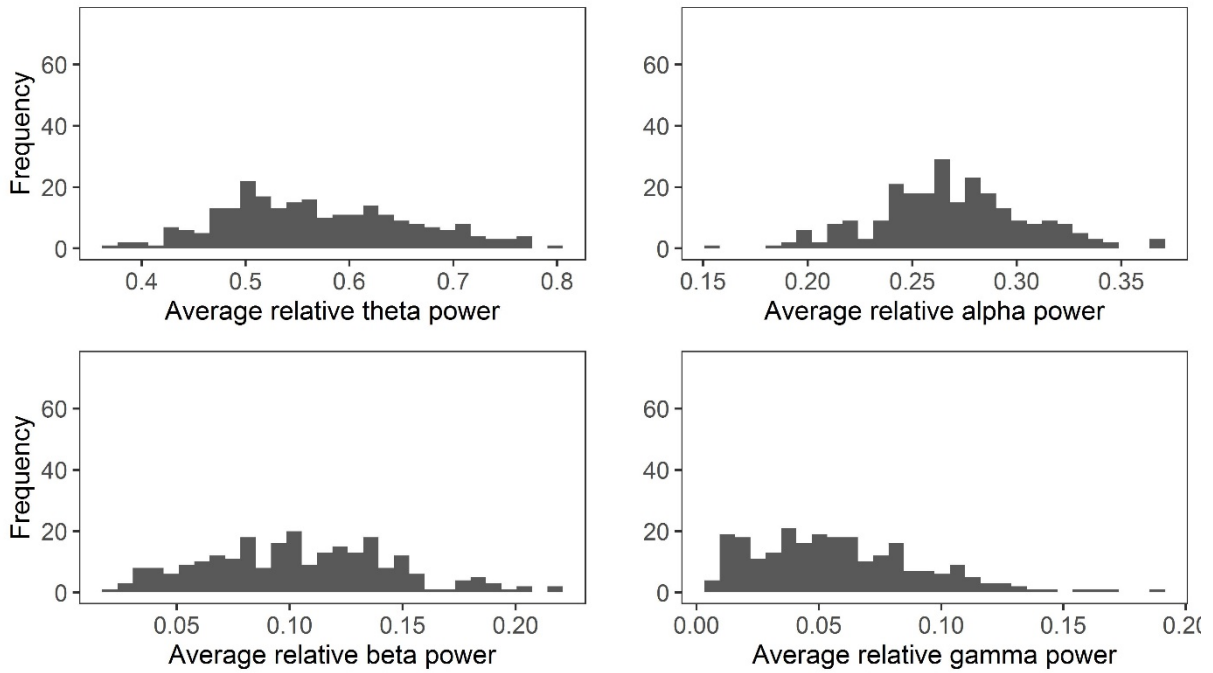


Figure 8 Histograms of relative theta, alpha, beta, and gamma power

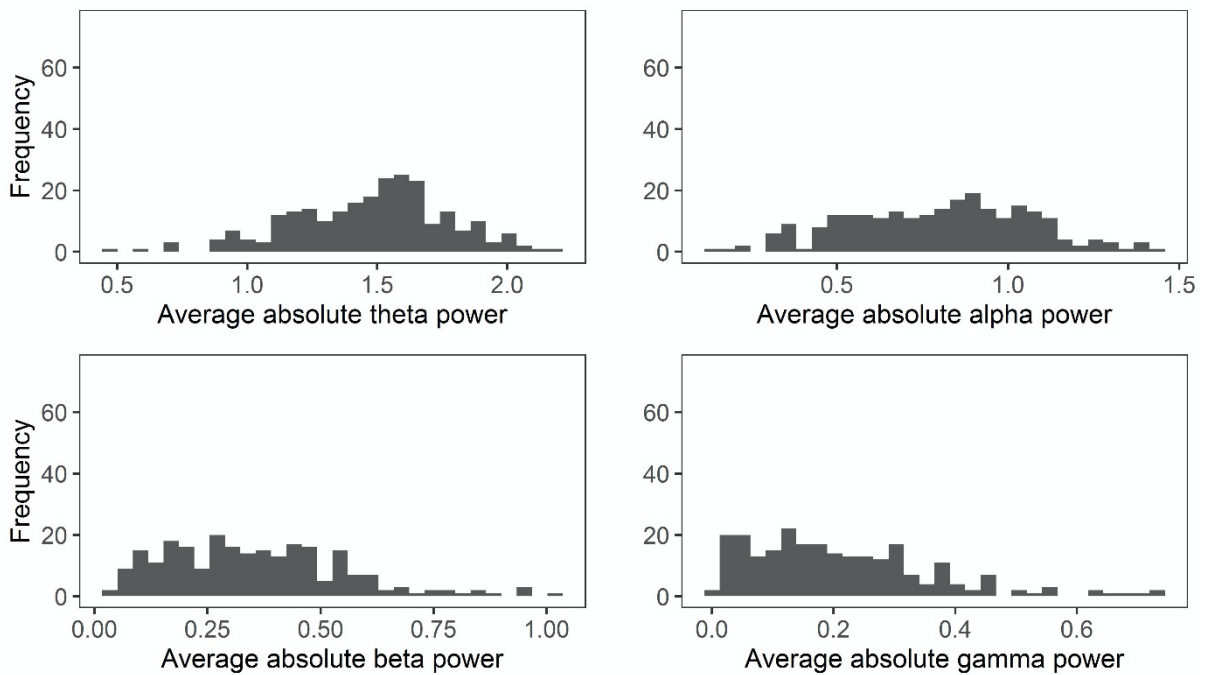


Figure 9 Histograms of absolute theta, alpha, beta, and gamma power ($\mu\text{V}^2/\text{Hz}$)

Relative power theta has a mean of 0.5769 (SD=0.090), relative power alpha has a mean of 0.268 (SD=0.0436), relative power beta has a mean of 0.104 (SD=0.041), and relative power gamma has a mean of 0.058 (SD=0.034). On the other hand, absolute theta power has a mean of 1.47 (SD=0.29), absolute alpha power has a mean of 0.80 (SD=0.26), absolute beta power

has a mean of 0.36 (SD=0.20), and relative gamma power has a mean of 0.21 (SD=0.15). As described in the methods chapter, a linear regression assumes that the error distribution is normal. When the underlying dependent variable is itself not normally distributed, this is usually taken to be an indicator that the error distribution will also not be normal. In this case, the positive skew for the gamma variable was problematic since the error distribution (in both relative and absolute power models) was heteroscedastic. This problem was solved by using robust regression.

4.4 Bivariate descriptive statistics for brain waves and breastfeeding, food insecurity

Table 14 shows a correlation matrix for the dependent variables and three independent variables. As we would expect, the relative and absolute measures are positively correlated – for example relative alpha power is positively associated with absolute alpha power. The same is true when comparing relative and absolute power for both gamma and beta frequencies. Interestingly, there is an exception to this pattern. Relative theta power has a strong negative correlation with all other types of brain wave frequencies – including absolute theta power. This paradox is explained by remembering that relative theta power is ultimately a proportion, where the numerator is absolute theta power, and the denominator is the sum of absolute theta, alpha, beta and gamma power. Proportions can decrease even as the numerator increases; this occurs when the increase in the denominator is large enough to offset the increase in the numerator. This pattern is happening here. Notice the positive correlation that absolute theta power has with the other absolute power measure (bolded in Table 14). As absolute theta power increases, so do all the other absolute measures. Focusing on relative theta power then, while its numerator increases as absolute power theta rises, its denominator (which is the sum of all absolute measures) increases even faster. This leads to the paradoxical finding that relative and absolute theta power are negative associated, and the relation is quite strong ($r = -0.66$).

In looking at the bivariate association between the dependent and independent variables (which ignores all other variables), ever breastfed has the strongest correlation with the four dependent variables – though its association is still weak in magnitude. For example, its highest correlation is with the frequency of relative alpha power ($r= 0.23$), followed closely by absolute theta power ($r=0.21$) and absolute alpha power ($r=0.21$). Breastfeeding duration has low bivariate associations with all four measures of brain wave frequencies, being under 0.10 in absolute value in every case. HFI has two correlations that rise above the 0.10 mark in absolute value: relative theta ($r=0.12$) and relative beta ($r= -0.11$).

Table 14 Correlation table for dependent and independent variables

	1	2	3	4	5	6	7	8	9	10	11
1. Relative theta power	1.00										
2. Absolute theta power	-0.66	1.00									
3. Relative alpha power	-0.60	0.70	1.00								
4. Absolute alpha power	-0.86	0.89	0.81	1.00							
5. Relative beta power	-0.93	0.51	0.29	0.69	1.00						
6. Absolute beta power	-0.91	0.59	0.31	0.76	0.97	1.00					
7. Relative gamma power	-0.86	0.39	0.15	0.57	0.90	0.88	1.00				
8. Absolute gamma power	-0.86	0.46	0.18	0.63	0.90	0.93	0.98	1.00			
9. Ever breastfed	-0.11	0.21	0.23	0.21	0.03	0.07	0.00	0.03	1.00		
10. Breastfeeding duration	-0.01	0.08	0.04	0.06	-0.01	0.01	0.00	0.01	0.48	1.00	
11. HFI	0.12	-0.02	-0.08	-0.06	-0.11	-0.09	-0.08	-0.07	0.03	0.04	1.00

Note: Relative theta, alpha, beta and gamma are ratios and absolute theta, alpha, beta and gamma power is measured in $\mu V^2/Hz$. “Rel.” and “Abs.” refer to “Relative” and “Absolute” respectively; “BF” refers to breastfeeding.

Tables 15 and 16 continue this bivariate look at the data through t-tests and find similar patterns. For example, Table 15 shows that absolute theta power and both relative and absolute alpha power are significantly related to ever breastfeeding. In all three cases, Cohen’s d is above 0.40, which Cohen placed in the moderate to large region. Breastfeeding behaviors were not significantly related to any other outcome measure.

Table 15 Independent t-tests ever breastfed and relative theta, alpha, gamma and beta power

Variable	Ever breastfed	Not breastfed	Cohen's <i>d</i>	p-value
	(n=187)	(n=56)		
	Mean (SD)	Mean (SD)		
Relative Theta power	0.56 (0.09)	0.59 (0.10)	-0.26	.093
Absolute Theta power	1.50 (0.29)	1.35 (0.28)	0.45	<.001
Relative Alpha power	0.27 (0.04)	0.25 (0.04)	0.57	.004
Absolute Alpha power	0.83 (0.27)	0.70 (0.24)	0.50	.001
Relative Beta power	0.10 (0.04)	0.10 (0.04)	0.08	.615
Absolute Beta power	0.36 (0.19)	0.33 (0.20)	0.16	.300
Relative Gamma power	0.06 (0.03)	0.06 (0.04)	-0.01	.973
Absolute Gamma power	0.21 (0.15)	0.20 (0.15)	0.06	.691

Note: Absolute theta, alpha, beta and gamma power measured in $\mu\text{V}^2/\text{Hz}$, relative theta, alpha, beta and gamma power are ratios. The t-test assumes the outcome variables are normally distributed which is tenable for all variables except for gamma.

Mirroring the weaker correlations that HFI had with the outcomes as compared to ever breastfeeding, Table 16 shows that HFI is not statistically associated with any of the outcome measures at the .05 level. HFI is marginally related to relative beta power ($p = .087$, Cohen's $d = -0.25$) and relative theta power ($p = .072$, Cohen's $d = 0.26$).

Table 16 Independent t-tests HFI and relative and absolute theta, alpha, gamma and beta power

Variable	Food insecurity	Food security	Cohen's <i>d</i>	p-value
	(n=67)	(n=176)		
	Mean (SD)	Mean (SD)		
Relative Theta power	0.59 (0.09)	0.56 (0.09)	0.26	.072
Absolute Theta power	1.46 (0.36)	1.47 (0.27)	-0.05	.707
Relative Alpha power	0.26 (0.04)	0.27 (0.04)	-0.19	.199
Absolute Alpha power	0.77 (0.30)	0.81 (0.25)	-0.13	.360
Relative Beta power	0.10 (0.04)	0.10 (0.04)	-0.25	.087
Absolute Beta power	0.33 (0.20)	0.37 (0.20)	-0.19	.181
Relative Gamma power	0.05 (0.03)	0.06 (0.04)	-0.18	.207
Absolute Gamma power	0.19 (0.14)	0.22 (0.15)	-0.17	.250

Note: Absolute theta, alpha, beta and gamma power measured in $\mu\text{V}^2/\text{Hz}$, relative theta, alpha, beta and gamma power are ratios. The t-test assumes the outcome variables are normally distributed which is tenable for all variables except for gamma.

Figures 10 through 15 visualize the bivariate associations between the dependent variables and independent variables. The conclusions reached in Tables 15 and 16 are

reinforced. Figures 10 and 11 show that ever breastfed has the strongest association with absolute theta (unexpected finding) and relative and absolute alpha power (expected finding).

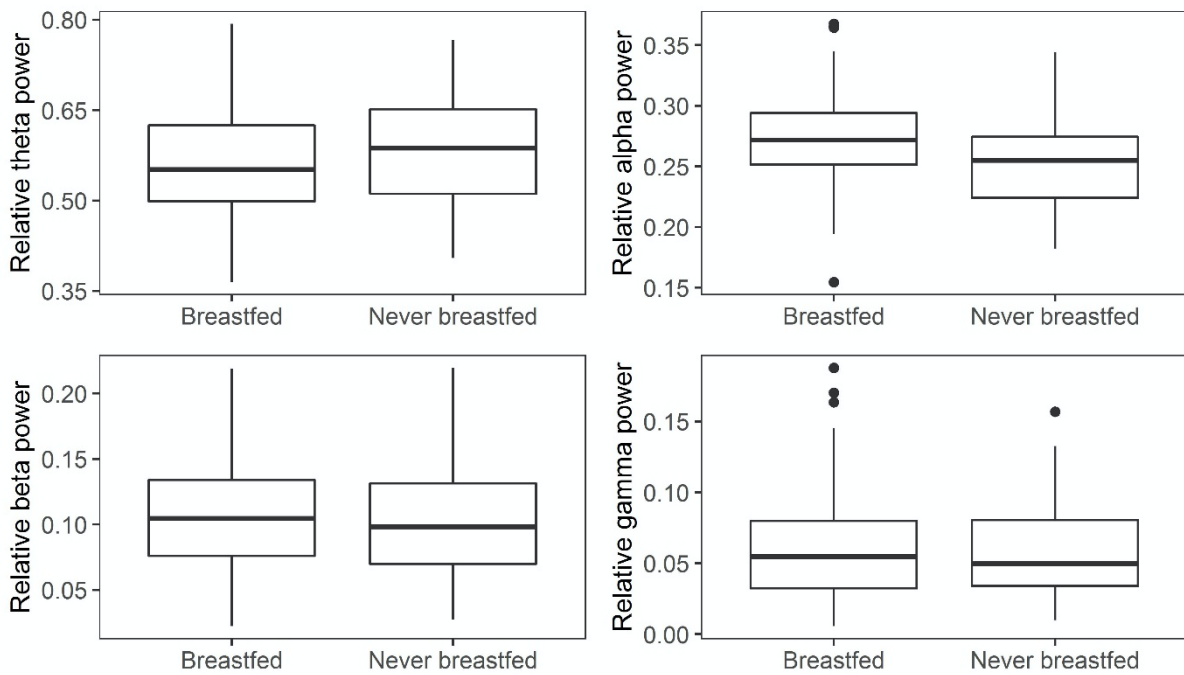


Figure 10 Boxplots of relative theta, alpha, beta, and gamma power split by whether an infant was ever breastfed or not

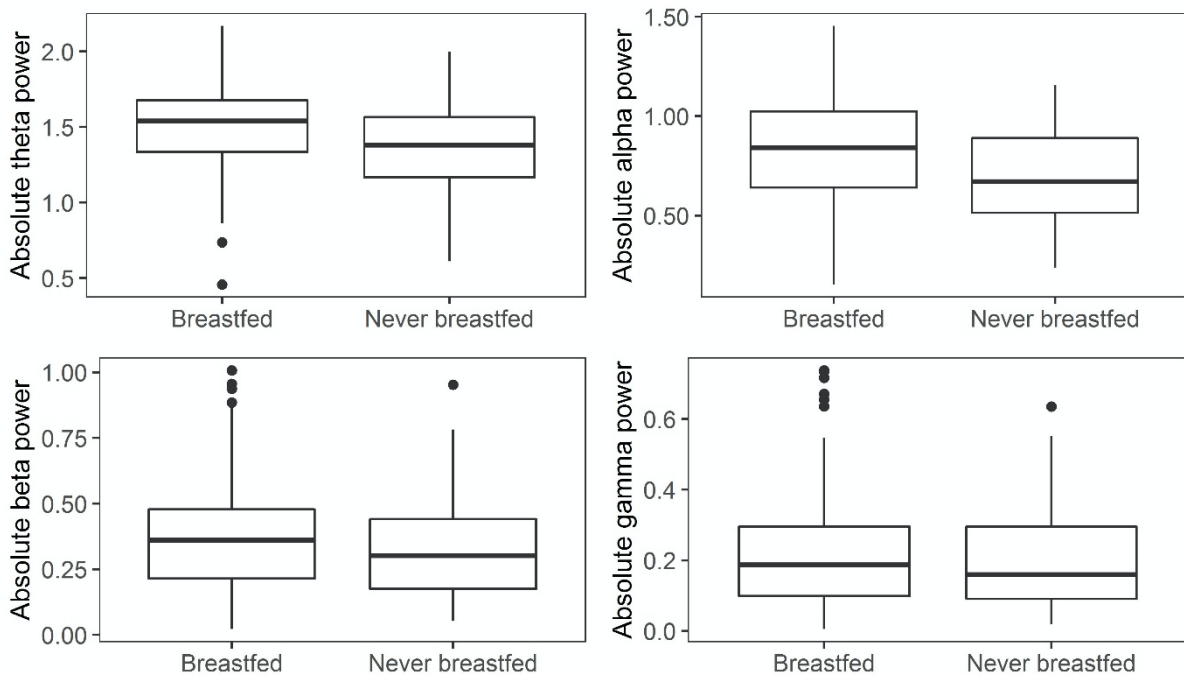


Figure 11 Boxplots of absolute theta, alpha, beta, and gamma power ($\mu\text{V}^2/\text{Hz}$) split by whether an infant was ever breastfed or not

Figures 12 and 13 show breastfeeding duration is generally unrelated to any of the brain wave frequency measures.

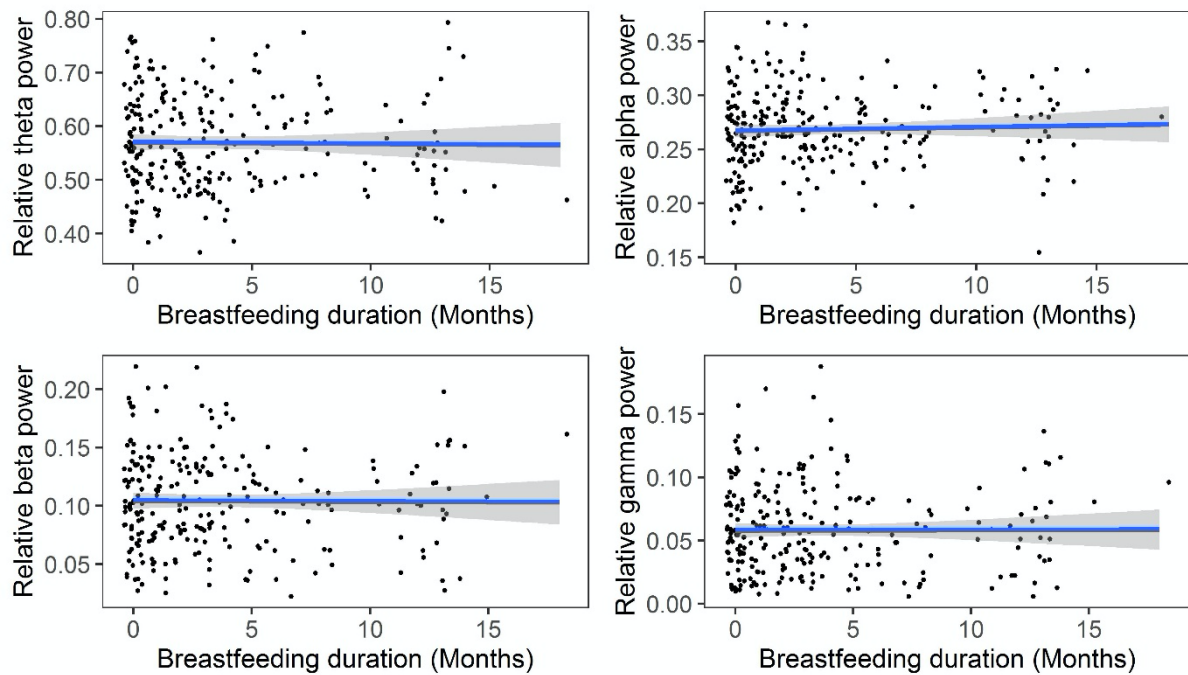


Figure 12 Scatterplots of relative theta, alpha, beta, and gamma power and breastfeeding duration (months)

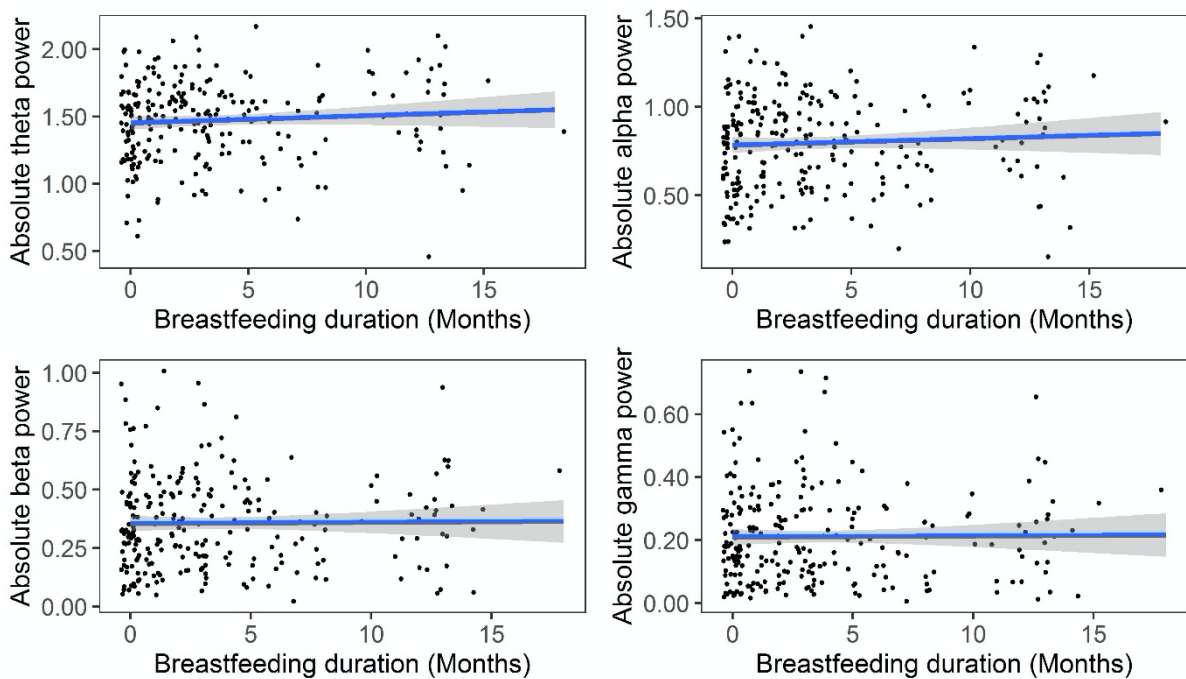


Figure 13 Scatterplots of absolute theta, alpha, beta, and gamma power ($\mu\text{V}^2/\text{Hz}$) and breastfeeding duration (months)

Household food insecurity is negatively associated with relative gamma power, while it is weakly positively related to relative theta power (Figures 14 and 15).

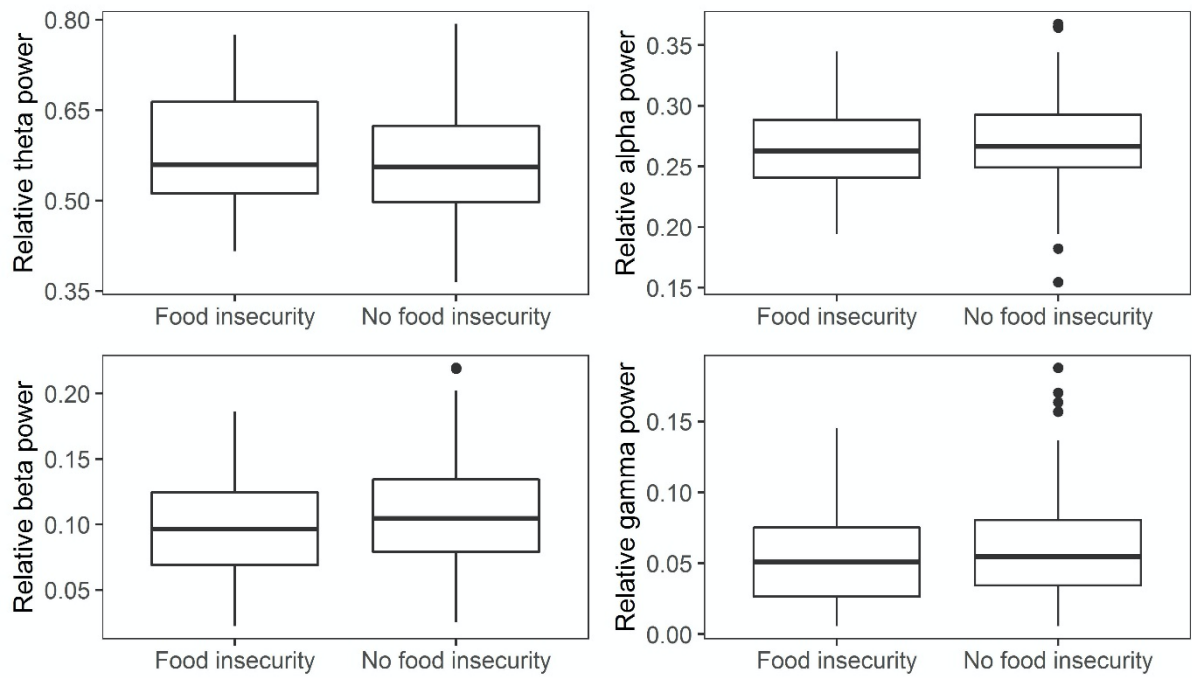


Figure 14 Box plots of relative theta, alpha, beta, and gamma power and Household Food Insecurity (HFI)

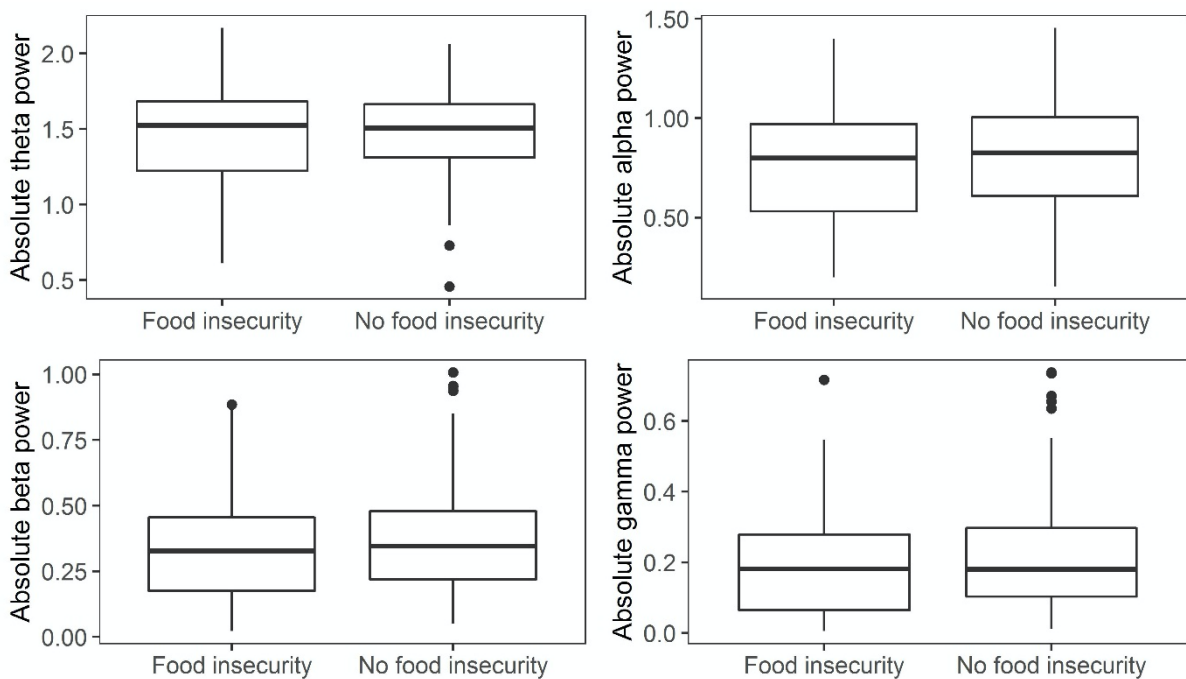


Figure 15 Box plots of absolute theta, alpha, beta, and gamma power ($\mu\text{V}^2/\text{Hz}$) and Household Food Insecurity (HFI)

4.5 Additional bivariate exploration for the household food insecurity and breastfeeding

The bivariate relationship between the independent variables and covariates are explored here. First, the bivariate association between the IVs (ever breastfed and HFI) and participation in SNAP and WIC is explored. Secondly, the association between the IVs and the covariates used in the MLR models is assessed. To understand how the independent variables covary with participation in SNAP and WIC, a series of contingency tables are displayed below. These tables show the counts and column percentages (e.g., in Table 17, 78% of mothers who did not participate in SNAP reported breastfeeding their infants, while 76% of mothers who participated in SNAP breastfed their infants). Additionally, each table reports a chi-square test of association. The null hypothesis of the chi-square test is no association. A significant chi-square test therefore indicates a statistically significant association between the two categorical variables.

Tables 17 through 19 shows that SNAP and WIC participation are generally unrelated with experiencing any food insecurity and breastfeeding behaviors.

Table 17 Bivariate association of SNAP participation and ever breastfed

	Did not Participate in SNAP	Participated in SNAP
Never breastfed	18 (22%)	38 (24%)
Ever breastfed	65 (78%)	122 (76%)

Chi-square test: $\chi^2(1) = 0.04$, $p = .840$

Table 18 Bivariate association of WIC participation and ever breastfed

	Did not Participate in WIC	Participated in WIC
Never breastfed	17 (39%)	39 (23%)
Ever breastfed	53 (13%)	134 (77%)

Chi-square test: $\chi^2(1) = 0.02$, $p = .901$

Table 19 Bivariate association of SNAP participation and food insecurity

	Did not Participate in SNAP	Participated in SNAP
Food security	62 (75%)	114 (71%)
Food insecurity	21 (25%)	46 (29%)

Chi-square test: $\chi^2(1) = 0.618, p=.675$

As seen in Table 20, there is an association between food insecurity and WIC participation which is significant at the .05 level ($p=.031$). The odds ratio is 2.22, meaning that the odds of participating in WIC are approximately twice as great for mothers who experienced food insecurity as compared to mothers who were rated as food secure.

Table 20 Bivariate association of WIC participation and food insecurity

	Did not Participate in WIC	Participated in WIC
Food security	58 (83%)	118 (68%)
Food insecurity	12 (17%)	55 (32%)

Chi-square test: $\chi^2(1) = 4.65, p=.031$

The relationship of the IVs (ever breastfed and HFI) to the study outcomes is assessed for all demographic covariates used in the MLR models that follow. Each demographic variable is broken down by the binary IVs and reported in Table 21 (ever breastfed) and Table 22 (HFI). As was done for looking at the bivariate association between the IVs and SNAP and WIC participation, the IVs were cross tabulated with all categorical demographic variables (race, site, depression status, physical health status, maternal alcohol status, maternal cigarette status, and financial worry), displaying column percentages and presenting chi-square results to determine whether the two variables are significantly related. In a single case (maternal race) where the core chi-square assumption of having a minimum expected frequency of five for each cell was violated, Fisher's Exact Test was used instead of the chi-square test. For numeric covariates (age, education, count of services), the mean and SD are shown for the two levels

of ever breastfed, while an independent samples t-test assuming equal variances was used to assess whether the two variables share a statistically significant relationship.

Table 21 shows that ever breastfed was significantly associated with many of the covariates – which highlights the importance of favoring the MLR regression results that follow over the bivariate t-tests displayed in Table 15.

Table 21 Covariates broken down by ever breastfed

		Ever breastfed (n=187)	Never breastfed (n=56)	<i>p</i> ^a
<i>Categorical variables</i>		Freq ^d (%)	Freq ^d (%)	
Maternal Race/Ethnicity	White	23 (12.3%)	11 (19.6%)	.003 ^b
	Black/African American	58 (31.0%)	30 (53.6%)	
	Hispanic, Latina, Spanish	86 (46.0%)	13 (23.2%)	
	Other	9 (4.8%)	1 (1.8%)	
	Multiracial	11 (5.9%)	1 (1.8%)	
Maternal mental health	Depressed (10 < PHQ8)	20 (10.7%)	12 (21.4%)	.063
	Not depressed (10 > PHQ8)	167 (89.3%)	44 (78.6%)	
Maternal physical health ^c	Good	148 (79.1%)	44 (78.6%)	.999
	Poor	39 (20.9%)	12 (21.4%)	
Maternal alcohol status	Never in the last year	115 (61.5%)	29 (51.8%)	.253
	Had drank in last year	72 (38.5%)	27 (48.2%)	
Maternal smoking status	Never in the last year	157 (84.0%)	33 (58.9%)	<.001
	Had smoked in last year	30 (16.0%)	23 (41.1%)	
Financial worry	Little to no worry	68 (36.4%)	18 (32.1%)	.674
	Moderate to high worry	119 (63.6%)	38 (67.9%)	
Site	Louisiana	38 (20.3%)	28 (50.0%)	<.001
	Minnesota	29 (15.5%)	5 (8.9%)	
	Nebraska	57 (30.5%)	16 (28.6%)	
	New York	63 (33.7%)	7 (12.5%)	
<i>Numeric variables</i>		Mean (SD)	Mean (SD)	
Maternal Age		26.8 (6.1)	27.0 (6.2)	.833
Maternal Education		12.2 (3.2)	11.4 (2.5)	.098
Count of Support Service Received		3.0 (1.6)	3.0 (1.8)	.807

^a P-values are based on chi-square (except for maternal race) for categorical variables, and a two-sample t-test for numeric variables.

^b P-value is based on Fisher’s Exact test since an assumption for the chi-square test is violated (see text).

^c Physical health was dichotomized (“Poor” and “Fair” vs “Good,” “Very Good” and “Excellent”).

^d Frequency (%) reported as the percentage of categorical variable within each category.

Regarding maternal race, mothers who reported breastfeeding their infants were more likely to be Hispanic – 46.0% of mothers who reported breastfeeding their infants were

Hispanic while only 23.2% of mothers who did not breastfeed their infants were Hispanic. This was by far the largest difference concerning the racial background of mothers who did or did not breastfeed their infants, leading to a statistically significant relationship between maternal race and breastfeeding behaviors ($p=.003$). Ever breastfed was also significantly related to maternal smoking status ($p<.001$) and site ($p=<.001$). Mothers who never breastfed their infants were more likely to report smoking at least once in the past year (41.1% vs 16.0% for mothers who had breastfed). When considering site, there was more balance in where the mothers lived among the subset of mothers who had reported breastfeeding their infants, ranging from 15.5% in Minnesota to 33.7% in New York. Their counterparts (the never breastfed mothers) came mostly from Louisiana (50%) and Nebraska (28.6%). Maternal depression was marginally significant at the 0.10 level ($p=.063$). Mothers who never breastfed their infants were more likely to be depressed (21.4% vs. 10.7% for mothers who breastfed). None of the remaining covariates (maternal physical health, alcohol status, financial stress, age, education, and count of federal support services participated in) exhibited a significant association with ever breastfed on the bivariate level.

Table 22 illustrates that HFI was significantly related to many of the covariates – again highlighting the value of relying on MLR models to assess the extent of relationship between this IV and the outcomes rather than simple bivariate tests which ignore background factors. HFI was significantly related to three covariates (mental health, physical health, financial worry) at the .05 level, and was marginally related to four covariates at the 0.10 level (maternal race, site, education, and count of participation in social services). Mothers who experienced food insecurity were more likely to be depressed ($p<.001$), have lower self-reported physical health ratings ($p<.001$), experienced more financial stress ($p<.001$), completed almost one year less of education on average ($p=.082$) and reported using more governmental support services ($p=.052$).

Table 22 Covariates broken down by household food insecurity (HFI)

		Food security (n=176)	Food insecurity (n=67)	<i>p</i> ^a
<i>Categorical variables</i>		Freq ^d (%)	Freq ^d (%)	
Maternal Race/Ethnicity	White	26 (14.8%)	8 (11.9%)	.060 ^b
	Black/African American	66 (37.5%)	22 (32.8%)	
	Hispanic, Latina, Spanish	73 (41.5%)	26 (38.8%)	
	Other	7 (4.0%)	3 (4.5%)	
	Multiracial	4 (2.3%)	8 (11.9%)	
Maternal mental health	Depressed (10 < PHQ8)	9 (5.1%)	23 (34.3%)	<.001
	Not depressed (10 > PHQ8)	167 (94.9%)	44 (65.7%)	
Maternal physical health ^c	Good	150 (85.2%)	42 (62.7%)	<.001
	Poor	26 (14.8%)	25 (37.3%)	
Maternal alcohol status	Never in the last year	106 (60.2%)	38 (56.7%)	.725
	Had drank in last year	70 (39.8%)	29 (43.3%)	
Maternal smoking status	Never in the last year	141 (80.1%)	49 (73.1%)	.316
	Had smoked in last year	35 (19.9%)	18 (26.9%)	
Financial worry	Little to no worry	81 (46.0%)	5 (7.5%)	<.001
	Moderate to high worry	95 (54.0%)	62 (92.5%)	
Site	Louisiana	53 (30.1%)	13 (19.4%)	.076
	Minnesota	20 (11.4%)	14 (20.9%)	
	Nebraska	56 (31.8%)	17 (25.4%)	
	New York	47 (26.7%)	23 (34.3%)	
<i>Numeric variables</i>		Mean (SD)	Mean (SD)	
Maternal Age		27.1 (6.3)	26.4 (5.5)	.491
Maternal Education		12.2 (3.1)	11.4 (2.8)	.082
Count of Support Service Received		2.8 (1.6)	3.3 (1.5)	.052

^a P-values are based on chi-square (except for maternal race) for categorical variables, and a two-sample t-test for numeric variables.

^b P-value is based on Fisher's Exact test since an assumption for the chi-square test is violated (see text).

^c Physical health was dichotomized ("Poor" and "Fair" vs "Good," "Very Good" and "Excellent").

^d Frequency (%) reported as the percentage of categorical variable within each category.

4.6 MLR Results Introduction

As reviewed in the methods chapter, a series of multiple linear regression (MLR) models are used to answer the research questions. Given the scales of the DVs (relative alpha power, for example had a mean of 0.27 and ranged from 0.05 to 0.37), standardized regression coefficients are reported to make the results easier to interpret. The key regression assumptions were checked prior to interpreting model results. Chapter 3 reported on the extent of

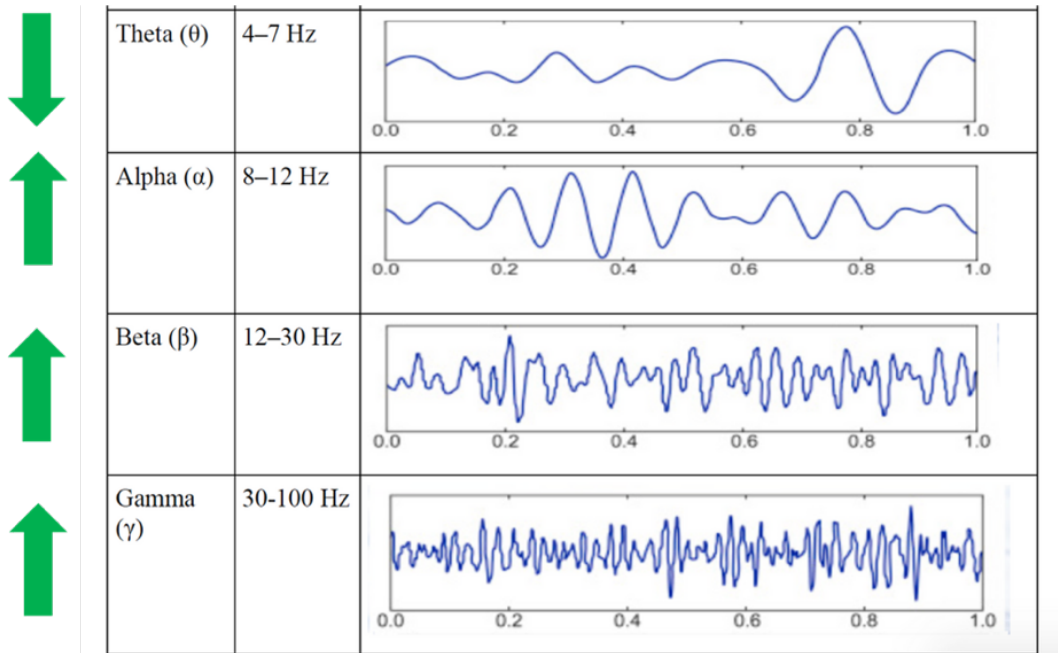
multicollinearity among the predictor variables (independent variables and covariates). To briefly summarize, multicollinearity is not strong in the current study since most predictors had relative low correlations (often below 0.20 in magnitude). A MLR model also assumes the error distribution is normal and homoscedastic (i.e., constant variance). These assumptions were tenable in every MLR that was estimated – except for the models (both relative and absolute) where gamma power was specified as the dependent variable. In these models, the error distribution was both skewed (i.e., not normal) and heteroscedastic – breaking two linear regression assumptions. Robust regression was therefore used (Midi, Rana & Imon, 2009) (see Chapter 3 for more of a discussion about this decision). As described earlier, the missing data strategy employed here is listwise deletion given the small missingness percentage across all variables. This led to a final sample size of 243 being used in the regression analyses.

The next four tables show MLR results for the outcomes of relative and absolute theta, alpha, beta, and gamma power. These models feature three key independent variables: ever breastfed (BF), breastfeeding duration (BFD), and household food insecurity (HFI). As discussed above, BF and BFD were separated out into two different sets of models to cope with the high level of collinearity between these two key variables ($r=0.48$). Results for each outcome variable are reported sequentially (theta, alpha, beta, then gamma).

Note that many of the predictor variables were dichotomized in these regression models, which was explained above. A mother's reported substance use of both alcohol (never used in past year vs those that did), smoking habits (those who never smoked in the past year vs those that did) and physical health ("Poor" and "Fair" vs "Good," "Very Good" and "Excellent") were dichotomized. Financial stress was also dichotomized from its original ordinal coding (mothers who reported being in the never, very rarely, and rarely categories were coded as 0, where any financial stress was coded as a 1). Maternal race and site are both nominal scaled variables; so a set of dummy variables were therefore used (being Hispanic and

from Nebraska were selected as the reference group since these groups had the largest sample size). Age (years), years of education, count of federal social services used, and epoch count were all inputted into the regression model as numeric predictor variables.

For the purpose of contextualizing the findings described in the next four sections, a review of developmental EEG literature follows. Developmental EEG literature shows that early adversity in many forms, including lower socioeconomic status (Tomalski et al., 2013), maternal stress (Troller-Renfree et al., 2020), and institutionalization (Marshall et al., 2004) may be associated with differences in the power of different EEG wavebands. Adversity during early childhood has been linked to lower frontal gamma power (Tomalski et al., 2013), increased theta power (Marshall et al., 2004, Troller-Renfree et al., 2020) and reduced alpha power (Marshall et al., 2004, Troller-Renfree et al., 2020). The pattern of increased low-frequency brain power (theta waves) and reduced high-frequency brain power (alpha, beta, and gamma waves) has been found to be associated with developmental delays, problems with learning and attention, and associations with vocabulary and working memory in adolescent children (Corning et al., 1986, Harmony et al., Maguire & Schneider, 2019, McLaughlin et al., 2010). This evidence is suggestive brain function, as measured by EEG may have consequential effects on neurocognitive functioning in adolescence. However, it is important to consider that these differences in brain function that may be detected in early childhood, particularly from children from low SES backgrounds, can be attributed to adaptive neuroplasticity. Research has shown that children from disadvantaged backgrounds may exhibit differences in brain function which can be attributed to the need to prioritize different skills during traditional developmental milestones that allow a child to better adapt to their environment (Ellis et al., 2020). For interpretation purposes, Figure 1 illustrates the expected directionality of effect size on relative and absolute power theta, alpha, beta, and gamma for breastfed infants who are food secure.



Note: green arrow suggests the adaptive directionality of effect size on measurements of brain power as seen in literature.

Figure 16 Theta, alpha, beta, and gamma brain waves with corresponding expected directionality for breastfed infants who are food secure

4.6.1 MLR results for relative and absolute theta power

Table 23 shows the MLR model output for the relative and absolute theta power outcome. Models 1 and 3 show a MLR with ever breastfed, HFI and the covariates as predictors, while Models 2 and 4 show a similar model but using breastfeeding duration rather than ever breastfed. The dependent variable for models 1 and 2 is relative power theta, while it is absolute theta power in Models 3 and 4. Regression tables for all other outcome measures (e.g., alpha, beta, and gamma power) are similarly organized.

Table 23 Relative and absolute theta power MLR results, effect size and standard errors reported

<i>Variables</i>	Relative power		Absolute power	
	Model 1	Model 2	Model 3	Model 4
Ever breastfed	-0.090 (0.066)		0.152* (0.064)	
Duration of breastfeeding		-0.002 (0.062)		0.017 (0.061)
HFI	0.100 (0.072)	0.092 (0.072)	0.001 (0.069)	0.012 (0.070)
Maternal race: White	0.135 (0.078)	0.140 (0.078)	-0.095 (0.075)	-0.105 (0.076)
Maternal race: Black	0.171 (0.089)	0.181* (0.089)	-0.272** (0.086)	-0.287** (0.087)
Maternal race: Other	-0.027 (0.066)	-0.030 (0.067)	-0.122 (0.064)	-0.118 (0.065)
Maternal race: Multiracial	0.092 (0.070)	0.091 (0.070)	-0.148* (0.068)	-0.146* (0.069)
Maternal age	-0.011 (0.061)	-0.006 (0.062)	-0.013 (0.060)	-0.023 (0.060)
Maternal mental health	-0.082 (0.070)	-0.068 (0.070)	0.008 (0.068)	-0.015 (0.068)
Maternal physical health	-0.115 (0.066)	-0.112 (0.066)	0.041 (0.064)	0.036 (0.065)
Maternal Education	0.128 (0.065)	0.115 (0.065)	-0.075 (0.063)	-0.055 (0.063)
Maternal substance use, smoking	-0.110 (0.071)	-0.093 (0.071)	0.055 (0.069)	0.028 (0.070)
Maternal substance use, alcohol	-0.055 (0.061)	-0.050 (0.062)	-0.052 (0.059)	-0.060 (0.060)
Financial hardship	0.099 (0.066)	0.104 (0.066)	-0.093 (0.064)	-0.101 (0.065)
Services count	0.149* (0.065)	0.151* (0.066)	0.000 (0.063)	-0.003 (0.064)
Site: LA	0.152 (0.083)	0.168* (0.083)	-0.124 (0.081)	-0.150 (0.081)
Site: NY	0.238** (0.083)	0.234** (0.084)	-0.270*** (0.080)	-0.262** (0.082)
Site: MN	-0.076 (0.070)	-0.085 (0.070)	0.095 (0.068)	0.112 (0.069)
Epoch count	0.252*** (0.061)	0.260*** (0.061)	-0.346*** (0.060)	-0.360*** (0.060)
Intercept	-0.090 (0.066)		0.152* (0.064)	
Model fit (R ²)	23.0%	22.4%	27.7%	25.9%

Notes: * = $p < .05$; ** = $p < .01$, *** = $p < .001$, effect sizes reported, standard errors in parenthesis, reference group for HFI (household food insecurity) was food security, reference group for maternal race is Hispanic, reference group for site is NE. Relative theta, alpha, beta and gamma power are ratios and absolute theta, alpha, beta and gamma power measured in $\mu V^2/Hz$.

Ever breastfed ($p=.173$, Model 1), breastfeeding duration ($p=.977$, Model 1), and food insecurity ($p=.163$, Model 2) were not significantly associated with relative theta power.

Turning to absolute theta power, ever breastfed is the only significant independent variable, being positively related to absolute theta power ($p=.017$). The effect size of 0.152 suggests a weak to moderate relationship between ever breastfed and absolute theta power. Models which specified ever breastfed as the IV rather than breastfeeding duration had slightly higher R^2 statistics, suggesting that ever breastfed might be a more useful operationalization of breastfeeding behavior in this study.

Some covariates had a significant association with relative and absolute theta power, though the pattern of significance differs to some extent when comparing the results for relative and absolute theta power. For example, the pairwise difference between Multiracial and Hispanic mothers was statistically significant with infants of Hispanic mothers having higher absolute theta power ($p=.030$, Model 3) – but this relation was not significant with relative theta power as the outcome. For absolute theta power, Black mothers had infants with significantly lower absolute theta power ($p=.001$, Model 3) as compared to infants of Hispanic mothers. This difference between infants of Black and Hispanic mothers was actually *positive* in the models with relative theta power as the outcome, a difference which was marginally significant in Model 1 ($p=.084$) at the 0.10 level and significant at the 0.05 level in Model 2 ($p=.044$). This reversal in direction of effect can be seen for other variables in Table 23. When comparing Models 1 and 2 for relative theta power to Models 3 and 4 for absolute theta power, the correlations of many of the covariates are in the opposite direction. This reflects the strong negative correlation between relative and absolute theta power ($r=-0.66$, Table 14) reported earlier. The positive association of living in New York or Louisiana as compared to Nebraska for relative theta power reverses to a negative relationship when the outcome is absolute theta power – though the effects for Louisiana are only significant at the 0.05 level in Model 2 ($p=.022$). In both cases, the magnitude of the association is similar, just in opposite directions depending on whether the dependent variable is relative or absolute theta power. A similar

pattern plays out for epoch count. Although epoch count is positively associated with relative theta power ($p=.008$), it is negatively associated with absolute theta power ($p<.001$). Again, these reversals are expected given the strong negative association ($r= -0.66$) between relative and absolute theta power, when relative theta power increases, absolute theta power decreases. The association of count of services and the outcomes provides an exception – although the number of services a mother reported participating in is associated with increases in relative theta power of their infants ($p=.230$), there was close to zero association between this covariate and absolute theta power.

4.6.2 MLR results for relative and absolute alpha power

Table 24 shows the MLR output for the relative and absolute alpha power outcome.

Table 24 Relative and absolute alpha power MLR model results, effect size and standard errors reported

<i>Variables</i>	Relative power		Absolute power	
	Model 1	Model 2	Model 3	Model 4
Ever breastfed	0.229** (0.070)		0.170** (0.065)	
Duration of breastfeeding		0.019 (0.067)		0.019 (0.062)
HFI	-0.043 (0.076)	-0.025 (0.077)	-0.040 (0.070)	-0.027 (0.072)
Maternal race: White	-0.089 (0.082)	-0.104 (0.084)	-0.128 (0.077)	-0.139 (0.078)
Maternal race: Black	-0.190* (0.094)	-0.214* (0.096)	-0.222* (0.088)	-0.239** (0.089)
Maternal race: Other	-0.095 (0.070)	-0.089 (0.072)	-0.085 (0.065)	-0.080 (0.066)
Maternal race: Multiracial	-0.084 (0.074)	-0.081 (0.076)	-0.100 (0.069)	-0.097 (0.070)
Maternal age	-0.046 (0.065)	-0.061 (0.066)	-0.005 (0.061)	-0.016 (0.061)
Maternal mental health	-0.014 (0.074)	-0.049 (0.075)	0.065 (0.069)	0.040 (0.070)
Maternal physical health	0.053 (0.070)	0.046 (0.071)	0.102 (0.065)	0.096 (0.066)
Maternal Education	-0.066 (0.069)	-0.035 (0.070)	-0.119 (0.064)	-0.096 (0.064)
Maternal substance use, smoking	0.065 (0.075)	0.023 (0.077)	0.080 (0.070)	0.050 (0.071)
Maternal substance use, alcohol	-0.068 (0.065)	-0.081 (0.066)	-0.027 (0.060)	-0.036 (0.061)
Financial hardship	-0.090 (0.070)	-0.103 (0.071)	-0.105 (0.065)	-0.114 (0.066)
Services count	-0.041 (0.069)	-0.045 (0.071)	-0.101 (0.064)	-0.105 (0.065)
Site: LA	0.039 (0.088)	0.000 (0.090)	-0.136 (0.082)	-0.165* (0.083)
Site: NY	-0.149 (0.087)	-0.137 (0.090)	-0.253** (0.081)	-0.244** (0.083)
Site: MN	0.124 (0.074)	0.149 (0.076)	0.073 (0.069)	0.092 (0.070)
Epoch count	-0.120 (0.065)	-0.104* (0.066)	-0.309*** (0.061)	-0.323*** (0.061)
Intercept	0.000 (0.062)	0.000 (0.063)	0.000 (0.058)	0.000 (0.058)
Model fit (R ²)	14.0%	9.8%	25.3%	23.1%

Notes: * = $p < .05$; ** = $p < .01$, *** = $p < .001$, effect sizes reported, standard errors in parenthesis, reference group for HFI was food security, reference group for maternal race is Hispanic, reference group for site is NY. Relative theta, alpha, beta and gamma power are ratios and absolute theta, alpha, beta and gamma power measured in $\mu V^2/Hz$.

There was no main effect of HFI or breastfeeding duration on relative or absolute alpha power. But infants who were breastfed at least one time as reported by their mothers had a significant increase in both relative ($p=.001$ in Model 1) and absolute ($p=.009$) alpha power – higher alpha is associated with positive developmental outcomes. The effect size of ever breastfed (0.22 in Model 1 and 0.17 in Model 2) is similar in both models. As was the case in the models with theta power as the outcome, R^2 is slightly higher (by approximately 4% and 2% in the models for relative and absolute alpha power respectively) in models where ever breastfed rather than breastfeeding duration is the independent variable.

The difference between infants of Black and Hispanic mothers ($p=.044$, Model 1) and epoch count ($p=.036$, Model 2; $p=.066$, Model 1) significantly related to both relative and absolute alpha power. Hispanic mothers had infants with greater relative and absolute alpha power, while epoch count was negatively associated with both outcomes. The effect size of these two predictors were larger in the models with absolute alpha power as the dependent variable. Infants from Louisiana had lower absolute alpha power ($p=.047$, Model 4) as compared to Nebraska – but only in Model 4 where breastfeeding rather than ever breastfed was the IV. We see a similar pattern in infants from New York, which was associated with lower absolute alpha power ($p=.002$, Model 4) as compared to infants in Nebraska.

4.6.3 MLR results for relative and absolute beta power

Table 25 shows the MLR model for the relative and absolute beta power outcome.

Table 25 Relative and absolute beta power MLR model results, effect size and standard errors reported

<i>Variables</i>	Relative power		Absolute power	
	Model 1	Model 2	Model 3	Model 4
Ever breastfed	0.002 (0.066)		0.036 (0.065)	
Duration of breastfeeding		-0.014 (0.062)		-0.004 (0.061)
HFI	-0.107 (0.072)	-0.106 (0.072)	-0.088 (0.071)	-0.084 (0.071)
Maternal race: White	-0.115 (0.078)	-0.115 (0.078)	-0.119 (0.077)	-0.121 (0.077)
Maternal race: Black	-0.126 (0.089)	-0.128 (0.089)	-0.130 (0.088)	-0.134 (0.088)
Maternal race: Other	0.083 (0.066)	0.084 (0.067)	0.034 (0.065)	0.035 (0.066)
Maternal race: Multiracial	-0.057 (0.070)	-0.058 (0.070)	-0.048 (0.069)	-0.047 (0.069)
Maternal age	0.022 (0.062)	0.022 (0.061)	0.024 (0.061)	0.022 (0.061)
Maternal mental health	0.083 (0.070)	0.081 (0.070)	0.095 (0.069)	0.089 (0.069)
Maternal physical health	0.115 (0.066)	0.114 (0.066)	0.148* (0.065)	0.146* (0.065)
Maternal Education	-0.118 (0.065)	-0.117 (0.065)	-0.162* (0.064)	-0.157* (0.064)
Maternal substance use, smoking	0.115 (0.071)	0.112 (0.071)	0.120 (0.070)	0.112 (0.070)
Maternal substance use, alcohol	0.088 (0.061)	0.086 (0.061)	0.055 (0.060)	0.052 (0.061)
Financial hardship	-0.081 (0.066)	-0.081 (0.066)	-0.073 (0.065)	-0.075 (0.065)
Services count	-0.167* (0.065)	-0.166* (0.065)	-0.169** (0.064)	-0.169** (0.065)
Site: LA	-0.213* (0.083)	-0.215* (0.083)	-0.231** (0.082)	-0.238** (0.082)
Site: NY	-0.205* (0.083)	-0.208* (0.083)	-0.219** (0.081)	-0.219** (0.082)
Site: MN	0.049 (0.070)	0.048 (0.070)	0.016 (0.069)	0.019 (0.069)
Epoch count	-0.241*** (0.062)	-0.242*** (0.061)	-0.301*** (0.061)	-0.304*** (0.060)
Intercept	0.000 (0.059)	0.000 (0.059)	0.000 (0.058)	0.000 (0.058)
Model fit (R ²)	22.8%	22.8%	25.0%	24.9%

Notes: * = $p < .05$; ** = $p < .01$, *** = $p < .001$, effect sizes reported, standard errors in parenthesis, reference group for HFI was food security, reference group for maternal race is Hispanic, reference group for site is NY. Relative theta, alpha, beta and gamma power are ratios and absolute theta, alpha, beta and gamma power measured in $\mu V^2/Hz$.

The main effects for ever breastfeeding and breastfeeding duration were not statistically significant at the 0.05 level of significance – for either relative or absolute beta power. Since breastfeeding behavior is unrelated to beta power, the R^2 are similar in magnitude regardless of which operationalization of breastfeeding behavior is used. HFI was also not significantly associated with either relative or absolute beta power.

There is a very strong association between relative and absolute beta power ($r=0.97$). This strong linear dependence shades the pattern of findings across the covariates for each outcome. Three of the significant covariates (count of participation in governmental social services, differences in sites, and epoch count) were significant and of similar magnitude for both relative and absolute beta power. For example, participating in more governmental services was associated with lower relative and absolute beta power ($p=.011$, Model 1). Infants of mothers in Nebraska had significantly greater relative and absolute beta power as compared to infants in Louisiana ($p=.011$, Model 1) and New York ($p=.013$, Model 1). Epoch count showed a negative and moderately strong association with relative ($p<.001$, Model 1) and absolute ($p<.001$, Model 3) beta power, with effects that are slightly larger when absolute power was the outcome. Two variables were significant predictors for absolute, but not relative, beta power. Good maternal physical health ($p=.024$, Model 3) was associated with higher absolute beta power. Years of maternal education was negatively related to absolute power beta ($p=.047$, Model 3). The effects for education and good maternal physical health were similar in size though opposite in direction, being right around 0.15 SDs.

4.6.4 MLR results for relative and absolute gamma power

Regression output for relative gamma power is shown in Table 26.

Table 26 Relative and absolute gamma power MLR model results, effect size and standard errors reported

<i>Variables</i>	Relative power		Absolute power	
	Model 1	Model 2	Model 3	Model 4
Ever breastfed	-0.008 (0.067)		0.020 (0.067)	
Duration of breastfeeding		0.003 (0.063)		0.005 (0.063)
HFI	-0.087 (0.073)	-0.088 (0.073)	-0.083 (0.073)	-0.081 (0.073)
Maternal race: White	-0.119 (0.080)	-0.118 (0.080)	-0.114 (0.079)	-0.116 (0.079)
Maternal race: Black	-0.094 (0.091)	-0.092 (0.091)	-0.085 (0.090)	-0.087 (0.090)
Maternal race: Other	0.071 (0.068)	0.070 (0.068)	0.036 (0.067)	0.036 (0.067)
Maternal race: Multiracial	-0.084 (0.072)	-0.084 (0.072)	-0.060 (0.071)	-0.059 (0.071)
Maternal age	0.052 (0.063)	0.052 (0.063)	0.048 (0.062)	0.047 (0.062)
Maternal mental health	0.128 (0.072)	0.130 (0.072)	0.128 (0.071)	0.125 (0.071)
Maternal physical health	0.106 (0.068)	0.107 (0.068)	0.142* (0.067)	0.141* (0.067)
Maternal Education	-0.121 (0.067)	-0.123 (0.066)	-0.162* (0.066)	-0.160* (0.065)
Maternal substance use, smoking	0.081 (0.073)	0.083 (0.073)	0.099 (0.072)	0.096 (0.072)
Maternal substance use, alcohol	0.110 (0.063)	0.110 (0.063)	0.079 (0.062)	0.078 (0.062)
Financial hardship	-0.067 (0.068)	-0.067 (0.067)	-0.056 (0.067)	-0.057 (0.067)
Services count	-0.145* (0.067)	-0.145* (0.067)	-0.158* (0.066)	-0.159* (0.066)
Site: LA	-0.179* (0.085)	-0.177* (0.085)	-0.204* (0.085)	-0.207* (0.084)
Site: NY	-0.216* (0.085)	-0.216* (0.085)	-0.219** (0.084)	-0.218* (0.084)
Site: MN	0.009 (0.072)	0.008 (0.072)	-0.021 (0.071)	-0.019 (0.071)
Epoch count	-0.240*** (0.063)	-0.240*** (0.063)	-0.280*** (0.062)	-0.282*** (0.062)
Intercept	0.000 (0.060)	0.000 (0.060)	0.000 (0.059)	0.000 (0.059)
Model fit (R^2)	19.1%	19.1%	20.8%	20.8%

Notes: * = $p < .05$; ** = $p < .01$, *** = $p < .001$, effect sizes reported, standard errors in parenthesis, reference group for HFI was food security, reference group for maternal race is Hispanic, reference group for site is NY. Relative theta, alpha, beta and gamma power are ratios and absolute theta, alpha, beta and gamma power measured in $\mu V^2/Hz$.

As noted above, the results in this table are based on robust standard errors since the regression assumption of normality and homoscedasticity were violated. The results below are almost an exact carbon copy of the results for relative and absolute beta power. This is the result of the strong relationship between beta and gamma power, with correlations around 0.90 (Table 14). The main effects of the two breastfeeding variables were not statistically different from zero for either relative or absolute gamma power. The R^2 was therefore similar in magnitude for both operationalizations of breastfeeding behavior. HFI was not found to be significantly associated with relative or absolute gamma power.

Echoing the results for relative and absolute beta power, the pattern of significance for relative and absolute gamma power is similar for the predictor variables (the two outcomes have a correlation of 0.98). The number of federal services that a mother participated in significantly and negatively related to relative gamma power ($p=.031$, Model 1), such that a 1 SD increase in the use of federal services led to a drop in relative gamma power by approximately 0.14. Epoch count ($p<.001$, Model 1) was negatively related to gamma brain wave activity for both the relative and absolute measures, with a moderate effect size around 0.25 SDs. Infants in Nebraska had higher relative gamma power as compared to infants in New York ($p=.011$, Model 1) and Louisiana ($p=.037$, Model 1). All of these covariates (use of governmental services, epoch count, and differences across sites) are significant of similar magnitudes for both relative and absolute gamma power. Good maternal physical health is positively associated with absolute gamma power ($p=.035$, Model 3), while education related negatively with absolute gamma power ($p=.014$, Model 3). Mirroring the results for beta power, neither covariate was significantly related to relative gamma power.

4.7 Interpretation of Findings

Unless otherwise noted, when evaluating the significance between the IVs and the DVs, the MLR results are used rather than the bivariate associations reported in Tables 15 and 16. The MLR are preferred since they adjust for key covariates, while the bivariate results do not. It is important to highlight the strong agreement between the bivariate t-tests and MLR results. Looking at the relation between ever breastfed and the outcomes, Table 15 shows that ever breastfed is significantly related to absolute theta, relative and absolute alpha. The MLR results agree – ever breastfed was only related to these three outcomes. For HFI, there was similarly high agreement between the bivariate and multivariate results. The bivariate tests showed HFI was not significantly associated with any outcome; a result which was replicated in the multivariate analyses.

4.8 Summary of MLR: Significant Main Effects

Table 27 summarizes MLR results.

Table 27 Summary of effect size on household food insecurity, ever breastfed, and breastfeeding duration for relative and absolute theta, alpha, beta, and gamma power

	Household Food Insecurity (HFI)		Ever Breastfed	Breastfeeding Duration
	Models 1,3	Models 2,4	Models 1,3	Model 2,4
Relative Theta Power	0.100	0.092	-0.090	-0.002
Absolute Theta Power	0.001	0.012	0.152*	0.017
Relative Alpha Power	-0.043	-0.025	0.229**	0.019
Absolute Alpha Power	-0.040	-0.027	0.170**	0.019
Relative Beta Power	-0.107	-0.106	0.002	-0.014
Absolute Beta Power	-0.088	-0.084	0.036	0.004
Relative Gamma Power	-0.087	-0.088	-0.008	0.003
Absolute Gamma Power	-0.083	-0.081	0.020	0.005

Notes: * = $p < .05$; ** = $p < .01$, *** = $p < .001$, effect sizes reported, bolded numbers indicate statistical significance, reference group for HFI was food security, relative theta, alpha, beta and gamma power are ratios and absolute theta, alpha, beta and gamma power measured in $\mu V^2/Hz$, models 1 and 3 included ever breastfed as an IV and models 2 and 4 included breastfeeding duration as an IV.

This table defines the magnitude of effect size and statistical significance of that effect size of HFI, ever breastfeeding, and breastfeeding duration on relative and absolute theta, alpha, beta, and gamma power. Since there were two MLRs that were calculated for each breastfeeding outcome variable, one with ever breastfed and the other with breastfeeding duration, a pair for effect sizes is shown for HFI where relative measures from models 1 and 2 and absolute measures from models 3 and 4 are reported in the table below.

It is seen in this summary table that ever breastfeeding was found to be significantly associated with absolute theta power and relative ($p < .01$) and absolute alpha power ($p < .001$). Breastfeeding duration and HFI on the other hand were not significantly associated with any of the outcome measures.

4.9 Summary of Additional Findings

Table 28 illustrates a summary of covariate interactions seen across the MLR models.

Table 28 Summary of significant covariate associations for relative and absolute theta, alpha, beta, and gamma power

	Race- Black	Race- multiracial	Physical health	Education	Services count	Epoch count
Rel. Theta Power M1/M2	--/ 0.181*	--	--	--	0.149* / 0.151*	0.252***/ 0.260***
Abs. Theta Power M3/M4	-0.272**/ -0.287**	-0.148*/ -0.146*	--	--	--	-0.346***/ -0.360***
Rel. Alpha Power M1/M2	-0.190*/ -0.214*	--	--	--	--	-- / -0.104*
Abs. Alpha Power M3/M4	-0.222*/ -0.239**	--	--	--	--	-0.309***/ -0.323***
Rel. Beta Power M1/M2	--	--	--	--	-0.167*/ -0.166*	-0.241***/ -0.242***
Abs. Beta Power M3/M4	--	--	0.148*/ 0.146*	-0.162*/ -0.157*	-0.169**/ -0.169**	-0.301***/ -0.304***
Rel. Gamma Power M1/M2	--	--	--	--	-0.145*/ -0.145*	-0.240***/ -0.240***
Abs. Gamma Power M3/M4	--	--	0.142*/ 0.141*	-0.162*/ -0.160*	-0.158*/ -0.159*	-0.280***/ -0.282***

Notes: * = $p < .05$; ** = $p < .01$, *** = $p < .001$, effect sizes reported, for relative power measurements values reported as model 1/model 2 and for absolute power measurements as model 3/model 4, models 1 and 3 include ever breastfeeding as an IV and models 2 and 4 include breastfeeding duration as an IV, reference group for maternal race is Hispanic, non-significant effect sizes not shown, rel. and abs. are short for relative and absolute, respectively.

Within each MLR model, ten covariates were included in order to control for confounders of breastfeeding and household food insecurity. These covariates included maternal race/ethnicity, maternal age, maternal mental health, maternal physical health, maternal education, maternal smoking and alcohol use, economic stress, use of social services, site, and epoch count. Patterns of significant associations between these confounders and brain function were detected, which are outlined in this section. Study site was significantly associated with several power outcomes, but due to the small sample sizes within these sites, this is not interpreted further within this section. Non-significant effect sizes are not shown in the table below.

Maternal race was significantly associated with relative and absolute power of theta and alpha brain waves, and it was primarily the difference between infants of Black and Hispanic mothers that was significant. Increased maternal physical health was significantly associated with increased absolute beta and gamma power. Maternal education was found to be significantly associated with decreased absolute theta power and increased absolute gamma power. The participation in social services was found to be significantly associated with lower relative and absolute beta and gamma power, while it was positively related to relative theta power. Finally, epoch count was found to be significantly associated with increased relative theta while it was negatively associated with absolute theta, relative and absolute alpha, beta and gamma power.

Chapter 5: Discussion

This chapter contextualizes the results of this dissertation in context with other relevant studies. This chapter also covers the limitations, strengths, and implications of this research.

5.1 Purpose and Main Findings

The current study aims to build additional understanding around the association of nutritional factors, in particular breastfeeding and food insecurity, with brain function during the first year of life, as observed by EEG. The main reason for focusing on this topic is that more research effort needs to be directed toward achieving a better understanding of the effects of poor nutrition as an adverse childhood experience on the neurodevelopment of vulnerable children (De Oliveira et al., 2020; Mackes et al., 2020). An improved understanding of how breastfeeding and food insecurity are related to the functioning of an infants' brain will encourage the design of public health policies and interventions to improve early childhood nutrition as a mechanism to affect brain development (Schwarzenberg et al., 2018). There is a growing body of literature that establishes patterns within the four brain waves of theta, alpha, beta, and gamma in early childhood development that suggests that increased low-frequency brain power (increased theta waves) and decreased high-frequency brain power (such as lower alpha, gamma, and beta waves) is associated with developmental outcomes such as poorer vocabulary and memory as well as problems with learning, developmental delays, and difficulties paying attention (Corning et al., 1986, Harmony et al., Maguire & Schneider, 2019, McLaughlin et al., 2010). As reviewed in Chapter 2, it is important to consider the framework that differences in brain function may be adaptive for children experiencing adversity as a result of their lower SES, amongst other factors. Research has shown significant association between

being from a lower SES as a child and outcomes including brain function and structure (Noble & Giebler, 2020). This body of literature highlights the finding that children from disadvantaged backgrounds and a lower SES may develop skills that are prioritized in supporting their experiences within their environment that are distinct from their higher SES peers (Ellis et al., 2020). For this reason, interpretations on differences in brain function within this chapter will be discussed as adaptive changes in brain function, rather than as deficits.

This study aimed to examine the associations of breastfeeding and household food insecurity and infant brain development, specifically measured as relative and absolute theta, alpha, beta, and gamma power. At present, it is unknown how both breastfeeding and household food insecurity are related to brain function in infants. There is an opportunity to add to the literature by examining the association of these experiences with infant brain development as measured by relative and absolute theta, alpha, beta, and gamma power. Resting state EEG has been shown to be sensitive enough to detect individual differences and enrichment and deprivation experiences during brain development (Bell & Fox, 1992; Raine et al. 2001, Marshall et al., 2004). Whether the relative or absolute power spectral densities of theta, alpha, beta, and gamma will increase or decrease in association to the presence and duration of breastfeeding and the presence of household food insecurity was previously unknown.

This dissertation examined the following research questions and through statistical analysis, presents the following results and discussion highlighted in four key takeaways which address these questions:

RQ1: To what extent is breastfeeding related to the brain function of infants at 12 months of age?

Key Takeaway #1: Ever breastfeeding an infant during the first year of life is associated with higher absolute theta power, an unexpected directionality and association.

Key Takeaway #2: Ever breastfeeding an infant during the first year of life is associated with higher relative and absolute alpha power, an expected directionality and association.

Key Takeaway #3: Breastfeeding duration was not associated with relative or absolute theta, alpha, beta or gamma power.

RQ2: To what extent is household food insecurity related to the brain function of infants at 12 months of age?

Key Takeaway #4: The presence of food insecurity was not associated was not associated with relative or absolute theta, alpha, beta or gamma power.

Key Takeaway #1

Ever breastfeeding an infant during the first year of life is associated with higher absolute theta power, an unexpected directionality and association.

In this study, the decision of a mother to ever breastfeed was associated with higher absolute theta power ($p < 0.05$). The effect size of 0.152 suggests a weak to moderate relationship between ever breastfed and absolute theta power, and is interpreted that for a 1-SD increase in ever breastfeeding within this sample, there was a statistically significant increase of 0.152-SDs of absolute theta power.

Theta waves reflect activity from the limbic system and hippocampal regions of the brain; however, the scalp distribution of theta rhythm in infants depends on age, reflecting the engagement of different brain networks during growth (Orekhova et al., 2006). At the age of one an infants' brain spends much of its time producing theta brainwave cycles, which ultimately declines as an infant reaches childhood (Perone et al., 2018). The modulation of

theta activity in infants is associated with the development of cognitive skills (Jones et al., 2010) and the regulation of responses (Michel et al., 2015).

This is a surprising finding from this research, considering that increased theta power has been found to be associated with adverse experiences in childhood (Marshall et al., 2004, Troller-Renfree et al, 2020). Breastfeeding as a behavior has been found to be associated with enhanced maternal sensitivity and ensured attachment between the mother and her child (Tharner et al., 2012). Furthermore, research has shown that mothers who breastfeed their children tend to touch their infants more, are more responsive to feeding needs, and display more eye-to-eye contact with infants during feeding (Pearson et al., 2011; Jansen et al., 2008). This research suggests that breastfeeding can be considered a beneficial experience within early childhood, which would hypothetically improve the experienced adversity of children from disadvantaged backgrounds. One explanation for the unexpected directionality of absolute theta power, which is significantly higher for ever breastfed infants compared to never breastfed infants is that this difference in brain function could be attributed to a circumstantial adaptation, although it is important to consider that the entire sample of infants within this study came from lower SES backgrounds.

An additional consideration is that the increase in absolute theta power could be in part modulated by differences in skull thickness or other factors that could impact the electrical impedance of the EEG cap. Absolute power measurements are measurements that are not standardized and therefore we must cautiously interpret findings within absolute power measurements due to the additional confounders that can be caused by the physiology of an infant, the data collection process, and the quality of data that was collected. Relative power measurements are ratios that allow researchers to standardize the magnitude of each brain wave's power spectral density by dividing, for example, absolute power theta measured for a participant by the sum of absolute power theta, alpha, beta, and gamma for that same

participant. Finally, it was found that there was a strong inverse relationship between relative and absolute power theta ($r=-0.66$), a relationship that was not seen between other relative and absolute power brain wave pairs. This paradox can be explained by the fact that as absolute theta power goes up, so does absolute alpha, beta, and gamma power – the increases in these other three bands of brain wave frequencies more than offsets the increase in absolute theta power. For these reasons, the significant association of increased absolute theta power for infants who were ever breastfed ($p<.05$) should be cautiously interpreted since relative power theta was not found to be significantly associated with being ever breastfed.

Key Takeaway #2

Ever breastfeeding an infant during the first year of life is associated with higher relative and absolute alpha power.

It was found that ever breastfeeding an infant was associated with higher relative and absolute power alpha ($p<.01$), the expected directionality of effect size. Ever breastfeeding an infant was not found to be associated with relative or absolute beta and gamma power or relative theta power. The effect size for relative and absolute alpha power was 0.229 and 0.170, respectively, which can be interpreted as for every 1-SD increase in ever breastfeeding within this sample there was a statistically significant increase in relative and absolute power by 0.229 and 0.170 SDs, respectively. Increased alpha power is associated with positive developmental outcomes in childhood (Corning et al., 1986, Harmony et al., Maguire & Schneider, 2019, McLaughlin et al., 2010). The pattern of agreement of magnitude and directionality of relative and absolute alpha power provides additional evidence that when controlled for by the ten covariates in this study, ever breastfeeding an infant was significantly associated with an increase in alpha power within this sample of infants.

Alpha waves reflect activity from the occipital lobes during wakeful relaxation, when the eyes are closed, and the brain is not processing a lot of information (Saby & Marshall,

2010). The highest levels of alpha power are associated with an elevated state of anxiety (Dadashi et al., 2016). By age two months, a precursor of the alpha wave (3-4-Hz) has established, increasing to 4 -5 Hz at age six months, reaching 5-7 Hz at age 12 months, and finally stabilizing within the normal adult alpha frequency range (8 -12 Hz) by age three years (St. Louis & Frey, 2016).

A large breadth of research has described the differences in behavior and cognition between breast-fed vs. formula-fed infants measured during childhood that persist throughout adolescence. Breast-fed infants have been shown to process speech differently from bottle-fed infants (Ferguson & Molfese, 2007; Pivik et al., 2011). In addition, breastfed infants have been shown to exhibit improved cognitive abilities in childhood, compared to formula-fed infants (Deoni et al., 2018; Huang et al., 2014; Mackes et al., 2016; Horta et al., 2015; Luby et al., 2016; Nyardi et al., 2013).

Key Takeaway #3

Breastfeeding duration was not associated with relative and absolute theta, alpha, beta or gamma power.

While breastfeeding duration and ever breastfeeding were found to be correlated with each other as operationalizations of the same behavior ($r=0.48$), only ever breastfeeding was found to be associated with brain function, and particularly, higher relative and absolute alpha power. This finding is interesting in context with literature that describes the associations of breastfeeding and enhanced maternal sensitivity and attachment as breastfeeding, mothers touch their infants and maintain eye contact more, among other attachment behaviors (Pearson et al., 2011; Jansen et al., 2008). It is possible that the increases in relative and absolute alpha power within the sample of infants who were ever breastfed are in part due to the emotional connection that breastfeeding elicits. In addition, mothers who make the decision to breastfeed may represent a subset of the sample who were able to dedicate more time and attention to their

infants in the form of breastfeeding. As shown in Chapter 4, mothers who never breastfed their infants were more likely to be Hispanic ($p=.003$, 23.2% vs 46%) and to have smoked at least once in the past year ($p<.001$, 41.1% vs 16% for mothers who had breastfed). Maternal depression was marginally significant at the 0.10 level ($p=.063$). Mothers who never breastfed their infants were more likely to be depressed (21.4% vs. 10.7% for mothers who breastfed). The decision to breastfeed may also be associated with other positive maternal behaviors that can be supportive of infant brain development and function. Finally, given that most mothers who ever breastfed (93.5% of the 187 mothers who ever breastfed) breastfed beyond one month, it is also possible that the nutritional benefits derived by an infant in the first month of breastfeeding are superior to the benefits relate to brain development in extended breastfeeding beyond one month. This could be explained by the way in which breast milk, which is a living tissue, changes as an infant grows and begins as colostrum which develops in the alveoli during the last month of pregnancy and contains high levels of protein and immunoglobulins but less glucose and fat than mature breastmilk. Transitional milk develops three days following birth as colostrum stops and by 10 days postpartum, breastmilk develops into mature milk.

Key Takeaway #4

The presence of food insecurity was not associated was not associated with relative or absolute theta, alpha, beta or gamma power.

This study utilized an adapted version of the U.S. Household FSS Module Short Form which was dichotomized to detect the presence of food insecurity in the households of 243 mother and infant pairs. 67 mothers and infant pairs or 27.6% of study participants were classified to be living within food insecure households for their selection of 2 or more affirmative responses of the 5-item food insecurity questions they were asked. This means that close to one third of the mother and infant dyads in this study were experiencing food insecurity when this data was collected, even though mothers within this study participated on average in

2.97 social support services ($SD=1.62$), with 65.8% of mothers participating in SNAP ($n=160$) and 71.2% participating in WIC ($n=173$). The parent study, Baby's First Year's, recruited low-income mothers in order to understand the impact of a monthly unconditional cash transfer on brain development in infants, so the presence of food insecurity in this population is not particularly surprising as low socioeconomic status can be considered a predictor of food insecurity (Coleman-Jensen, 2010).

Food insecurity was not found to be associated with relative or absolute theta, alpha, beta or gamma power within the MLR models run in this study nor within the independent t-tests (Table 16 in Chapter 4). The inadvertent elimination of one of the items of the U.S. Household FSS Module short form eliminated the ability to detect very low food insecurity within this sample, which in turn could have impacted the statistical detection of differences of brain function within this sample with respect to food security, low food insecurity, and very low food insecurity as the tool is designed to detect. The elimination of this question led to the dichotomization of participants into two categories, food secure and food insecure, which may have reduced the variance in this measure within this study's sample.

Household food insecurity is a complex variable because of its relationship to many other aspects of a family's life including income, education, job status, nutrition, among many others. For infants and children, food insecurity can be considered as an adversity experienced in early childhood which could be impacting brain development in a variety of capacities including through nutrition, stress pathways, and other familial experiences that are associated with the presence of food insecurity. As seen in Table 20 in Chapter 4, there was an association detected between food insecurity and WIC participation which is significant at the .05 level ($p=.031$). The odds ratio of 2.22 means that the odds of participating in WIC are more than twice as great for mothers who experienced food insecurity as compared to mothers who were rated as food secure. In addition, household food insecurity was significantly related to three

out of ten demographic covariates. Mothers who experienced food insecurity were more likely to be depressed ($p < .001$), experience moderate to high financial worry ($p < .001$) and have lower self-reported physical health ratings ($p < .001$). While this study did not identify significant associations between food insecurity and brain function in early childhood, the aforementioned differences in demographic characteristics between food secure and food insecure mothers underscores the importance for further research to understand the associations between food insecurity and brain function in early childhood.

5.2 Additional Findings

Table 28 in Chapter 4 illustrates a summary of covariate interactions seen across the MLR models and these patterns of association are expounded upon further in this section.

Maternal race was significantly associated with relative and absolute power of several brain waves. The pairwise difference for Black and Hispanic mothers was statistically significant, where infants of Black mothers had, on average, higher relative theta power, lower absolute theta power and lower relative and absolute alpha power. Finally, the pairwise difference for multiracial and Hispanic mothers was statistically significant, where infants of multiracial mothers had, on average, lower absolute theta power. This finding demonstrates that racial differences in brain function persist in a sample of infants at age one year from lower SES backgrounds, a meaningful finding that corroborates knowledge that racial experiences in the United States are varied, and it is possible that these differences in race may be adaptations that are the result of adverse childhood experiences.

Increased maternal physical health was significantly associated with increased absolute beta and gamma power. These patterns of association imply that better physical health of a mother is associated with the directionality seen with improved cognitive outcomes in other literature and not the directionality associated with experiences of adversity. Better physical

health of a mother may therefore improve the experiences of a child that allows for the detection of these changes in brain function.

Maternal education was found to be significantly associated with increased relative theta power and decreased relative and absolute beta and gamma power. This pattern of association is inversed from the pattern seen with maternal physical health and is an unexpected outcome. One explanation for this outcome could be that the variability of education is low within this sample size, with an average of 11.97 years of education ($SD=3.03$), meaning that within 1-SD of the mean within this sample, mothers had between 8.94 and 15.00 years of education, which is up to middle school and one year shy of completing a bachelor's degree.

The participation in social services was found to be significantly associated with higher relative theta power and lower relative and absolute beta and gamma power. This is interpreted that as a mother's participation in social services increases, relative theta power increases while relative and absolute beta and gamma power decrease significantly. This is an additionally perplexing finding as this is not the expected pattern of association if one was to consider the participation of social services to be advantageous for a child and mother's environment and experiences. However, it may be that this variable is also proxy for the needs of a family that mirrors the stress a mother or family can face when needing additional resources in the form of social services to improve living conditions and/or experiences.

Finally, epoch count was found to be significantly associated with increased relative theta, decreased absolute theta, and decreased relative and absolute alpha, beta, and gamma power. Epoch count can be considered as a proxy for the real-life environment of data collection with infants as study subjects. Epoch count is the number of segments the EEG data was spliced into for analysis. This range is variable depending on the length of data initially available for analysis and cleaning, which is dependent upon the real-life conditions of an infant tolerating an EEG cap for a period of around 5 minutes. Within developmental EEG data

collection, these segments are often between 1-2s long as infant EEG data often contains “noise” resulting from movement, eye blinks, or other sources. Within this study sample, infants had at minimum 20 artifact-free epochs for analysis purposes, which excluded participants with too few epochs who may not have cooperated well with data collection. If we can consider that epoch count may be a proxy for the executive function abilities of an infant to remain calm during data collection, then the patterns of association are the expected directionalities of improved cognitive functioning. The only exception is for decreased absolute theta power, this reflects the strong negative correlation between relative and absolute theta power ($r = -0.70$) reported earlier.

5.3 Limitations

There are several limitations to consider when contextualizing the results of this research study. First and foremost, as a cross-sectional study that derived all data through individual, single-session, visits around an infant’s first birthday, we are only able to understand associations between breastfeeding and food insecurity with respect to brain function. While cross-sectional research is not designed to define mechanisms of action or to confirm longitudinal impact of a behavior, there is value that is derivable through robust cross-sectional research. The manipulation of a mother’s breastfeeding behaviors or the presence of food security for a household with an infant would be unethical. Beyond ethics, a cross-sectional study as described in this dissertation does not require extensive funding. While the parent study, Baby’s First Years, was allocated more than \$30M in funding, largely in part to cover the experimental unconditional cash transfers, the study described in this dissertation did not require additional funding to complete, rather it was a time investment that allowed for the completion of this work.

The COVID-19 pandemic influenced the ability for researchers to conduct in person data collection and therefore, the experience of the pandemic can be considered a limitation of

this study. Because of the pandemic, age 1 data collection was prematurely halted in March of 2020 when New York City shutdown resulting in a much smaller sample size than the expected 600 mother and infant dyads which was reduced to 243 mother and infant dyads.

With respect to food insecurity, a clear limitation of this study is the inability to detect very low food insecurity, as defined as the USDA. The U.S. Household FSS Module Short Form is a six-item questionnaire that is both validated and reliable for the detection of food security, low food insecurity, and very low food insecurity. The parent study, *Baby's First Years*, inadvertently eliminated the following question: "In the last 12 months, were you ever hungry but didn't eat because there wasn't enough money for food?" from the age 1 survey and therefore only five of the six items of the tool were used for data collection. Therefore, the HFI variable was dichotomized due to the elimination of one question from the U.S. Household FSS Module short form in age 1 data collection by the parent study, *Baby's First Years*. As was previously discussed in Chapter 3, a report by the USDA Economic Research Service (ERS) (2019) demonstrated that no food secure households had selected yes to the question about experiencing hunger. The omission of this question only limits the ability to discern a distinction between those with low food security and very low food security, which are scored as 2-4 affirmations and 5-6 affirmations to the U.S. Household FSS Module short form, respectively. For this reason, the HFI variable was dichotomized to allow for the detection of any level of food insecurity, but ultimately, this modification of the tool limited the ability to perceive significant differences in brain function within infants whose mothers may be experiencing very low food insecurity.

Finally, it is important to recognize that this study was able to understand breastfeeding duration as measured in months, however, there was no data that was collected to understand if breastfeeding mothers were supplementing with formula and if they were supplementing with formula, to what degree they were doing so. It is plausible, given the way in which the

breastfeeding duration question was asked, that a mother could have been breastfeeding for comfort or infrequently, while supplementing with formula, and still affirm that they had been breastfeeding for a duration of 12 months, due to the non-specificity of the question. In addition, 71.2% of the moms participating in this study were receiving WIC benefits for the past one year, and one of the benefits that is provided by WIC is formula. Today, WIC provides formula based upon the breastfeeding status of an infant. For fully breastfed infants, a mother's WIC benefit would include more food and milk items whereas a partially breastfed infant's mother would receive some formula, and less food and milk products. Finally, a fully formula fed infant would receive more formula, almost enough to exclusively formula feed, and the mothers would receive less food and milk items due to this increase in formula. It is likely that some of the 173 mothers receiving WIC benefits within this study population would be using formula to supplement breastfeeding if they were breastfeeding their infants. It is important to note that there was no significant difference in WIC participation for moms who ever breastfed vs never breastfed. This may be attributed to the fact that even breastfeeding moms can receive WIC benefits as an advantageous social service for the benefit of their family, which is further supported by the high level of WIC participation within this sample. Ultimately, it may be that the specificity of the breastfeeding duration question was not able to detect differences in brain function in this sample due to the uncontrolled confounder of formula feeding.

5.4 Strengths

It is because of the careful and purposeful research work executed by the Baby's First Years research team that there are significant strengths of this research study. Sampling for the Baby's First Years study was very carefully executed to ensure that mothers did not feel coerced into participating in the study. During recruitment, participants were offered their unconditional cash transfer without the requirement to participate in the study. Participants were recruited from four states (NY, NE, LA, and MN) shortly after giving birth within a

hospital. The study sample was ultimately selected following a very careful screening process that ensured that the mothers were low-income and diverse, amongst other characteristics. The sample of mothers ultimately included in this study were derived from the control group of the parent study, Baby's First Years, which allowed for the detection of significant associations with respect to brain function without intervention.

Another strength of this study was the quality of EEG data collection. Researchers of the parent study conducted a pilot of the in-home EEG data collection process in advance of beginning the RCT funded by the NIH (Troller-Renfree et al., 2021). This pilot of over 400 one year old infants from diverse backgrounds allowed researchers to advance their understanding of the feasibility of in-home EEG data collection with respect to equipment recommendations, data collection, and data analysis. This pilot demonstrated that the developed methodology for in-home EEG data collection yielded high quality data with good internal consistency reliability. In addition, the Baby's First Years research team processed EEG data, which was retrieved for use and analysis in this dissertation. Because skilled researchers who had considerable experience processed the EEG data, there is an increased confidence in the quality of the data utilized in this study.

Independent variables, including breastfeeding duration, ever breastfed, and household food insecurity as well as many of the covariates included in this study were derived from validated and reliable survey tools that demonstrates the fidelity of each variable in measuring with it purports to measure. The reliability of the self-reported answers about infant feeding is reported to be moderately high among mothers of infants up to 35 months old. The six-item U.S. Household FSS module has been validated as a food insecurity screener by Blumberg et al., 1999, where the shorter module was found to correctly classify food insecurity 97.7% of 44,647 households participating in the 1995 Current Population Survey's food security module whose food security was measured using an 18-item scale. This instrument is also reported to

identify food insecure households with a high level of sensitivity (i.e., an accurate true positive rate) and with a high level of specificity (i.e., an accurate true negative rate) (Gulliford et al., 2004). Within the subgroup of 243 mothers in this sample, the PHQ-8, a tool to measure depression, showed good reliability with a Cronbach's alpha of 0.84. This estimate is like Shin et al. (2019), who reported a Cronbach's alpha of 0.89 for the PHQ-8. Shin et al. (2019) also report evidence about convergent validity for the PHQ-8. As expected, the PHQ-8 is strongly correlated with the Hamilton depression rating scale (Spearman correlation= 0.62). The BFY instrument also includes items extracted from the Global Health Tool (Idler & Beryamini, 1997) to measure maternal physical health of the mothers, and items extracted from the instrument devised by Kling, Liebman, Katz (2007) to measure maternal substance abuse, specifically alcohol and smoking cigarettes.

Finally, although the sample size for this study was reduced due to the pandemic, COVID-19, there was still sufficient statistical power for the inclusion of 10 covariates as well as independent variables in the MLR models, which allowed for the controlling of many confounders that are associated both with the presence of food insecurity as well as breastfeeding behaviors in mothers. As discussed in the additional findings section above, several of these covariates illustrate patterns of significance with respect to the relative and absolute power of theta, alpha, beta, and gamma. There are undoubtedly additional confounders, such as formula feeding, that were not included in these models, but the 10 covariates that were included do allow for increased confidence in the significant associations detected and described in this chapter.

5.5 Implications

There are important implications of this research, especially in context with literature reviewed in this chapter. This research demonstrates the significant associations between ever breastfeeding an infant with brain function in a population of infants from diverse, low SES

backgrounds. In contextualizing these changes in brain function as plausible adaptations that infants are developing due to their experiences, an opportunity exists to further explore these associations with brain function to understand the skills that low SES infants are developing during the first year of life. While there is significant research that contextualizes breastfeeding as related to cognition and academic performance in childhood, it is not yet understood through which mechanisms of action these associations exist. It may be possible that ever breastfed infants, like those in this study, exhibit higher absolute theta power and higher relative and absolute alpha power as adaptive changes that are related to skill developments to cope with family experiences that could be related to the decision of a mother to initiate breastfeeding.

The bivariate exploration of differences in demographics between food insecure and food secure mothers and mothers who ever breastfed or did not initiate breastfeeding illustrated that there are in fact characteristic differences that can contextualize the differences in environmental experiences infants are having within these groups. Mothers who experienced food insecurity were more likely to be depressed ($p<.001$), experience moderate to high financial worry ($p<.001$) and have lower self-reported physical health ratings ($p<.001$). Mothers who reported never breastfeeding their infants were more likely to be Hispanic ($p<.01$, 23.2% vs 46%) and to have smoked at least once in the past year ($p<.001$, 41.1% vs 16% for mothers who had breastfed).

There are future opportunities to continue to explore the relationship between breastfeeding, food insecurity, and brain function in early childhood. Given that breastfeeding duration was not found to be significantly associated with brain function within this study's sample of infants, but ever breastfeeding an infant was, the question arises — what are the mechanisms of action by which breastfeeding is associated with brain function and development? Evidence illustrates that both the behavior of breastfeeding and attachment between a mother and a breastfeeding infant as well as the nutritional composition of

breastmilk can explain some differences in brain structure, but the understanding of how these two distinct factors of a breastfeeding relationship contribute together to brain development is not yet known and offers opportunity for future study. In addition, as household food insecurity was not found to be associated with brain function in this sample of infants, there are future opportunities to study infants from low-SES backgrounds to identify associations between household food insecurity and brain function that can leverage the entire six-item U.S. Household Food Security Survey (FSS) Module Short Form or other tools that are designed to detect childhood food insecurity more specifically.

In addition to further research, there are policy implications from this research and other research like this. The illustration of changes of brain function in early childhood associated with ever breastfeeding an infant is powerful in context with important policy discussions that postulate opportunities to impact children long term through early interventions. Within the United States, programs such as WIC and SNAP already are designed to improve both food security, and in the context of WIC, encourage breastfeeding. Considering mothers within this study participated in an average of three social service programs but there was still a 28% rate of food insecurity in population, opportunity exists to pursue novel programming to better target food security in low-income families. We must reflect on further opportunities to improve services provided to mothers and infants from low-SES backgrounds in the United States to encourage healthier childhood development, inclusive of brain development, by mitigating circumstances that can create adverse childhood experiences. This is work that is being pioneered by the BFY study which is poised to demonstrate the impact of unconditional cash transfers on brain function in early childhood as an opportunity for intervention that can have a lasting impact on children. The Biden administration has already worked to implement programs that parallel the intervention of the BFY study through the Child Tax Credit, which in the span of one year will allocate \$105 billion to families in the United States through

monthly \$250-\$300 payments for each child, a service that will reach 90% of America's 74 million children. In context with this policy in the wake of the pandemic, the BFY study is poised to study the associations of this additional payment to mothers of infants within both the treatment and control groups on brain function in early childhood. It is research like this, set upon the backdrop of innovative social policy, that can cause meaningful policy changes that may improve the experiences and development of America's most vulnerable infants.

References

- Adane, Akilew Awoke, Gita D. Mishra, and Leigh R. Tooth. "Maternal pre-pregnancy obesity and childhood physical and cognitive development of children: a systematic review." *International Journal of Obesity* 40.11 (2016): 1608-1618.
- Agostoni, Carlo, et al. "Free glutamine and glutamic acid increase in human milk through a three-month lactation period." *Journal of Pediatric Gastroenterology and Nutrition* 31.5 (2000): 508-512.
- Agresti, A. *Categorical data analysis* (3rd ed.). New York: Wiley. 2013.
- Ahbang, P.A., Bharti, W., & Mehrotra, S.C. Technological basics of EEG recording and operation of apparatus. In: *Introduction to EEG and Speech-based emotion recognition*. Chapter 2. pp. 19-50. (2016). Mumbai, India: Elsevier.
- Ajibola, Gbolahan, et al. "HIV exposure and formula feeding predict under-2 mortality in HIV-uninfected children, Botswana." *The Journal of Pediatrics* 203 (2018): 68-75.
- Alaimo, K., Olson, C. M., & Frongillo, E. A. Food insufficiency and American school-aged children's cognitive, academic, and psychosocial development. *Pediatrics*, 108(1), 2001:44-53.
- Al-Chalabi, Mustafa, and Ihsan Alsalman. "Physiology, Prolactin." *StatPearls [Internet]*. StatPearls Publishing, 2019.
- Allen, J., and Hector, D. "Benefits of breastfeeding." *New South Wales Public Health Bulletin* 16.4 (2005): 42-46.
- Almeida, Mara Ribeiro, et al. "Maternal vitamin B6 deficient or supplemented diets on expression of genes related to GABAergic, serotonergic, or glutamatergic pathways in hippocampus of rat dams and their offspring." *Molecular Nutrition & Food Research* 60.7 (2016): 1615-1624.
- Aloisio, Irene, et al. "Three-month feeding integration with bifidobacterium strains prevents gastrointestinal symptoms in healthy newborns." *Frontiers in nutrition* 5 (2018): 39.
- Altman, D.A., Machin, D., Bryant, T., & Gardner, M. *Statistics with confidence: Confidence intervals and statistical guidelines*. London, UK: BMJ Books.
- Alvarenga, Willyane de Andrade, et al. "Mothers living with HIV: replacing breastfeeding by infant formula." *Revista Brasileira de Enfermagem* 72.5 (2019): 1153-1160.
- American Academy of Pediatrics. (2012). Breastfeeding and the use of human milk. *Pediatrics*, 129 (3), e827-e841. doi: <https://doi.org/10.1542/peds.2011-3552>
- Amrhein, V., Greenland, S., & McShane, B. (2019) Scientists rise up against statistical significance. *Nature* 567, 305–307.

- Andersen, Stine Linding, et al. "Mechanisms in endocrinology: neurodevelopmental disorders in children born to mothers with thyroid dysfunction: evidence of fetal programming?" *European Journal of Endocrinology* 177.1 (2017): R27-R36.
- Anderson, George, et al. "Breast feeding and melatonin: Implications for improving perinatal health." *Journal of Breastfeeding Biology* 1.1 (2016): 8-20.
- Anderson, Philip O. "Treating diabetes during breastfeeding." *Breastfeeding Medicine* 13.4 (2018): 237-239.
- Anderson, Sue Ann, ed. "Core indicators of nutritional state for difficult-to-sample populations." *The Journal of Nutrition* 120.suppl_11 (1990): 1555-1600.
- Andreas, Nicholas J., Beate Kampmann, and Kirsty Mehring Le-Doare. "Human breast milk: A review on its composition and bioactivity." *Early Human Development* 91.11 (2015): 629-635.
- Aneesh, M., & Ghugre, P. (2019). *Early nutrition and cognitive functions*. 4, 102–108.
- Arora, Samir, et al. "Major factors influencing breastfeeding rates: Mother's perception of father's attitude and milk supply." *Pediatrics* 106.5 (2000): e67-e67.
- Asgarshirazi, Masoumeh, et al. "Comparison of fecal calprotectin in exclusively breastfed and formula or mixed fed infants in the first six months of life." *Acta Medica Iranica* (2017): 53-58.
- Aubert-Broche, Bérengère, et al. "A new method for structural volume analysis of longitudinal brain MRI data and its application in studying the growth trajectories of anatomical brain structures in childhood." *Neuroimage* 82 (2013): 393-402.
- Augustine, Rachael A., et al. "Prolactin regulation of oxytocin neurone activity in pregnancy and lactation." *The Journal of Physiology* 595.11 (2017): 3591-3605.
- Avci, Zekai, et al. "Involuntary movements and magnetic resonance imaging findings in infantile cobalamin (vitamin B12) deficiency." *Pediatrics* 112.3 (2003): 684-686.
- Baltaci, Abdulkemim Kasim, and Kemal Yuce. "Zinc transporter proteins." *Neurochemical Research* 43.3 (2018): 517-530.
- Barra, Rafael, et al. "Facts and hypotheses about the programming of neuroplastic deficits by prenatal malnutrition." *Nutrition Reviews* 77.2 (2019): 65-80.
- Bartfeld, Judith, and Fei Men. "Food insecurity among households with children: the role of the state economic and policy context." *Social Service Review* 91.4 (2017): 691-732.
- Bauer, Christopher E., et al. "Breastfeeding Duration Is Associated with Regional, but Not Global, Differences in White Matter Tracts." *Brain Sciences* 10.1 (2020): 19.

- Beck, Kristen L., et al. "Comparative proteomics of human and macaque milk reveals species-specific nutrition during postnatal development." *Journal of Proteome Research* 14.5 (2015): 2143-2157.
- Begus, Katarina, and Elizabeth Bonawitz. "The rhythm of learning: theta oscillations as an index of active learning in infancy." *Developmental Cognitive Neuroscience* (2020): 100810.
- Bekdash, Rola A. "Neuroprotective effects of choline and other methyl donors." *Nutrients* 11.12 (2019): 2995.
- Belfield, Clive R., and Inas Rashad Kelly. "The benefits of breast feeding across the early years of childhood." *Journal of Human Capital* 6.3 (2012): 251-277.
- Bellando, J., McCorkle, G., Spray, B., Sims, C. R., Badger, T. M., Casey, P. H., ... & Andres, A. (2020). Developmental assessments during the first 5 years of life in infants fed breast milk, cow's milk formula, or soy formula. *Food Science & Nutrition*.
- Bell, M. A., & Fox, N. A. (1992). The relations between frontal brain electrical activity and cognitive development during infancy. *Child development*, 63(5), 1142-1163.
- Benton, David. "The influence of dietary status on the cognitive performance of children." *Molecular Nutrition & Food Research* 54.4 (2010): 457-470.
- Berg, J. M., J. L. Tymoczko, and L. Stryer. "Section 10.2: Hemoglobin Transports Oxygen Efficiently by Binding Oxygen Cooperatively." *Biochemistry* (2002).
- Berger, P. K., Plows, J. F., Jones, R. B., Alderete, T. L., Yonemitsu, C., Poulsen, M., ... & Goran, M. I. (2020). Human milk oligosaccharide 2'-fucosyllactose links feedings at 1 month to cognitive development at 24 months in infants of normal and overweight mothers. *PLoS one*, 15(2), e0228323.
- Bernal, Juan. "Thyroid hormones and brain development." *Vitamins & Hormones* 71 (2005): 95-122.
- Bernard, Jonathan Y., et al. "Breastfeeding duration and cognitive development at 2 and 3 years of age in the EDEN mother-child Cohort." *The Journal of Pediatrics* 163.1 (2013): 36-42.
- Bhatnagar, Shinjini, and Sunita Taneja. "Zinc and cognitive development." *British journal of nutrition* 85.S2 (2001): S139-S145.
- Bhinder, Ganive, et al. "Milk fat globule membrane supplementation in formula modulates the neonatal gut microbiome and normalizes intestinal development." *Scientific Reports* 7 (2017): 45274.
- Bickel, Gary, Mark Nord, Cristofer Price, William Hamilton, and John Cook: Guide to Measuring Household Food Security, Revised 2000. U.S. Department of Agriculture, Food and Nutrition Service, Alexandria VA. March, 2000.

- Black, Maureen M. "The evidence linking zinc deficiency with children's cognitive and motor functioning." *The Journal of Nutrition* 133.5 (2003): 1473S-1476S.
- Blumberg, S. J., Bialostosky, K., Hamilton, W. L., & Briefel, R. R. (1999). The effectiveness of a short form of the Household Food Security Scale. *American journal of public health*, 89(8), 1231-1234.
- Bode, Lars, and Evelyn Jantscher-Krenn. "Structure-function relationships of human milk oligosaccharides." *Advances in Nutrition* 3.3 (2012): 383S-391S.
- Boquien, Clair-Yves. "Human milk: An ideal food for nutrition of preterm newborn." *Frontiers in Pediatrics* 6 (2018): 295.
- Borra, Cristina, Maria Iacovou, and Almudena Sevilla. "New evidence on breastfeeding and postpartum depression: the importance of understanding women's intentions." *Maternal and Child Health Journal* 19.4 (2015): 897-907.
- Bourke, Claire D., James A. Berkley, and Andrew J. Prendergast. "Immune dysfunction as a cause and consequence of malnutrition." *Trends in Immunology* 37.6 (2016): 386-398.
- Bovell-Ammon, Allison, et al. "Trends in food insecurity and SNAP participation among immigrant families of US-born young children." *Children* 6.4 (2019): 55.
- Braarud, H. C., Markhus, M. W., Skotheim, S., Stormark, K. M., Frøyland, L., Graff, I. E., & Kjellevoid, M. (2018). Maternal DHA status during pregnancy has a positive impact on infant problem solving: A Norwegian prospective observation study. *Nutrients*, 10(5), 529.
- Brandstatter, E., & Kepler, J. (1999). Confidence intervals as an alternative to significance testing. *Methods of Psychological Research Online*, 4(2), 33-46.
- Brennan, Patricia A., et al. "Protocol for the Emory University African American maternal stress and infant gut microbiome cohort study." *BMC Pediatrics* 19.1 (2019): 246.
- Bresnahan, Mary, et al. "Made to feel like less of a woman: The experience of stigma for mothers who do not breastfeed." *Breastfeeding Medicine* 15.1 (2020): 35-40.
- Briggs, T. et al. "Breastfeeding or Formula Feeding: A Mother's Choice." (2020): 1.
- Brion, Luc P., et al. "Zinc deficiency limiting head growth to discharge in extremely low gestational age infants with insufficient linear growth: a cohort study." *Journal of Perinatology* (2020): 1-11.
- Brito, N.H., Troller-Renfree, S.V., Leon-Santos, A., Isler, J.R., Fifer, W.P., & Noble, K. (2020). Associations among the home language environment and neural activity during infancy. *Developmental Cognitive Neuroscience*, 43, 100780. <https://doi.org/10.1016/j.dcn.2020.100780>

- Britton, J.W., Frey, L.C. & Hoop, J.L. (2016). *Electroencephalography (EEG): An Introductory text and atlas of normal and abnormal findings in adults, children, and infants*. Chicago: American Epilepsy Society.
- Britton, John R., Helen L. Britton, and Virginia Gronwaldt. "Breastfeeding, sensitivity, and attachment." *Pediatrics* 118.5 (2006): e1436-e1443.
- Butt, N.F., Fox, M.K., Briefel, R.R., Dwyer, J.T., Deming, D.M et al. (2010). Nutrient intakes of US infants, toddlers, and preschoolers meet or exceed dietary reference intakes. *Journal of the Academy of Nutrition and Dietetics*, 110 (12), S27-S37.
- Buzzell, G. A., Barker, T. V., Troller-Renfree, S. V., Bernat, E. M., Bowers, M. E., Morales, S., ... & Fox, N. A. (2019). Adolescent cognitive control, theta oscillations, and social observation. *NeuroImage*, 198, 13-30.
- Can, Dilara Deniz, Todd Richards, and Patricia K. Kuhl. "Early gray-matter and white-matter concentration in infancy predict later language skills: a whole brain voxel-based morphometry study." *Brain and Language* 124.1 (2013): 34-44.
- Cantiani, Chiara, et al. "Oscillatory gamma activity mediates the pathway from socioeconomic status to language acquisition in infancy." *Infant Behavior and Development* 57 (2019): 101384.
- Caparros-Gonzalez, Rafael A., et al. "Maternal and Neonatal Hair Cortisol Levels and Psychological Stress Are Associated With Onset of Secretory Activation of Human Milk Production." *Advances in Neonatal Care* 19.6 (2019): E11-E20.
- Cardoso, C., Afonso, C., & Bandarra, N. M. Dietary DHA, bioaccessibility, and neurobehavioral development in children. *Critical Reviews in Food Science and Nutrition*, 58(15) (2018): 2617-2631.
- Carlson, Alexander L., et al. "Infant gut microbiome associated with cognitive development." *Biological Psychiatry* 83.2 (2018): 148-159.
- Casas, Maribel, et al. "Maternal pre-pregnancy obesity and neuropsychological development in pre-school children: a prospective cohort study." *Pediatric Research* 82.4 (2017): 596-606.
- Casella, Erasmo Barbante, et al. "Vitamin B12 deficiency in infancy as a cause of developmental regression." *Brain and Development* 27.8 (2005): 592-594.
- Castrogiovanni, Paola, and Rosa Imbesi. "The role of malnutrition during pregnancy and its effects on brain and skeletal muscle postnatal development." *Journal of Functional Morphology and Kinesiology* 2.3 (2017): 30.
- Caudill, Marie A., et al. "Maternal choline supplementation during the third trimester of pregnancy improves infant information processing speed: A randomized, double-blind, controlled feeding study." *The FASEB Journal* 32.4 (2018): 2172-2180.

- Centers for Disease Control and Prevention. Facts, Key Breastfeeding Indicators 2020, <https://www.cdc.gov/breastfeeding/data/facts.html>. Accessed 24 Oct 2020.
- Centers for Disease Control and Prevention. Breastfeeding Among U.S. Children Born 2010–2017, CDC National Immunization Survey, 29 Sept 2020, https://www.cdc.gov/breastfeeding/data/nis_data/results.html. Accessed 24 Oct 2020.
- Cerdó, Tomás, Estefanía Diéguez, and Cristina Campoy. "Infant growth, neurodevelopment and gut microbiota during infancy: which nutrients are crucial?" *Current Opinion in Clinical Nutrition & Metabolic Care* 22.6 (2019): 434-441.
- Chabrol, H., Walburg, V., Teissedre, F., Armitage, J., & Santrisse, K. (2004). Influence of mother's perceptions on the choice to breastfeed or bottle-feed: perceptions and feeding choice. *Journal of reproductive and infant psychology*, 22(3), 189-198.
- Chatterjee, N., & Saumitra, M. (Developmental outcomes in children with malnutrition. *Journal of Nepal Pediatric Society* (2016): 36(2), 170.
- Child Welfare Information Gateway. *Understanding the effects of maltreatment on brain development*. Washington, DC: U.S. Department of Health and Human Services, Children's Bureau. 2015
- Choi, Hye Jeong, Su Kyoung Kang, and Mi Ra Chung. "The relationship between exclusive breastfeeding and infant development: A 6-and 12-month follow-up study." *Early Human Development* 127 (2018): 42-47.
- Clarke, G., et al. "Priming for health: gut microbiota acquired in early life regulates physiology, brain and behaviour." *Acta Paediatrica* 103.8 (2014): 812-819.
- Claumarchirant, L., et al. "Addition of milk fat globule membrane as an ingredient of infant formulas for resembling the polar lipids of human milk." *International Dairy Journal* 61 (2016): 228-238.
- Cleveland, L. M. "Breastfeeding recommendations for women who receive medication-assisted treatment for opioid use disorders: AWHONN Practice Brief Number 4." *Nursing for Women's Health* 20.4 (2016): 432-434.
- Çoban, Sümeyra, Ebru Yılmaz Keskin, and Mahir İğde. "Association between maternal and infantile markers of cobalamin status during the first month post-delivery." *The Indian Journal of Pediatrics* 85.7 (2018): 517-522.
- Coleman-Jensen, Alisha, Matthew P. Rabbitt, Christian A. Gregory, and Anita Singh. 2020. Household Food Security in the United States in 2019, ERR-275, U.S. Department of Agriculture, Economic Research Service.
- Coleman-Jensen, Alisha, and Mark Nord. "Food insecurity among households with working-age adults with disabilities." *USDA-ERS Economic Research Report* 144 (2013).

- Coleman-Jensen, A. J. (2010). US food insecurity status: toward a refined definition. *Social Indicators Research*, 95(2), 215-230.
- Collier, D., Sekhon, J.S., & Stark, P. Statistical models and causal inference, a dialogue with the social sciences. Cambridge: Cambridge University Press. 2010.
- Corning, W. C., Steffy, R. A., & Chaprin, I. C. (1982). EEG slow frequency and WISC-R correlates. *Journal of abnormal child psychology*, 10(4), 511-530.
- Couperus J.W., & Nelson, C.A. (2006). Early brain development and plasticity. In: McCartney K, Phillips D, eds. *The Blackwell Handbook of Early Childhood Development*.
- Cowan, Caitlin SM, Timothy G. Dinan, and John F. Cryan. "Annual Research Review: Critical windows—the microbiota–gut–brain axis in neurocognitive development." *Journal of Child Psychology and Psychiatry* 61.3 (2020): 353-371.
- Cumming, G., & Fidler, F. Confidence intervals: Better answers to better questions. *Zeitschrift für Psychologie*, 217 2009: 15–26.
- Cushing, A. H., et al. "Breastfeeding reduces risk of respiratory illness in infants." *American Journal of Epidemiology* 147.9 (1998): 863-870.
- Cusick, S.E., & Georgieff, M.K. The role of nutrition in brain development: the golden opportunity of the "first 1000 days" *Journal of Pediatrics*, 175 (2016): 16–21.
- Da Costa, A.G., et al. "Prevalence and risk factors for iron deficiency anemia and iron depletion during pregnancy: A prospective study." *Acta Medica Portuguesa* 29.9 (2016): 514-518.
- Dadashi, M., Birashk, B., Taremian, F., Asgarnejad, A.A., & Montazi, S. Effects of increase in amplitude of occipital alpha & theta brain waves on global functioning level of patients with GAD. *Basic Clinical Neuroscience*, 6(1) (2015): 14–20.
- Daniali, Seyede Shahrbanoo, et al. "Association of cord blood zinc level and birth weight in a sample of Iranian neonates." *International Journal of Preventive Medicine* 11 (2020).
- Dauncy, M.J. New insights into nutrition and cognitive neuroscience: Symposium on Early nutrition and later disease: current concepts, research and implications. *Proceedings of the Nutrition Society*, 68(4) (2009): 408-415.
- Debnath, R., Salo, V. C., Buzzell, G. A., Yoo, K. H., & Fox, N. A. (2019). Mu rhythm desynchronization is specific to action execution and observation: Evidence from time-frequency and connectivity analysis. *Neuroimage*, 184, 496-507.
- Debnath, R., Buzzell, G. A., Morales, S., Bowers, M. E., Leach, S. C., & Fox, N. A. (2020). The Maryland analysis of developmental EEG (MADE) pipeline. *Psychophysiology*, 57(6), e13580.

- DeBoer, T., Scott, L. S., & Nelson, C. A. (2007). Methods for acquiring and analyzing infant event-related potentials. *Infant EEG and event-related potentials*, 500, 5-37.
- De Capo, Madison, et al. "Perinatal nutrition and programmed risk for neuropsychiatric disorders: a focus on animal models." *Biological Psychiatry* 85.2 (2019): 122-134.
- De la Garza Puentes, Andrea, et al. "The Effect of Maternal Obesity on Breast Milk Fatty Acids and Its Association with Infant Growth and Cognition—The PREOBE Follow-Up." *Nutrients* 11.9 (2019): 2154.
- Demir, Ö. E., Prado, J., & Booth, J. R. (2015). Parental socioeconomic status and the neural basis of arithmetic: differential relations to verbal and visuo-spatial representations. *Developmental Science*. doi:10.1111/desc.12268
- De Oliveira, K. H. D., de Almeida, G. M., Gubert, M. B., Moura, A. S., Spaniol, A. M., Hernandez, D. C., & Buccini, G. Household food insecurity and early childhood development: Systematic review and meta-analysis. *Maternal & Child Nutrition* 2020: e12967.
- De Palma, Giada, et al. "Influence of milk-feeding type and genetic risk of developing coeliac disease on intestinal microbiota of infants: the PROFICEL study." *PloS one* 7.2 (2012): e30791.
- De Souza, Amanda Santos, Flávia Spreafico Fernandes, and Maria das Graças Tavares do Carmo. "Effects of maternal malnutrition and postnatal nutritional rehabilitation on brain fatty acids, learning, and memory." *Nutrition Reviews* 69.3 (2011): 132-144.
- Dean, D.C., et al. "Characterizing longitudinal white matter development during early childhood." *Brain Structure and Function* 220.4 (2015): 1921-1933.
- Dellschaft, N. S., et al. "The dietary form of choline during lactation affects maternal immune function in rats." *European Journal of Nutrition* 57.6 (2018): 2189-2199.
- Delorme, A., & Makeig, S. (2004). EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of neuroscience methods*, 134(1), 9-21.
- Demontigny, F., et al. "The role of fathers during breastfeeding." *Midwifery* 58 (2018): 6-12.
- Deoni, S., Dean, D., Joelson, S., O'Regan, J., & Schneider, N. Early nutrition influences developmental myelination and cognition in infants and young children. *Neuroimage*, 178 (2018): 649-659.
- Deoni, S et al. "Investigating white matter development in infancy and early childhood using myelin water fraction and relaxation time mapping." *NeuroImage* 63.3 (2012): 1038-53.
- Deoni, S., et al. "Early nutrition influences developmental myelination and cognition in infants and young children." *Neuroimage* 178 (2018): 649-659.

- Desky, Fitria, Hermanto Tri Joewono, and Widjiati Widjiati. "FR 50% in pregnancy results in different neuron and glial cell count (astrocytes, oligodendrocytes, and microglia) in the cerebrum and cerebellum of newborn *Rattus norvegicus*." *Majalah Obstetri & Ginekologi* 27.2 (2019): 56-65.
- Destailats, F., Oliveira, M., Bastic Schmid, V., Masserey-Elmelegy, I., Giuffrida, F., Thakkar, S. K., ... & Cruz-Hernandez, C. (2018). Comparison of the incorporation of DHA in circulatory and neural tissue when provided as triacylglycerol (TAG), monoacylglycerol (MAG) or phospholipids (PL) provides new insight into fatty acid bioavailability. *Nutrients*, 10(5), 620.
- Dhobale, M. "Neurotrophic factors and maternal nutrition during pregnancy." *Vitamins and Hormones*. 104. Academic Press, 2017. 343-366.
- Donath, S, & Amir, L.H. "Relationship between prenatal infant feeding intention and initiation and duration of breastfeeding: a cohort study," *Acta Paediatr.* 92.3 (2013): 352-356.
- Dong, Y., et al. "Preventing mother to child transmission of HIV: lessons learned from China." *BMC Infectious Diseases* 20.1 (2020): 1-10.
- Donovan, S.M., and Comstock, S.S. "Human milk oligosaccharides influence neonatal mucosal and systemic immunity." *Annals of Nutrition and Metabolism* 69.Suppl. 2 (2016): 41-51.
- Dowd, M.D. (2017). Early adversity, toxic stress, and resilience: pediatrics for today. *Pediatrics Annals*, 1(46) (2017): e246-e249.
- Dror, D. K., and Allen, L.H. "Effect of vitamin B12 deficiency on neurodevelopment in infants: current knowledge and possible mechanisms." *Nutrition Reviews* 66.5 (2008): 250-255.
- Edlow, A.G. "Maternal obesity and neurodevelopmental and psychiatric disorders in offspring." *Prenatal Diagnosis* 37.1 (2017): 95-110.
- El Din, Ebtissam M. Salah, et al. "Potential Risk Factors of Developmental Cognitive Delay in the First Two Years of Life." *Open Access Macedonian Journal of Medical Sciences* 7.12 (2019): 2024-2030.
- Ellingsen, K.M. "Standardized assessment of cognitive development: Instruments and issues." *Early Childhood Assessment in School and Clinical Child Psychology*. Springer, New York, NY, 2016. 25-49.
- Ellis, B. J., Abrams, L. S., Masten, A. S., Sternberg, R. J., Tottenham, N., & Frankenhuis, W. E. (2020). Hidden talents in harsh environments. *Dev Psychopathol*, 1, 1-19. doi:10.1017/S0954579420000887
- Ellwood-Lowe, M. E., Whitfield-Gabrieli, S., & Bunge, S. A. (2020). What is an adaptive pattern of brain network coupling for a child? It depends on their environment. *bioRxiv*.

- Etowa, Josephine, et al. "Social Determinants of Breastfeeding Preferences among Black Mothers Living with HIV in Two North American Cities." *International Journal of Environmental Research and Public Health* 17.18 (2020): 6893.
- Ettinger de Cuba, S., Chilton, M., Bovell-Ammon, A., Knowles, M., Coleman, S. M., Black, M. M., ... & Frank, D. A. (2019). Loss of SNAP is associated with food insecurity and poor health in working families with young children. *Health Affairs*, 38(5), 765-773.
- Farashahi, S., et al. "Metaplasticity as a neural substrate for adaptive learning and choice under uncertainty." *Neuron* 94.2 (2017): 401-414.
- Faul, F., Erdfelder, E., Buchner, A., & Lang, A.-G. Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. *Behavior Research Methods*, 41 (2009) 1149-1160.
- Fauzi, A., Widjiati, W., & Joewono, H. T. (2018). Fifty percent of food restriction during gestation reduced the dendritic density of cerebrum and cerebellum of *Rattus norvegicus* newborn. *Majalah Obstetri & Ginekologi*, 26(3), 112-117.
- Félix, L.M., et al. "Ketamine induction of p53-dependent apoptosis and oxidative stress in zebrafish (*Danio rerio*) embryos." *Chemosphere* 201 (2018): 730-739.
- Ferguson, C.F. (An effect size primer: a guide for clinicians and researchers. *Professional Psychology: Research and Practice*, 40 (2009): 532-538.
- Ferguson, M., & Molfese, P. J. Breast-fed infants process speech differently from bottle-fed infants: evidence from neuro-electrophysiology. *Developmental Neuropsychology*, 31(3), (2007): 337-347.
- Fernandez, A., Meechan, D. W., Karpinski, B. A., Paronett, E. M., Bryan, C. A., Rutz, H. L., ... & Rothblat, L. A. Mitochondrial dysfunction leads to cortical under-connectivity and cognitive impairment. *Neuron*, 102(6), (2019): 1127-1142.
- Fields, D.A., et al. "Associations between human breast milk hormones and adipocytokines and infant growth and body composition in the first 6 months of life." *Pediatric Obesity* 12 (2017): 78-85.
- Flensburg-Madsen, Trine, Marie Grønkjær, and Erik Lykke Mortensen. "Predictors of early life milestones: Results from the Copenhagen Perinatal Cohort." *BMC pediatrics* 19.1 (2019): 420.
- Food and Agriculture Organization. The state of food insecurity in the world. Rome: Food and Agriculture Organization of the United Nations. 2013.
- Fox, S.E., Levitt, P., & Nelson, C.A. Review: How the timing and quality of early experiences influence the development of brain architecture. *Child Development*, 81(1), (2010): 28-40.

- Fram, M.S. et al. "Child experience of food insecurity is associated with child diet and physical activity." *The Journal of Nutrition* 145.3 (2015): 499-504.
- Franke, H.A. Toxic stress: Effects, prevention and treatment. *Children*, 1(3), (2014): 390-402.
- Fumagalli, M., et al. "From early stress to 12-month development in very preterm infants: Preliminary findings on epigenetic mechanisms and brain growth." *PloS one* 13.1 (2018): e0190602.
- Garcia, M., Mamedova, L. K., Barton, B., & Bradford, B. J. Choline regulates the function of bovine immune cells and alters the mRNA abundance of enzymes and receptors involved in its metabolism in vitro. *Frontiers in Immunology* 9 (2018): 2448.
- Garwolińska, D., et al. "Chemistry of human breast milk—A comprehensive review of the composition and role of milk metabolites in child development." *Journal of Agricultural and Food Chemistry* 66.45 (2018): 11881-11896.
- Genc, S, et al. "Neurite density index is sensitive to age related differences in the developing brain." *Neuroimage* 148 (2017): 373-380.
- Georgieff M.K., Brunette, K.E., & Tran, P.V. Early life nutrition and neural plasticity. *Development and Psychopathology*. 27, (2015): 411–423.
- Georgieff, M.K., Ramel, S.E., & Cusick, S.E. (2018). Nutritional influences on brain development. *Acta Paediatrica*, 107(8), <https://doi.org/10.1111/apa.14287>
- Georgieff, M.K. "Iron assessment to protect the developing brain." *The American Journal of Clinical Nutrition* 106.suppl_6 (2017): 1588S-1593S.
- Ghiani, C.A., et al. "Early effects of lipopolysaccharide-induced inflammation on foetal brain development in rat." *ASN Neuro* 3.4 (2011): AN20110027.
- Goehring, K. C., et al. "Similar to those who are breastfed, infants fed a formula containing 2'-fucosyllactose have lower inflammatory cytokines in a randomized controlled trial." *The Journal of Nutrition* 146.12 (2016): 2559-2566.
- González, M.D.R., et al. "Prevalence of breastfeeding and factors associated with the start and duration of exclusive breastfeeding in the Community of Madrid among participants in the ELOIN." *Anales de Pediatría (English Edition)* 89.1 (2018): 32-43.
- Gray, K. D., et al. "Influence of Early Lactation Assistance on Inpatient Exclusive Breastfeeding Rates." *Journal of Human Lactation* (2020): 0890334420957967.
- Groer, M.WW., et al. "Development of the preterm infant gut microbiome: a research priority." *Microbiome* 2.1 (2014): 38.
- Guaraldi, F., and Guglielmo S. "Effect of breast and formula feeding on gut microbiota shaping in newborns." *Frontiers in Cellular and Infection Microbiology* 2 (2012): 94.

- Guerrini, R., and Parrini, E. "Neuronal migration disorders." *Neurobiology of Disease* 38.2 (2010): 154-166.
- Gulliford, M.C., Mahabir, D., & Rocke, D. "Reliability and validity of a short form household food security scale in a Caribbean community". *BMC Public Health* 4 (2004): 22, <https://doi.org/10.1186/1471-2458-4-22>
- Gundersen, C., and Ziliak, J.P. "Food insecurity research in the United States: Where we have been and where we need to go." *Applied Economic Perspectives and Policy* 40.1 (2018): 119-135.
- Gupta, D. S., et al. "Temporal Structure of Neural Processes Coupling Sensory, Motor and Cognitive Functions of the Brain." *Frontiers in Computational Neuroscience* 14 (2020).
- Gurnida, D. A., Rowan, A. M., Idjradinata, P., Muchtadi, D., & Sekarwana, N. (2012). Association of complex lipids containing gangliosides with cognitive development of 6-month-old infants. *Early human development*, 88(8), 595-601.
- Guyatt, G.H., Oxman, A.D., Kunz, R., Vist., G.E., Falck-Ytter, Y., & Schunemann, H.J. (2008). What is "quality of evidence" and why is it important to clinicians? *British Medical Journal (Clinical Research Edition)*, 336 (7651), 995-998.
- Haenlein, M., & Kaplan, A. A beginner's guide to partial least squares analysis. *Understanding Statistics*, 3, (2004): 283-297
- Hair, J., Anderson, R. E., Babin, B. J., Tatman, R. L., & Black, W. C. *Multivariate data analysis*. Upper Saddle River, NJ: Prentice Hall. 2010.
- Hair, J. F., Hult, G. T. M., Ringle, C. M., & Sarstedt, M. A primer on partial least squares structural equation modeling (PLS-SEM) (2nd ed.). Thousand Oaks, CA: Sage. 2017.
- Hansen-Pupp, I., et al. "Postnatal decrease in circulating insulin-like growth factor-I and low brain volumes in very preterm infants." *The Journal of Clinical Endocrinology & Metabolism* 96.4 (2011): 1129-1135.
- Hanson, K.L., & Connor, L.M. "Food insecurity and dietary quality in US adults and children: a systematic review." *The American Journal of Clinical Nutrition* 100.2 (2014): 684-692.
- Harmony, T., Hinojosa, G., Marosi, E., Becker, J., Rodriguez, M., Reyes, A., & Rocha, C. (1990). Correlation between EEG spectral parameters and an educational evaluation. *International Journal of Neuroscience*, 54(1-2), 147-155.
- Haskins, J. "Healthy People 2030 to Create Objectives for the Health of the Nation." *American Journal of Public Health* 107.10 (2017): 1528.
- Hassan, R., MacMillan, H. L., Saigal, S., & Schmidt, L. A. Brain, interrupted: alpha/delta EEG ratio in survivors of pre-and post-natal adversity. *International Journal of Neuroscience*, 1-7.2020. <https://doi.org/10.1080/00207454.2020.1797724>

- Hayes, A. F. Introduction to mediation, moderation, and conditional process analysis. A regression-based approach. New York, NY: Guildford Press. 2013.
- Hernell, O., et al. "Clinical benefits of milk fat globule membranes for infants and children." *The Journal of Pediatrics* 173 (2016): S60-S65.
- Hobbs, S., & King, C. The unequal impact of food insecurity on cognitive and behavioral outcomes among 5-year-old urban children. *Journal of Nutrition Education and Behavior*, 50, (2018): 687–694.
- Hodyl, N A., et al. "Child neurodevelopmental outcomes following preterm and term birth: What can the placenta tell us?" *Placenta* 57 (2017): 79-86.
- Holland, D., et al. "Structural growth trajectories and rates of change in the first 3 months of infant brain development." *JAMA Neurology* 71.10 (2014): 1266-1274.
- Horta, B.L., de Mola, C.L., & Victora, C.G. "Breastfeeding and intelligence: a systematic review and meta-analysis." *Acta Paediatrica* 104 (2015): 14-19.
- Houweling, T., Becker, R. & Hervais-Adelman, A. "The noise-resilient brain: Resting-state oscillatory activity predicts words-in-noise recognition." *Brain and Language* 202 (2020): 104727.
- Hovey, D., et al. "The effect of intranasal oxytocin on visual processing and salience of human faces." *Translational Psychiatry* 10.1 (2020): 1-9.
- Hu, Xiaona, et al. "Perinatal iron deficiency-induced hypothyroxinemia impairs early brain development regardless of normal iron levels in the neonatal brain." *Thyroid* 26.7 (2016): 891-900.
- Huang, J., Peters, K. E., Vaughn, M. G., & Witko, C. Breastfeeding and trajectories of children's cognitive development. *Developmental Science*, 17(3), (2014): 452-461.
- Huang, L, et al. "Maternal prepregnancy obesity and child neurodevelopment in the Collaborative Perinatal Project." *International journal of epidemiology* 43.3 (2014): 783-792.
- Huang, Y,, et al. "Low-mineral direct drinking water in school may retard height growth and increase dental caries in schoolchildren in China." *Environment International* 115 (2018): 104-109.
- Hunegnaw, Melkamu Tamir, Kassahun Alemu Gelaye, and Bekri Mohammed Ali. "Factors associated with the time to cessation of breastfeeding among mothers who have index children aged two to three years in Debre Markos, northwest Ethiopia: a retrospective follow-up study." *BMC Pediatrics* 18.1 (2018): 77.
- Hung, M., Bounsanga, J., & Voss, M.W. Interpretation of correlations in clinical research. *Postgraduate Medicine*, 129(8), (2017): 902–906.

- Hurlbert, S.H., & Lombardi, C.M. Final collapse of the Neyman-Pearson decision theoretic framework and rise of the neoFisherian. *Annales Zoologici Fennici*, 46, 3(2009): 11-349.
- Hwang, Hye Mee, Ray Yueh Ku, and Kazue Hashimoto-Torii. "Prenatal environment that affects neuronal migration." *Frontiers in Cell and Developmental Biology* 7 (2019): 138.
- Ichim, Gabriel, Servane Tauszig-Delamasure, and Patrick Mehlen. "Neurotrophins and cell death." *Experimental Cell Research* 318.11 (2012): 1221-1228.
- Idler, E. L., & Benyamini, Y. Self-rated health and mortality: a review of twenty-seven community studies. *Journal of Health and Social behavior*, (1997): 21-37.
- Inguaggiato, E., G. Sgandurra, and G. Cioni. "Brain plasticity and early development: implications for early intervention in neurodevelopmental disorders." *Neuropsychiatrie de l'Enfance et de l'Adolescence* 65.5 (2017): 299-306.
- Innis S.M. Dietary omega 3 fatty acids and the developing brain. *Brain Research*, 1237, (2008): 35-43.
- Innis, S. M. Impact of maternal diet on human milk composition and neurological development of infants. *The American Journal of Clinical Nutrition*, 99(3), (2014): 734S-741S.
- Institute of Medicine. Dietary Reference Intakes Research Synthesis: Workshop Summary. Washington, DC: The National Academies Press. 2007.
- Isaacs, E. B., Fischl, B. R., Quinn, B. T., Chong, W. K., Gadian, D. G., & Lucas, A. Impact of breast milk on intelligence quotient, brain size, and white matter development. *Pediatric Research*, 67(4), (2010): 357-362.
- Islam, Md Jahirul, et al. "Exploring the influence of psychosocial factors on exclusive breastfeeding in Bangladesh." *Archives of Women's Mental Health* 20.1 (2017): 173-188.
- Jansen, Jarno, Carolina de Weerth, and J. Marianne Riksen-Walraven. "Breastfeeding and the mother-infant relationship—a review." *Developmental Review* 28.4 (2008): 503-521.
- Jiang, N. M., Tofail, F., Moonah, S. N., Scharf, R. J., Taniuchi, M., Ma, J. Z., ... & Haque, R. Febrile illness and pro-inflammatory cytokines are associated with lower neurodevelopmental scores in Bangladeshi infants living in poverty. *BMC Pediatrics*, 14(1), (2014), 50.
- Jing, H., Gilchrist, J. M., Badger, T. M., & Pivik, R. T. A longitudinal study of differences in electroencephalographic activity among breastfed, milk formula-fed, and soy formula-fed infants during the first year of life. *Early Human Development*, 86(2), (2010): 119-125.
- Johnson, A. D., & Markowitz, A. J. Associations between household food insecurity in early childhood and children's kindergarten skills. *Child Development*, 89, (2018): e1-e17.
- Johnson, Anna D., and Anna J. Markowitz. "Food insecurity and family well-being outcomes among households with young children." *The Journal of Pediatrics* 196 (2018): 275-282.

- Johnson, M.H. Functional brain development in infants: elements of an interactive specialization framework *Child Development*, 71.1 (2003): <https://doi.org/10.1111/1467-8624.00120>
- Jones, Candace, et al. "Fetal programming and eating disorder risk." *Journal of Theoretical Biology* 428 (2017): 26-33.
- Jones, E. J. H., et al. "Infant EEG theta modulation predicts childhood intelligence." *Scientific reports* 10.1 (2020): 1-10.
- Jyoti, Diana F., Edward A. Frongillo, and Sonya J. Jones. "Food insecurity affects school children's academic performance, weight gain, and social skills." *The Journal of Nutrition* 135.12 (2005): 2831-2839.
- Kafouri, Salomi, et al. "Breastfeeding and brain structure in adolescence." *International Journal of Epidemiology* 42.1 (2013): 150-159.
- Kaul, P., et al. "Association between maternal diabetes, being large for gestational age and breast-feeding on being overweight or obese in childhood." *Diabetologia* 62.2 (2019): 249-258
- Kim, P., Feldman, R., Mayes, L. C., Eicher, V., Thompson, N., Leckman, J. F., & Swain, J. E. Breastfeeding, brain activation to own infant cry, and maternal sensitivity. *Journal of Child Psychology and Psychiatry*, 52(8), (2011): 907-915.
- Kim, Su Yeong, and Dae Yong Yi. "Components of human breast milk: from macronutrient to microbiome and microRNA." *Clinical and Experimental Pediatrics* 63.8 (2020): 301.
- Kim, Yong Joo. "Pivotal roles of prolactin and other hormones in lactogenesis and the nutritional composition of human milk." *Clinical and Experimental Pediatrics* 63.8 (2020): 312.
- King, J. C. "A summary of pathways or mechanisms linking preconception maternal nutrition with birth outcomes." *The Journal of Nutrition* 146.7 (2016): 1437S-1444S.
- Kinney, Hannah C., and Joseph J. Volpe. "Myelination events." *Volpe's Neurology of the Newborn*. Elsevier, 2018. 176-188.
- Klemm, Sarah. "Eating Right During Pregnancy." EatRight, Academy of Nutrition and Dietetics, 8 Jan. 2019, eatright.org/health/pregnancy/what-to-eat-when-expecting/eating-right-during-pregnancy
- Kling, J.R., Liebman, J.B., Katz, L.F. Experimental analysis of neighborhood effects. *Econometrica*, 75(1), (2007): 83-119.
- Knickmeyer, Rebecca C., et al. "A structural MRI study of human brain development from birth to 2 years." *Journal of Neuroscience* 28.47 (2008): 12176-12182.
- Kock, N. *Hypothesis testing with confidence intervals and P values*. Laredo, TX: ScriptWarp Systems. 2015.

- Kolb, B., & Gibb, R. (2011). Brain plasticity and behaviour in the developing brain. *Journal of the Canadian Academy of Child and Adolescent Psychiatry*, 20(4), 265.
- Koleilat, Maria, and Shannon E. Whaley. "Reliability and validity of food frequency questions to assess beverage and food group intakes among low-income 2-to 4-year-old children." *Journal of the Academy of Nutrition and Dietetics* 116.6 (2016): 931-939.
- Kominiarek, Michelle A., et al. "Stress during pregnancy and gestational weight gain." *Journal of Perinatology* 38.5 (2018): 462-467.
- Krebs, N.F., Lozoff, B and Georgieff, M.K. "Neurodevelopment: the impact of nutrition and inflammation during infancy in low-resource settings." *Pediatrics* 139.Supplement 1 (2017): S50-S58.
- Kroenke, K. & Spitzer, R.L. The PHQ-9: a new depression diagnostic and severity measure. *Psychiatric Annals*, 32(9) (2002): 509-515.
- Krogsrud, S. K., Fjell, A. M., Tamnes, C. K., Grydeland, H., Mork, L., Due-Tønnessen, P., ... & Walhovd, K. B. Changes in white matter microstructure in the developing brain—A longitudinal diffusion tensor imaging study of children from 4 to 11 years of age. *Neuroimage*, 124, (2016): 473-486.
- Krol, K. M., et al. "Duration of exclusive breastfeeding is associated with differences in infants' brain responses to emotional body expressions." *Frontiers in Behavioral Neuroscience* 8 (2015): 459.
- Kronenfeld, N., et al. "Chronic use of psychotropic medications in breastfeeding women: Is it safe?" *PloS one* 13.5 (2018): e0197196.
- Kvestad, I., et al. "Vitamin B-12 status in infancy is positively associated with development and cognitive functioning 5 y later in Nepalese children." *The American Journal of Clinical Nutrition* 105.5 (2017): 1122-1131.
- Lamb, C.A., Fabris, V.T. and Lanari. C. "Progesterone and breast." *Best Practice & Research Clinical Obstetrics & Gynaecology* (2020).
- Landry, M. J., van den Berg, A. E., Asigbee, F. M., Vandyousefi, S., Ghaddar, R., & Davis, J. N.. Child-report of food insecurity is associated with diet quality in children. *Nutrients*, 11(7), (2019): 1574.
- Laouar, A. "Maternal leukocytes and infant immune programming during breastfeeding." *Trends in Immunology* 41.3 (2020): 225-239.
- Laurberg, P., et al. "Dynamics and predictors of serum TSH and fT4 reference limits in early pregnancy: a study within the Danish National Birth Cohort." *The Journal of Clinical Endocrinology & Metabolism* 101.6 (2016): 2484-2492.
- Lauritzen, Lotte, et al. "DHA effects in brain development and function." *Nutrients* 8.1 (2016): 6.

- Le Doare, Kirsty, et al. "Mother's milk: a purposeful contribution to the development of the infant microbiota and immunity." *Frontiers in Immunology* 9 (2018): 361.
- Label, C., & Deon, S. "The development of brain white matter microstructure." *Neuroimage* 182 (2018): 207-218.
- Lee, Sooyeon, and Shannon L. Kelleher. "Biological underpinnings of breastfeeding challenges: the role of genetics, diet, and environment on lactation physiology." *American Journal of Physiology-Endocrinology and Metabolism* 311.2 (2016): E405-E422.
- Lehtonen, J., Valkonen-Korhonen, M., Georgiadis, S., Tarvainen, M.P., Lappi, H., et al. Nutritive sucking induces age-specific EEG-changes in 0–24 week-old infants. *Infant Behavior and Development*, 45, (2016): 98-108.
- Leitz, D. "Identifying the risk factors for food insecurity in the United States." *Major Themes in Economics* 20.1 (2018): 49-71.
- Lenehan, S. M., Boylan, G. B., Livingstone, V., Fogarty, L., Twomey, D. M., Nikolovski, J., ... & Murray, D. M. (2020). The impact of short-term predominate breastfeeding on cognitive outcome at 5 years. *Acta Paediatrica*, 109(5), 982-988.
- Leonard, J. A., Romeo, R. R., Park, A. T., Takada, M. E., Robinson, S. T., Grotzinger, H., . . . Mackey, A. P. (2019). Associations between cortical thickness and reasoning differ by socioeconomic status in development. *Developmental Cognitive Neuroscience*, 36, 100641.
- Leppink J, Winston K, & O'Sullivan P. (2016). Statistical significance does not imply a real effect. *Perspectives on Medical Education*, 5, 122–144.
- Lessa, Iara, and Rocha, Celia. "Regrounding in infertile soil: Food insecurity in the lives of new immigrant women." *Canadian Social Work Review/Revue Canadienne de Service Social* (2012): 187-203.
- Lester, Barry M., et al. "Epigenetic programming by maternal behavior in the human infant." *Pediatrics* 142.4 (2018).
- Lewis, E. D., Richard, C., Goruk, S., Wadge, E., Curtis, J. M., Jacobs, R. L., & Field, C. J. Feeding a mixture of choline forms during lactation improves offspring growth and maternal lymphocyte response to ex vivo immune challenges. *Nutrients*, 9(7), (2017): 713.
- Li, Huili, Jing Zhang, and Lee Niswander. "Zinc deficiency causes neural tube defects through attenuation of p53 ubiquitylation." *Development* 145.24 (2018).
- Lien, E. L., C. Richard, and D. R. Hoffman. "DHA and ARA addition to infant formula: Current status and future research directions." *Prostaglandins, Leukotrienes and Essential Fatty Acids* 128 (2018): 26-40.

- Lien, Yu-Chin, et al. "Dysregulation of neuronal genes by fetal-neonatal iron deficiency anemia is associated with altered DNA methylation in the rat hippocampus." *Nutrients* 11.5 (2019): 1191.
- Liu, J., Leung, P., & Yang, A. Breastfeeding and active bonding protects against children's internalizing behavior problems. *Nutrients*, 6(1), (2014): 76–89.
- Liu, Xiaohui, et al. "Folic acid supplementation, dietary folate intake and risk of preterm birth in China." *European Journal of Nutrition* 55.4 (2016): 1411-1422.
- Liu, Zheng, et al. "The effects of breastfeeding versus formula-feeding on cerebral cortex maturation in infant rhesus macaques." *Neuroimage* 184 (2019): 372-385.
- Lönnerdal, Bo. "Human milk: bioactive proteins/peptides and functional properties." *Protein in Neonatal and Infant Nutrition: Recent Updates*. Vol. 86. Karger Publishers, 2016. 97-107.
- Luby, Joan L., et al. "Breastfeeding and childhood IQ: The mediating role of gray matter volume." *Journal of the American Academy of Child & Adolescent Psychiatry* 55.5 (2016): 367-375.
- Mackes, N.K., Golm, D., Sarkar, S, Kumsta, R., Rutter M. et al..Breastfeeding and childhood IQ: The mediating role of grey matter volume. *Journal of the American Academy of Child & Adolescent Psychiatry*, 55(5), (2016): 367-375.
- Mackes, N.K., Golm, D., Sarkar, S., Kumsta, R., Rutter, M. et al. Early childhood deprivation is associated with alterations in adult brain structure despite subsequent environmental enrichment. *Proceedings of the National Academy of Sciences of the United States of America*, 117.1 (2020): 641-649.
- Maguire, M. J., & Schneider, J. M. (2019). Socioeconomic status related differences in resting state EEG activity correspond to differences in vocabulary and working memory in grade school. *Brain and cognition*, 137, 103619.
- Maharlouei, Najmeh, and Amirhosein Pourhaghighi. "Factors affecting exclusive breastfeeding, using adaptive LASSO regression." *International Journal of Community Based Nursing and Midwifery* 6.3 (2018): 260.
- Makropoulos, Antonios, et al. "Regional growth and atlasing of the developing human brain." *Neuroimage* 125 (2016): 456-478.
- Mann, C.J. Observational research methods: Research designs II: Cohort, cross sectional, and case-control studies. *Emergency Medical Journal*, 20(1), (2003):554-560.
- Marciniak, Aleksandra, et al. "Fetal programming of the metabolic syndrome." *Taiwanese Journal of Obstetrics and Gynecology* 56.2 (2017): 133-138.

- Marshall, P.J., Fox, N.A., & BEIP Core Group. "A comparison of the electroencephalogram between institutionalized and community children in Romania." *Journal of Cognitive Neuroscience* 16.8 (2004): 1327-1338.
- Martin, Camilia R., Pei-Ra Ling, and George L. Blackburn. "Review of infant feeding: key features of breast milk and infant formula." *Nutrients* 8.5 (2016): 279.
- Masum, A. K. M., et al. "Physicochemical properties of spray-dried model infant milk formula powders: Influence of whey protein-to-casein ratio." *International Dairy Journal* 100 (2020): 104565.
- Matsunaga, M., et al. "Breastfeeding dynamically changes endogenous oxytocin levels and emotion recognition in mothers." *Biology Letters* 16.6 (2020): 20200139.
- Mazzocchi, Alessandra, et al. "Hormones in breast milk and effect on infants' growth: a systematic review." *Nutrients* 11.8 (2019): 1845.
- McClain, Amanda C., Katherine L. Dickin, and Jamie Dollahite. "Life course influences on food provisioning among low-income, Mexican-born mothers with young children at risk of food insecurity." *Appetite* 132 (2019): 8-17.
- McKinney, C. O., et al. "Racial and ethnic differences in breastfeeding." *Pediatrics* 138.2 (2016): 1-12.
- McLaughlin, K. A., Fox, N. A., Zeanah, C. H., Sheridan, M. A., Marshall, P., & Nelson, C. A. (2010). Delayed maturation in brain electrical activity partially explains the association between early environmental deprivation and symptoms of attention-deficit/hyperactivity disorder. *Biological psychiatry*, 68(4), 329-336.
- McLeod LD, Cappelleri J & Hays R. Best (but oft-forgotten) practices: expressing and interpreting associations and effect sizes in clinical outcome assessments. *American Journal of Clinical Nutrition* 103 (2016): 685-693
- Melchior, Maria et al. "Mental health context of food insecurity: a representative cohort of families with young children." *Pediatrics* 124.4 (2009): e564-72.
- Menard, S. *Logistic regression: from introductory to advanced concepts and applications*. Thousand Oaks, CA: Sage Publications. 2010.
- Mestan, K., et al. "Cord blood biomarkers of the fetal inflammatory response." *The Journal of Maternal-Fetal & Neonatal Medicine* 22.5 (2009): 379-387.
- Michel, C., Stets, M., Parise, E., Reid, V., Striano, T., & Hoehl, S. Theta- and alpha-band EEG activity in response to eye gaze cues in early infancy. *Neuro Image*, 118, (2015): 576-583.
- Miller, Suzanne L., Petra S. Huppi, and Carina Mallard. "The consequences of fetal growth restriction on brain structure and neurodevelopmental outcome." *The Journal of Physiology* 594.4 (2016): 807-823.

- Mills, Kathryn L., et al. "Structural brain development between childhood and adulthood: Convergence across four longitudinal samples." *Neuroimage* 141 (2016): 273-281.
- Midi, H., Rana, L., & Imon, R. (2009). Robust Estimation of Regression Parameters with Heteroscedastic Errors in the Presence of Outliers. In *WSEAS International Conference. Proceedings. Mathematics and Computers in Science and Engineering* (No. 8). World Scientific and Engineering Academy and Society.
- Milner, E. M., Fiorella, K. J., Mattah, B. J., Bukusi, E., & Fernald, L. C. H. Timing, intensity, and duration of household food insecurity are associated with early childhood development in Kenya. *Maternal and Child Nutrition*, 14, (2018): e12543. <https://doi.org/10.1111/mcn.12543>
- Miranda, Rosiane A., Egberto Gaspar de Moura, and Patrícia Cristina Lisboa. "Tobacco smoking during breastfeeding increases the risk of developing metabolic syndrome in adulthood: lessons from experimental models." *Food and Chemical Toxicology* (2020): 111623.
- Miranda, A., & Sousa, N. (2018). Maternal hormonal milieu influence on fetal brain development. *Brain and behavior*, 8(2), e00920.
- Missana, Manuela, et al. "Discrimination of fearful and happy body postures in 8-month-old infants: an event-related potential study." *Frontiers in Human Neuroscience* 8 (2014): 531.
- Miyake, Yoshihiro, et al. "Maternal B vitamin intake during pregnancy and childhood behavioral problems in Japan: The Kyushu Okinawa maternal and child health study." *Nutritional Neuroscience* 23.9 (2020): 706-713.
- Monk, C., Georgieff M.K., & Osterholm, E.A. Research review: Maternal prenatal distress and poor nutrition-mutually influencing risk factors affecting infant neurocognitive development. *Journal of Child Psychology and Psychiatry*, 54, (2013): 115-130.
- Moore, Julia E., et al. "The effects of exposure to an enhanced preschool program on the social-emotional functioning of at-risk children." *Early Childhood Research Quarterly* 32 (2015): 127-138.
- Morgan, B. L. C, and Winick. M. "Institute of Human Nutrition Columbia University College of Physicians & Surgeons New York, New York." *Nutritional Pathology: Pathobiochemistry of Dietary Imbalances* (2020): 38.
- Morris S.S., Cogill B., & Uauy, R. Effective international action against undernutrition: why has it proven so difficult and what can be done to accelerate progress? *Lancet*, 371, (2008): 608–621.
- Morrison, J.L., and Regnault, T.R.H. "Nutrition in pregnancy: optimising maternal diet and fetal adaptations to altered nutrient supply." (2016): 342.

- Morrissey, T.W., et al. "Neighborhood poverty and children's food insecurity." *Children and Youth Services Review* 66 (2016): 85-93.
- Mosca, F., & Gianni, M. L. (2017). Human milk: composition and health benefits.
- Moukarzel, S, et al. "Milk fat globule membrane supplementation in formula-fed rat pups improves reflex development and may alter brain lipid composition." *Scientific reports* 8.1 (2018): 1-9.
- Mullen, E.M. *Mullen scales of early learning*. Circle Pines, MN: AGS, 1995.
- Munblit, D., et al. "Colostrum and mature human milk of women from London, Moscow, and Verona: determinants of immune composition." *Nutrients* 8.11 (2016): 695.
- Musser, E. D., Heidemarie Kaiser-Laurent, and Ablow, J.C. "The neural correlates of maternal sensitivity: an fMRI study." *Developmental Cognitive Neuroscience* 2.4 (2012): 428-436.
- Musumeci, Giuseppe, et al. "Fetal Programming: Maternal Diets, Tryptophan, and Postnatal Development." *Diet, Nutrition, and Fetal Programming*. Humana Press, Cham, 2017. 325-337.
- Napso, Tina, et al. "The role of placental hormones in mediating maternal adaptations to support pregnancy and lactation." *Frontiers in Physiology* 9 (2018): 1091.
- Nassar, May F., et al. "Language skills and intelligence quotient of protein energy malnutrition survivors." *Journal of Tropical Pediatrics* 58.3 (2012): 226-230.
- National Library of Medicine (U.S.). (2018, May-2022, July). *Household income and child development in the first three years of life*. Identifier NCT03593356. <https://clinicaltrials.gov/ct2/show/NCT03593356>
- Nelson III, Charles A., and Laurel J. Gabard-Durnam. "Early Adversity and Critical Periods: Neurodevelopmental Consequences of Violating the Expectable Environment." *Trends in Neurosciences* 43.3 (2020): 133-143.
- Newton, Edward R. "Lactation and breastfeeding." *Gabbe's Obstetrics Essentials: Normal & Problem Pregnancies E-Book* (2018): 171-176.
- Nguyen, P.H., et al. "Preconception micronutrient supplementation with iron and folic acid compared with folic acid alone affects linear growth and fine motor development at 2 years of age: a randomized controlled trial in Vietnam." *The Journal of Nutrition* 147.8 (2017): 1593-1601.
- Noble, E.E., and Scott E. K. "Early life exposure to obesogenic diets and learning and memory dysfunction." *Current Opinion in Behavioral Sciences* 9 (2016): 7-14.
- Noble, K. G., & Giebler, M. A. (2020). The neuroscience of socioeconomic inequality. *Current opinion in behavioral sciences*, 36, 23-28.

- Nord, M., Coleman-Jensen A., Andrews M., & Carlson S. Household food security in the United States, 2009. *Advances in Nutrition*, 2(2), (2009): 153-154.
- Nyardi, A., Li, J., Hickling, S., Foster, J., & Oddy, W.H. The role of nutrition in children's neurocognitive development, from pregnancy through childhood. *Frontiers of Human Neuroscience*, 7, 97. (2013): doi: 10.3389/fnhum.2013.00097
- Offenbacher, S., et al. "Effects of maternal *Campylobacter rectus* infection on murine placenta, fetal and neonatal survival, and brain development." *Journal of Periodontology* 76 (2005): 2133-2143.
- Ogbo, Felix A et al. "Prevalence and determinants of cessation of exclusive breastfeeding in the early postnatal period in Sydney, Australia." *International Breastfeeding Journal* 12.16 (2017).
- O'Muircheartaigh, J., et al. "White matter development and early cognition in babies and toddlers." *Human brain mapping* 35.9 (2014): 4475-4487.
- Ong, M.H.A., & Puteh, F. Quantitative data analysis: choosing between SPSS, PLS and AMOS in social science research. *International Interdisciplinary Journal of Scientific Research*, 3(1), (2017): 14-25.
- Orehova, E., Stroganova, T., Posikera, I.N., & Elam, M. EEG theta rhythm in infants and preschool children. *Clinical Neurophysiology* 117(5), (2006): 1047-62
- Ortiz-Mantilla, Silvia, et al. "Oscillatory dynamics underlying perceptual narrowing of native phoneme mapping from 6 to 12 months of age." *Journal of Neuroscience* 36.48 (2016): 12095-12105.
- Osborne, J W. & Overbay, A. The power of outliers (and why researchers should always check for them). *Practical Assessment, Research & Evaluation*, 9(6), (2004): doi <https://doi.org/10.7275/qf69-7k43>
- Osborne, J.W, & Waters, E. Four assumptions of multiple regression that researchers should always test. *Practical Assessment, Research & Evaluation* 8 (2002): 1-7.
- O'Sullivan, E. J., & Rasmussen, K. M. (2017). Development, construct validity, and reliability of the questionnaire on infant feeding: A tool for measuring contemporary infant-feeding behaviors. *Journal of the Academy of Nutrition and Dietetics*, 117(12), 1983-1990.
- Ou, Jinghua, and Sam-Po Law. "Induced gamma oscillations index individual differences in speech sound perception and production." *Neuropsychologia* 121 (2018): 28-36.
- Ou, X., et al. "Voxel-based morphometry and fMRI revealed differences in brain gray matter in breastfed and milk formula-fed children." *American Journal of Neuroradiology* 37.4 (2016): 713-719.

- Palar, K., et al. "Food insecurity is associated with HIV, sexually transmitted infections and drug use among men in the United States." *AIDS (London, England)* 30.9 (2016): 1457.
- Palmeira, Patricia, and Magda Carneiro-Sampaio. "Immunology of breast milk." *Revista da Associação Médica Brasileira* 62.6 (2016): 584-593.
- Pang, Wei Wei, et al. "Nutrients or nursing? Understanding how breast milk feeding affects child cognition." *European journal of nutrition* 59.2 (2020): 609-619.
- Parsons, Emilee, Katerina Claud, and Elaine O. Petrof. "The infant microbiome and implications for central nervous system development." *Progress in Molecular Biology and Translational Science* 171 (2020): 1-13.
- Pavarini, Gabriela, et al. "The role of oxytocin in the facial mimicry of affiliative vs. non-affiliative emotions." *Psychoneuroendocrinology* 109 (2019): 104377.
- Pavlakakis, A. E., et al. "Brain imaging and electrophysiology biomarkers: is there a role in poverty and education outcome research?" *Pediatric Neurology* 52.4 (2015): 383-388.
- Pearl, J. Causal inference in statistics: an overview. *Statistics Surveys*, 4 (2009): 96-146.
- Pearson, R. M., S. L. Lightman, and J. Evans. "The impact of breastfeeding on mothers' attentional sensitivity towards infant distress." *Infant Behavior and Development* 34.1 (2011): 200-205.
- Perone, S., Palanisamy, J., & Carlson, S. M. Age-related change in brain rhythms from early to middle childhood: Links to executive function. *Developmental Science* (2018): e12691. doi: 10.1111/desc.12691.
- Perrine, C. G., Galuska, D. A., Thompson, F. E., & Scanlon, K. S. Breastfeeding duration is associated with child diet at 6 years. *Pediatrics*, 134(Supplement 1), (2014): S50-S55.
- Pierre, W.C., et al. "Neonatal microglia: the cornerstone of brain fate." *Brain, Behavior, and Immunity* 59 (2017): 333-345.
- Pineda, R., Raney, M., and Smith, J. "Supporting and enhancing NICU sensory experiences (SENSE): Defining developmentally-appropriate sensory exposures for high-risk infants." *Early Human Development* 133 (2019): 29-35.
- Pivik, R. T., Andres, A., and Badger, T.M. "Diet and gender influences on processing and discrimination of speech sounds in 3-and 6-month-old infants: a developmental ERP study." *Developmental Science* 14.4 (2011): 700-712.
- Prado, E.L., & Dewey, K.G. Nutrition and brain development in early life. *Nutrition Reviews* 72(4) (2014): 267-284.

- Prince, Calais S., Alina Maloyan, and Leslie Myatt. "Maternal obesity alters brain derived neurotrophic factor (BDNF) signaling in the placenta in a sexually dimorphic manner." *Placenta* 49 (2017): 55-63.
- Pundir, Shikha, et al. "Maternal influences on the glucocorticoid concentrations of human milk: The STEPS study." *Clinical Nutrition* 38.4 (2019): 1913-1920.
- Pundir, Shikha, et al. "Variation of human milk glucocorticoids over 24-hour period." *Journal of Mammary Gland Biology and Neoplasia* 22.1 (2017): 85-92.
- Qiu, Anqi, Susumu Mori, and Michael I. Miller. "Diffusion tensor imaging for understanding brain development in early life." *Annual Review of Psychology* 66 (2015): 853-876.
- QS Medeiros, Pedro Henrique, et al. "A murine model of diarrhea, growth impairment and metabolic disturbances with *Shigella flexneri* infection and the role of zinc deficiency." *Gut Microbes* 10.5 (2019): 615-630.
- Quigley, M. A., Hockley, C., Carson, C., Kelly, Y., Renfrew, M. J., & Sacker, A. Breastfeeding is associated with improved child cognitive development: a population-based cohort study. *The Journal of Pediatrics* 160(1) (2012): 25-32.
- Ranganathan, P., Pramesh. C.S., & Buysee, M. Common pitfalls in statistical analysis: Clinical versus statistical significance. *Perspectives in Clinical Research* 6, (2015): 169-170.
- Raine, A., Venables, P.H., Dalais, C., Mellingen, K., Reynolds, C., & Mednick, S.A. (2001). Early educational and health enrichment at age 3–5 years is associated with increased autonomic and central nervous system arousal and orienting at age 11 years: Evidence from the Mauritius Child Health Project. *Psychophysiology*, 38, 254–266.
- Ratcliffe, Caroline, Signe-Mary McKernan, and Sisi Zhang. "How much does the Supplemental Nutrition Assistance Program reduce food insecurity?" *American Journal of Agricultural Economics* 93.4 (2011): 1082-1098.
- Rawlings, J.O., Pantula, S.G., & Dickey, D.A. *Applied regression analysis: a research tool*. New York, NY: Springer. 2013.
- Reichelt, A.C. Adolescent maturational transitions in the prefrontal cortex and dopamine signaling as a risk factor for the development of obesity and high fat/high sugar diet induced cognitive deficits. *Frontiers in Behavioral Neuroscience* 10, (2016): 189.
- Rescorla, Leslie, Josephine Nyame, and Pedro Dias. "Vocabulary development in European Portuguese: A replication study using the Language Development Survey." *Journal of Speech, Language, and Hearing Research* 59.6 (2016): 1484-1490.
- Richard, C., Lewis, E. D., Goruk, S., Wadge, E., Curtis, J. M., Jacobs, R. L., & Field, C. J. Feeding a mixture of choline forms to lactating dams improves the development of the immune system in sprague-dawley rat offspring. *Nutrients*, 9(6), (2017): 567.

- Rudolph, Johanna M., and Laurence B. Leonard. "Early language milestones and specific language impairment." *Journal of Early Intervention* 38.1 (2016): 41-58.
- Saad, Antonio F., et al. "High-fructose diet in pregnancy leads to fetal programming of hypertension, insulin resistance, and obesity in adult offspring." *American Journal of Obstetrics and Gynecology* 215.3 (2016): 378-e1.
- Sabri, Nur 'Amirah 'Inani, et al. "Factors associated with cognitive and motor delays in Malaysian infants aged 6–12 months." *Early Child Development and Care* (2020): 1-14.
- Saby, J.N., & Marshall, P.J. The utility of EEG band power analysis in the study of infancy and early childhood. *Developments in Neuropsychology*, 37(3), (2012): 253-73.
- Saha, K. K., Tofail, F., Frongillo, E. A., Rasmussen, K. M., Arifeen, S. E., Persson, L. Å., & Hamadani, J. D. Household food security is associated with early childhood language development: Results from a longitudinal study in rural Bangladesh. *Child: Care, Health and Development*, 36, (2010): 309–316
- Salone, Lindsey Rennick, William F. Vann Jr, and Deborah L. Dee. "Breastfeeding: an overview of oral and general health benefits." *The Journal of the American Dental Association* 144.2 (2013): 143-151.
- Sanders, T. R., Kim, D. W., Glendining, K. A., & Jasoni, C. L. (2014). Maternal obesity and IL-6 lead to aberrant developmental gene expression and deregulated neurite growth in the fetal arcuate nucleus. *Endocrinology*, 155(7), 2566-2577.
- Savanur, M. and Ghure, P.D. "Early nutrition and cognitive functions." *International Journal of Food Science and Nutrition*, 4.1 (2019): 102-108.
- Schipper, Lidewij, Gertjan van Dijk, and Eline M. van der Beek. "Milk lipid composition and structure; the relevance for infant brain development." *OCL* 27 (2020): 5.
- Schmatz, M., et al. "Maternal obesity: the interplay between inflammation, mother and fetus." *Journal of Perinatology* 30.7 (2010): 441-446.
- Shin, C. et al. "Comparison of the usefulness of the PHQ-8 and PHQ-9 for screening for major depressive disorder: Analysis of psychiatric outpatient data". *Psychiatry Investigation* 2019 16(4): 300–305.
- Published online 2019 Apr 24. doi: 10.30773/pi.2019.02.01
- Schoon, Ingrid, et al. "Family hardship, family instability, and cognitive development." *J Epidemiol Community Health* 66.8 (2012): 716-722.
- Schwarzenberg, S.J., Georgieff, M.K., and Committee on Nutrition. Advocacy for improving nutrition in the first 1000 days to support childhood development and adult health. *Pediatrics*, 141 (2) (2018): e20173716. doi: <https://doi.org/10.1542/peds.2017-3716>

- Shackman, J. E., Shackman, A. J., & Pollak, S. D. (2007). Physical abuse amplifies attention to threat and increases anxiety in children. *Emotion*, 7(4), 838.
- Shankar, Priya, Rainjade Chung, and Deborah A. Frank. "Association of food insecurity with children's behavioral, emotional, and academic outcomes: a systematic review." *Journal of Developmental & Behavioral Pediatrics* 38.2 (2017): 135-150.
- Sharps, Megan C., et al. "Increased placental macrophages and a pro-inflammatory profile in placentas and maternal serum in infants with a decreased growth rate in the third trimester of pregnancy." *American Journal of Reproductive Immunology* 84.3 (2020): e13267.
- Smith, Phillip, et al. "Age-Period-Cohort Analyses of Public Health Data Collected from Independent Serial Cross-Sectional Complex Probability Sample Surveys." *Centers for Disease Control and Prevention* (2006): 3735-3739.
- Soldateli, B., Vigo, A., & Giugliani, E. R. J. Effect of pattern and duration of breastfeeding on the consumption of fruits and vegetables among preschool children. *PLoS One*, 11.2 (2016).
- Stevens, C., Lauinger, B., & Neville, H. (2009). Differences in the neural mechanisms of selective attention in children from different socioeconomic backgrounds: an event-related brain potential study. *Dev Sci*, 12(4), 634-646. doi:10.1111/j.1467-7687.2009.00807.x
- St. John, Ashley M., et al. "Maternal cortisol slope at 6 months predicts infant cortisol slope and EEG power at 12 months." *Developmental Psychobiology* 59.6 (2017): 787-801.
- St. Louis, E.K., & Frey, L.C. *Electroencephalography (EEG): An introductory text and atlas of normal and abnormal findings in adults, children, and infants*. Chicago, IL, American Epilepsy Society. 2016.
- Sudfield, C.R., McCoy, D.C., Fink, G., Muhihi, A., Bellinger, D.C. et al. Malnutrition and Its determinants are associated with suboptimal cognitive, communication, and motor development in Tanzanian children. *Journal of Nutrition*, 145 (12), (2015): 2705–2714.
- Sullivan, R., Perry, R., Sloan, A., Kleinhaus, K., & Burtchen, N. Infant bonding and attachment to the caregiver: Insights from basic and clinical science. *Clinical Perinatology*, 48(4), (2011): 643-655.
- Tabachnick, B.G., & Fidell, L.S. *Using multivariate statistics* (6th ed.). Boston, MA: Allyn & Bacon. 2013.
- Taboada-Crispi, A., Bringas-Vega, M.L., Bosch-Bayard, J., Galan-Garcia, L., Bryce, C., et al. Quantitative EEG tomography of early childhood malnutrition. *Frontiers of Neuroscience*, (2016): <https://doi.org/10.3389/fnins.2018.00595>
- Talabi, Mehret Birru, and Megan EB Clowse. "Antirheumatic medications in pregnancy and breastfeeding." *Current Opinion in Rheumatology* 32.3 (2020): 238-246.

- Tanaka, K et al. "The pilot study: sphingomyelin-fortified milk has a positive association with the neurobehavioural development of very low birth weight infants during infancy, randomized control trial." *Brain & Development* vol. 35,1 (2013): 45-52.
- Tanda, Rika, et al. "The impact of prepregnancy obesity on children's cognitive test scores." *Maternal and Child Health Journal* 17.2 (2013): 222-229.
- Taq, J. Causality in qualitative and quantitative research. *Qualitative and Quantitative*, 35 (2011): 263-291.
- Tharner, A., et al. "Breastfeeding and its relation to maternal sensitivity and infant attachment." *Journal of Developmental & Behavioral Pediatrics* 33.5 (2012): 396-404.
- Thatcher, R.W. Validity and reliability of quantitative electroencephalography. *Journal of Neurotherapy* 14.2 (2010): <https://doi.org/10.1080/10874201003773500>
- Thingholm, T. E., L. Rönstrand, and P. A. Rosenberg. "Why and how to investigate the role of protein phosphorylation in ZIP and ZnT zinc transporter activity and regulation." *Cellular and Molecular Life Sciences* (2020): 1-18.
- Thompson, B., Diamond, K.E., McWilliam, R., Snyder, P., & Snyder, S. W. Evaluating the quality of evidence from correlational research for evidence-based practice. *Exceptional Children* 71(2), (2005): 181-194
- Tierney, Adrienne L, and Charles A Nelson 3rd. "Brain Development and the Role of Experience in the Early Years." *Zero to Three* 30.2 (2009): 9-13.
- Tomalski, P., Moore, D. G., Ribeiro, H., Axelsson, E. L., Murphy, E., Karmiloff-Smith, A., & Kushnerenko, E. Socioeconomic status and functional brain development—associations in early infancy. *Developmental Science*, 16(5), (2013): 676-687.
- Toro-Campos, Rosario, et al. "Effect of feeding mode on infant growth and cognitive function: study protocol of the Chilean infant Nutrition randomized controlled Trial (ChiNuT)." *BMC Pediatrics* 20 (2020): 1-11.
- Tozuka, Yusuke, et al. "Maternal obesity impairs hippocampal BDNF production and spatial learning performance in young mouse offspring." *Neurochemistry International* 57.3 (2010): 235-247.
- Troller-Renfree, S., Nelson, C. A., Zeanah, C. H., & Fox, N. A. (2016). Deficits in error monitoring are associated with externalizing but not internalizing behaviors among children with a history of institutionalization. *Journal of Child Psychology and Psychiatry*, 57(10), 1145-1153.
- Troller-Renfree, S. V., Brito, N. H., Desai, P. M., Leon-Santos, A. G., Wiltshire, C. A., Motton, S. N., ... & Noble, K. G. Infants of mothers with higher physiological stress show alterations in brain function. *Developmental Science*, (2020): e12976.

- Troller-Renfree, S. V., Morales, S., Leach, S. C., Bowers, M. E., Debnath, R., Fifer, W. P., ... & Noble, K. G. (2021). Feasibility of assessing brain activity using mobile, in-home collection of electroencephalography: methods and analysis. *Developmental Psychobiology*.
- Tuthill, E. L., et al. "'In the United States, we say, 'No breastfeeding,' but that is no longer realistic": provider perspectives towards infant feeding among women living with HIV in the United States." *Journal of the International AIDS Society* 22.1 (2019): e25224.
- U.S. Household Food Security Survey Module: Three-Stage Design, With Screeners Economic Research Service. United States Department of Agriculture, (Revised-September 2012). <https://www.ers.usda.gov/media/8271/hh2012.pdf>. Accessed 12 Nov 2020.
- Uhlhaas, P.J., et al. "Neural synchrony and the development of cortical networks." *Trends in Cognitive Sciences* 14.2 (2010): 72-80.
- United States Department of Agriculture. Food Security Status of U.S. Households in 2019, <https://www.ers.usda.gov/topics/food-nutrition-assistance/food-security-in-the-us/key-statistics-graphics.aspx>. Accessed 24 Oct 2020.
- U.S. Department of Agriculture and U.S. Department of Health and Human Services. Dietary Guidelines for Americans, 2020-2025. 9th Edition. December 2020. Available at [DietaryGuidelines.gov](https://www.dietaryguidelines.gov).
- United States National Library of Medicine. Clinical Trials, Baby's First Years (BFY), 2020, <https://clinicaltrials.gov/ct2/show/NCT03593356>. Accessed 24 Oct 2020.
- UvnäsMoberg, Kerstin, et al. "Maternal plasma levels of oxytocin during breastfeeding—A systematic review." *PloS one* 15.8 (2020): e0235806.
- Vallat, R. Compute the average band power of an EEG signal. (2018): <https://raphaelvallat.com/bandpower.html>. Accessed 24 Oct 2020
- Van Lieshout, R. J., V. H. Taylor, and M. H. Boyle. "Pre-pregnancy and pregnancy obesity and neurodevelopmental outcomes in offspring: a systematic review." *Obesity reviews* 12.5 (2011): e548-e559.
- Vanderwert, R. E., Marshall, P. J., Nelson III, C. A., Zeanah, C. H., & Fox, N. A. (2010). Timing of intervention affects brain electrical activity in children exposed to severe psychosocial neglect. *PLoS One*, 5(7), e11415.
- Veena, S. R., Krishnaveni, G. V., Srinivasan, K., Wills, A. K., Muthayya, S., Kurpad, A. V., ... & Fall, C. H. (2010). Higher maternal plasma folate but not vitamin B-12 concentrations during pregnancy are associated with better cognitive function scores in 9-to 10-year-old children in South India. *The Journal of nutrition*, 140(5), 1014-1022.
- Veit, J., et al. "Cortical gamma band synchronization through somatostatin interneurons." *Nature Neuroscience* 20.7 (2017): 951.

- Verd, Sergio, et al. "Variation in the protein composition of human milk during extended lactation: a narrative review." *Nutrients* 10.8 (2018): 1124.
- Vieau, Didier, et al. "Perinatal undernutrition and brain-derived neurotrophic factor." *Handbook of Behavior, Food and Nutrition*. Springer, New York, NY, 2011. 2055-2068.
- Vieira Borba, Vânia, Kassem Sharif, and Yehuda Shoenfeld. "Breastfeeding and autoimmunity: Programming health from the beginning." *American Journal of Reproductive Immunology* 79.1 (2018): e12778.
- Vinzi, E.V., Trinchera, L., & Amato, S. *Handbook of partial least squares*. Springer Handbooks of Computational Statistics. Berlin Heidelberg: Springer-Verlag. 2010.
- Vitillo, L., et al. "Integrin-associated focal adhesion kinase protects human embryonic stem cells from apoptosis, detachment, and differentiation." *Stem Cell Reports* 7.2 (2016): 167-176.
- Wachs, T.D., Georgieff, M., Cusick, S., & McEwen, B.S. Review: Issues in the timing of integrated early interventions: contributions from nutrition, neuroscience, and psychological research. *Annals of the New York Academy of Sciences* 1308 (2014): 89-106.
- Wade, Mark, et al. "Cumulative psychosocial risk, parental socialization, and child cognitive functioning: A longitudinal cascade model." *Developmental Psychology* 54.6 (2018): 1038.
- Walker, H.I., Ford, W., Park, J-W., Mathur, R., Hotchkiss, N... et al. Partial Least Squares (PLS) applied to medical bioinformatics. *Procedia Computer Science* 6 (2011): 273-278.
- Walker, W. A. "Initial intestinal colonization in the human infant and immune homeostasis." *Annals of Nutrition and Metabolism* 63.Suppl. 2 (2013): 8-15.
- Wallenborn, J. T., et al. "Knowledge of breastfeeding recommendations and breastfeeding duration: A survival analysis on infant feeding practices II." *Breastfeeding Medicine* 12.3 (2017): 156-162.
- Wambach, K., and Spencer, B. *Breastfeeding and human lactation*. Jones & Bartlett Learning, 2019.
- Ward, A. Spurious correlations and causal inference. *Erkenntnis*, 78 (2013): 669-712.
- Ward, Tonya L., Dan Knights, and Cheryl A. Gale. "Infant fungal communities: current knowledge and research opportunities." *BMC Medicine* 15.1 (2017): 30.
- Wasserstein, R., Schirm, A.L., & Lazar, N.A. Moving to a world beyond "p < 0.05". *The American Statistician*, 73, (2019):1-9.
- Wasserstein, R.L., & Lazar, N.A. The ASA's statement on p-values: Context, process, and purpose. *The American Statistician*, 70, (2016): 129-133.
- Wessels, Inga, Martina Maywald, and Lothar Rink. "Zinc as a gatekeeper of immune function." *Nutrients* 9.12 (2017): 1286.

- Wilke, Marko, et al. "Bright spots: correlations of gray matter volume with IQ in a normal pediatric population." *Neuroimage* 20.1 (2003): 202-215.
- Wong, Eugene C., et al. "Trends in multivitamin use among women of reproductive age: United States, 2006–2016." *Journal of Women's Health* 28.1 (2019): 37-45.
- World Health Organization. Breastfeeding, 2020 https://www.who.int/health-topics/breastfeeding#tab=tab_1. Accessed 24 Oct 2020.
- Wu, Qiong, Robin L. Harwood, and Xin Feng. "Family socioeconomic status and maternal depressive symptoms: Mediation through household food insecurity across five years." *Social Science & Medicine* 215 (2018): 1-6.
- Yatsunenکو, Tanya, et al. "Human gut microbiome viewed across age and geography." *Nature* 486.7402 (2012): 222-227.
- Yoo, W., Mayberry, R., Sejong, B., Singh, K., He, Q., & Lillard, J.W.. A study of effects of multicollinearity in the multivariable analysis. *International Journal of Applied Science and Technology*, 4(5), (2014): 9-19
- Zeisel, Steven H., Kevin C. Klatt, and Marie A. Caudill. "Choline." *Advances in Nutrition* 9.1 (2018): 58-60.
- Żelaźniewicz, Agnieszka, and Bogusław Pawłowski. "Maternal breast volume in pregnancy and lactation capacity." *American Journal of Physical Anthropology* 168.1 (2019): 180-189.
- Zhang, Yuyao, et al. "Neonate and infant brain development from birth to 2 years assessed using MRI-based quantitative susceptibility mapping." *Neuroimage* 185 (2019): 349-360.
- Zhang, Zhiying, et al. "Amino acid profiles in term and preterm human milk through lactation: a systematic review." *Nutrients* 5.12 (2013): 4800-4821.
- Zheng, Ju-Sheng, et al. "Pre-conceptional intake of folic acid supplements is inversely associated with risk of preterm birth and small-for-gestational-age birth: a prospective cohort study." *British Journal of Nutrition* 115.3 (2016): 509-516.
- Zielińska, D., & Kolożyn-Krajewska, D. (2018). Food-origin lactic acid bacteria may exhibit probiotic properties. *BioMed research international*, 2018.

