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Effects of Premature Birth and/or Low Birthweight on Developmental Outcomes

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EFFECTS OF PREMATURE BIRTH AND/OR LOW BIRTHWEIGHT ON DEVELOPMENTAL OUTCOMES

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TABLE OF CONTENTS

LIST OF ABBREVIATIONS

β	Correlation coefficient
B	Unstandardized Regression Coefficient
SE_B	Standard Error of the Coefficient
ADHD	Attention-Deficit/Hyperactive Disorder
ADP	Adaptive Domain
ANOVA	Analysis for the Analysis of Variance
ASD	Autism Spectrum Disorder
BDI-2	Battelle Developmental Inventory, Second Edition
BISCUIT	Baby and Infant Screen for Children with aUtIsm Traits
COG	Cognitive Domain
COMM	Communication Domain
CP	Cerebral Palsy
DD	Developmental Disabilities
DQ	Developmental Quotient
ELBW	Extremely Low Birthweight
EPT	Extremely Preterm
FT	Full Term
ID	Intellectual Disabilities
IQ	Intelligence Quotient
IUGR	Intrauterine Growth Retardation
LBW	Low Birthweight
LPT	Late Preterm
MANOVA	Multiple Analysis for the Analysis of Variance
MOT	Motor Domain
MRI	Magnetic Resonance Imaging
P-S	Personal-Social
PLBW	Premature and Low Birthweight
PRE	Premature
PVL	Periventricular Leukomalacia
SGA	Small for gestational Age
VLBW	Very Low Birthweight
VPT	Very Preterm
WHO	World Health Organization

ABSTRACT

Advances in neonatal technology have improved survival rates of children born at lower and lower birthweight and after fewer and fewer weeks of gestation. However, these children are at increased risk of experiencing developmental delays. As weeks of gestation and birthweight decrease, the risk of developmental impairment and severity increases. Yet to be determined is whether premature birth and low birthweight (LBW) effect development differentially, and if the combined, have an additive effect on developmental outcomes. The first part of this study aimed to examine the independent effects of preterm birth and LBW in children at risk for developmental delays. Using the Battelle Developmental Inventory, Second Edition (BDI-2), differences in overall developmental quotient (DQ) scores and domain scores (i.e., adaptive, personal-social, communication, motor, cognitive) were assessed. In Part 1, were noted different developmental profiles for children born premature and/or LBW. Additionally, premature birth and low birthweight (PLBW) children exhibited the greatest impairment in all areas of development evaluated compared to their premature, LBW, and full term peers. The second part of this study aimed to examine the predictive value of weeks of gestation, birthweight, age, gender, and race on developmental outcomes. For Part 2, weeks of gestation, birthweight, age, gender, and race predicted statistically significant impairments in all the areas of development assessed with to varying degrees. These findings support the institution of early intervention, before clinical manifestations appear, and the importance of highly individualized interventions.

CHAPTER 1: INTRODUCTION

The increased use of assisted ventilation in delivery rooms, surfactant therapy, and overall advances in neonatal care that emerged in the 1960s is credited with the boost in survival rates of very low birthweight and premature infants and declines in the rates of cerebral palsy (CP) and other neurodevelopmental disabilities (Hack & Fanaroff, 1999; Hack, Klein, & Taylor, 1995). These improvements in survival rates continued to occur through the 1970s and 1980s with the wider spread use of cesarean delivery, phototherapy, intravenous nutrition, and neonatal monitoring of blood pressure, heart rate, and respiration. However, more recently, despite new advances, the rate of CP and neurodevelopmental disabilities among low birthweight (LBW) and preterm infants has remained stable. This factor has resulted in an overall increase not only in the number of surviving LBW and preterm infants, but also in the number of children with disabilities (Congress of the US, Office of Technology Assessment, 1987; Hack et al., 1995).

LBW and preterm birth have been associated with a range of problems such as feeding difficulties, motor skill deficits, cardiovascular regulation, impaired cognitive skills, and the increased likelihood of mental health problems such as Attention-Deficit/Hyperactive Disorder (ADHD; Bhutta, Cleves, Casey, Cradock, & Anand, 2002). Historically, researchers have not distinguished between infants born preterm and those born at LBW. Most research to date has examined the combined effect of LBW and prematurity or simply includes participants that are designated as premature and/or LBW. Prematurity is often a cause for LBW; however, infants born full term may also be LBW, commonly referred to as small-for-date (Vohr et al., 2012).

Advances in neonatal technology allowing for increased survival of infants born at lower birthweight and at earlier gestational ages, have led to an expansion of potential lifelong consequences for these infants, underscore the importance of studying these problems in more depth, and the need to diagnose high risk infants and initiate early interventions (Lee, Zhai, Brooks-Gunn, Han, & Waldfogel, 2014). Studying the implications of preterm birth and LBW separately may improve our understanding of the distinct implications they have on development and how we may mitigate the consequences. Associated delays can be pervasive, resulting in marked difficulties in achieving normal development (Verkerk, Jeukens-Visser, van Wassenaer-Leemhuis, Kok, & Nollet, 2014).

The overarching goal of this study was to add to the body of knowledge regarding potentially significant differences in the effects of premature birth and/or LBW on developmental outcomes in children at risk for developmental delays. The specific aims were to determine how LBW and prematurity, separately and combined, effect developmental outcomes in the areas of adaptive, personal-social, communication, motor and cognitive skills, and to examine how and the degree to which age, gender, race, birthweight, and weeks of gestation influence and predict developmental outcomes.

CHAPTER 2: PREMATURE BIRTH

Premature birth is defined as delivery that occurs before 37 weeks of gestation. Risk factors for premature delivery include maternal age, substance use, low socioeconomic status, low level of maternal education, infection or inflammation, uteroplacental ischaemia, uterine overdistension, stress, and/or immunologically mediated processes (Goldenberg et al., 2008; Romero et al., 2006). The World Health Organization (WHO) reported in 2012 that more than one in 10 infants was born prematurely, amounting to about 15 million infants. Of these infants, the vast majority, 12 million, were born between 32 and 37 weeks of gestation, 1.6 million were born between 28 and 32 weeks of gestation, and 780,000 were born prior to 28 weeks of gestation (Blencowe et al., 2013). The three widely accepted classifications of preterm birth are: extremely preterm (EPT; <26weeks), very preterm (VPT; 26-33 weeks), and late preterm (LPT; 34-36 weeks; Johnson & Marlow, 2011; Xiong, Gonzalez, & Mu, 2012). Limited data are available comparing the developmental outcomes of these three groups, prior work has primarily focused on premature children as a single group.

Developmental Outcomes

As advances in technology have allowed doctors to save infants born prematurely at increasingly earlier weeks of gestation; it has also been found that the fewer weeks of gestation, the higher the risk of disability. For example, CP is estimated to affect 1-2% of infants born FT. Rates of CP increase to 9% for infants born earlier than 32 weeks of gestation and 18% for infants born at 26 weeks of gestation (Abbott, 2015). Some data suggests as many as half of children born prematurely develop both cognitive and behavioral problems (Abbott, 2015; Larroque et al., 2008). A five year follow up study of children born between 22 and 32 weeks of gestation reported that close to half presented with some disability by the age of 5 years (Larroque et al., 2008). Additionally, impairments in cognitive development were found to increase as weeks of gestation decreased. Cognitive impairment was observed in 44% of participants born between 24 and 25 weeks of gestation and 26% of participants born at 32 weeks, compared with 12% of FT controls (Larroque et al., 2008). In children born before 33 weeks of gestation, intelligence quotient (IQ) scores decrease by 1.3 to 1.7 points for each week of shortened gestation (Allen, Cristofalo, & Kim, 2011; Bhutta et al., 2002). When cognitive function was examined, excluding children with CP, intellectual disabilities (ID), and severe sensory impairments, children born preterm still had lower average cognitive functioning scores compared to their FT peers (Allen et al., 2011; Bhutta et al., 2002).

Cognitive functioning is not the only area found to be impacted by preterm birth. The rate of motor dysfunction, visual deficiency, and hearing deficiency followed a similar pattern; shorter gestational age, and greater cognitive impairment (Larroque et al., 2008). Brain injury as a result of preterm birth has been associated with motor impairments. Premature birth increases the risk of periventricular leukomalacia (PVL), a form of white matter brain injury. A magnetic resonance imaging (MRI) study of children born preterm who had PVL at infancy found significant correlations between severity of motor dysfunction and the extent of pyramidal tract injury and total white matter volume (Allen et al., 2011; Staudt, Pavlova, Böhm, Grodd, & Krägeloh-Mann, 2003).

Children and adolescents born prematurely also appear to be at increased risk for vision and hearing impairments compared to their full term peers. Visual impairment occurs in 1% of children born before 30 weeks gestation and increase in incidence as weeks of gestation decrease; 1% to 2% born before 27 weeks gestation, and 9% to 12% born before 25 to 26 weeks gestation. Common visual impairments include myopia and strabismus (Allen et al., 2011).

Hearing and vision impairments that go unidentified at an early age can have a significant impact on language development in subsequent years.

Disability related to premature birth often persists into adulthood. Eryigit and colleagues (2015) conducted a longitudinal study of participants born between 26 and 31 weeks of gestation and found that most participants who exhibited cognitive impairments at 6 years of age presented with impairments at 26 years of age. Further, the authors reported that not only did impairments persist into adulthood, many of the participants continued to show impairments despite special education support during childhood (Eryigit Madzwamuse, Baumann, Jaekel, Bartmann, & Wolke, 2015). Another study suggested that children born before 32 weeks of gestation are six times more likely to be in special education by school age years than peers born full term (Holm & Crosbie, 2010).

Brain Development

The increased rates of disability reported in children born prematurely is thought to result from a disruption in the pattern of brain development (Kapellou et al., 2006). Typically, the surface area of the brain develops at a faster rate than the volume of the brain. Between 24 and 30 weeks of gestation, a fourfold increase in cortical volume occurs as a result of neuronal and axonal growth, myelination, synaptogenesis, and focused apoptosis (Kerstjens, De Winter, Bocca-Tjeertes, Bos, & Reijneveld, 2012). However, when a child is born prematurely, this pattern is interrupted, resulting in less cortical surface and cortical gray matter (Ajayi-Obe, Saeed, Cowan, Rutherford, & Edwards, 2000; Inder, Warfield, Wang, Hüppi, & Volpe, 2005).

The reduced growth of cortical area attributed to premature birth is thought to be a result of less connectivity rather than a reduced number of cortical neurons (Ajayi-Obe et al., 2000). It has been postulated that when the brain undergoes significant phases of development while the child is no longer in the womb, it receives signals from the environment it may not be ready to receive, in turn affecting how neurons are linked into networks (Fischi-Gomez et al., 2014). This is exemplified in the work of Fischi-Gomez et al (2014), who compared the brains of 6 year old children born prematurely to children born full term. The children born prematurely exhibited less organization in their neural tracts suggesting less efficiency. Fischi-Gomez suggested that the differences in organization compared to full term children was correlated to poorer social and cognitive skills (Fischi-Gomez et al., 2014). Additional work supports the concept that the slower the rate of surface area growth to volume, the greater the risk of developmental delays (Kapellou et al., 2006; MacKay, Smith, Dobbie, & Pell, 2010).

CHAPTER 3: LOW BIRTHWEIGHT

In 2011, the worldwide rate of infants born LBW was reported to be 15.5%, with 95.6% occurring in developing counties (World Health Organization, 2011). In the United States, the most recent estimate of infants born LBW is 8% (Martin, Hamilton, Osterman, Curtin, & Mathews, 2015). The WHO defines LBW as weight at birth of less than 2,500 grams (5.5 lbs). LBW can be a consequence of premature birth, small size for gestational age (SGA), or a combination of both (Valero de Bernabé et al., 2004). SGA is usually attributed to intrauterine growth retardation (IUGR), defined as slower than normal velocity of fetal growth. The three most common classification criteria based on birthweight are: extremely low birthweight (ELBW; <1000g), very low birthweight (VLBW; 1001 - 1500g), and low birthweight (LBW; 1501 - 2500g; Johnson & Marlow, 2011; Xiong et al., 2012).

Developmental Outcomes

Infants born at a LBW are at risk of motor and neurodevelopmental delays (Shah & Kingdom, 2011; Verkerk et al., 2014), and these delays are likely to persist over time (Duvall, Erickson, MacLean, & Lowe, 2015). Cognitive impairment, academic difficulties, psychological disorders, ADHD, and increased behavioral problems and/or social problems are prevalent (Aarnoudse-Moens, Weisglas-Kuperus, Goudoever, & Oosterlaan, 2009; Allen, 2002; Houtzager, Gorter-Overdiek, Van Sonderen, Tamminga, & Van Wassenaer, 2010).

CP is the most common major neurological abnormality that manifests in LBW infants. As birthweight decreases, the risk of developing CP increases. Additionally, approximately 20% of infants born at less than 1,000 grams had been diagnosed with CP, microcephaly, hydrocephaly, seizures, blindness, and/or deafness. In comparison, rates are about 14 to 17% for infants 1,000 to 1,500 grams, 6 to 8% for infants 1,500 to 2,499 grams, and below 5% in infants born at normal birthweight (Hack et al., 1995; Petersen, Greisen, Kovacs, Munck, & Friis-Hansen, 1990; Saigal, Szatmari, Rosenbaum, Campbell, & King, 1991).

In regard to neuropsychological outcomes, compared to children delivered at a normal birthweight, LBW children score significantly lower on tests of intelligence. These findings remain after controlling for sociodemographic risks factors and neurological abnormalities (Hack et al., 1995). LBW children perform lower than their normal birthweight peers in not just overall cognitive function, but also in more specific functions such as memory, attention, language abilities, fine and gross motor coordination, perceptual motor skills, problem solving, and nonverbal reasoning (Hack et al., 1995; Klein, Hack, & Breslau, 1989; Saigal et al., 1991; Teplin, Burchinal, Johnson-Martin, Humphry, & Kraybill, 1991). Further, impairments in neuropsychological outcomes appear to increase with decreasing birthweight. These latter findings may be related to the greater rate of medical complication associated with increasingly lower birthweight (Hack et al., 1995).

Once LBW children reach school age, they are more likely to receive supplementary services. McCormick et al (1990) found that 34% of LBW children compared to 14% of normal birthweight children experienced grade repetition or placement in special education. Correcting for sociodemographic variables did not explain this difference (McCormick, Gortmaker, & Sobol, 1990). Consistent with these findings LBW children have been reported to require increasing levels of assistance as they progress through the educational system (Carran & And Others, 1989).

Brain Development

Causes of IUGR include either inadequate supply of nutrients to the growing fetus or excess utilization of nutritional resources. When the fetus does not receive an adequate supply of essential nutrients, it develops an adaptive response in which blood is diverted from the liver, muscles, skin, and subcutaneous tissues to the brain, heart, and adrenals. The persistent lack of nutrients to the brain impairs growth and development (Shah & Kingdom, 2011). IURG is also associated with "secondary" placental dysfunction, which results from negative maternal behaviors such as maternal drug use, maternal stress, and undernutrition (Grissom & Reyes, 2013).

The placenta is a source of neurotransmitters and neuromodulators, such as serotonin, leptin, and BDNF for the developing fetus. It has been purported that even minor abnormalities in placental development or function adversely affect brain development (Bonnin & Levitt, 2012; Grissom & Reyes, 2013). Additionally, fetal malnutrition has a negative effect on brain development, causing deficits in neural connectivity and myelination (Hall & Wolke, 2012; Rees, Harding, & Walker, 2008). The consequences are white matter abnormalities, reduced volumes of both white and grey matter, and ventricular enlargement. Poorer early developmental outcomes are associated with reduced cortical white and grey matter subcortical grey matter volumes and larger ventricle size (Taylor et al., 2011).

CHAPTER 4: PREMATURE AND LOW BIRTHWEIGHT

Data on the combined effects of preterm birth and LBW is limited. Most research to date focused specifically on one or the other, or did not distinguish between the two. The consequence is that in some cases participants who are preterm, LBW, and/or preterm and low birthweight (PLBW) are frequently combined into a single sample. Hence, potential differences among these subgroups can go unrecognized and potential differences resulting from the combined effects on development often remain unexplored. Preterm birth and LBW both clearly increase the risk of disability, whether there are differential effects is yet to be determined. Goldenberg and colleagues (1996) examined the combined influence of preterm and LBW on cognitive function. At age 5 years, the IQ of infants that were LBW averaged 4 points lower than infants born at term and within a normal weight range; for infants that were PLBW, their IQ averaged 6 points lower (Goldenberg et al., 1996). Some researchers have indicated that by age 2 years, children born PLBW have weaker language skills than children born full term, with differences in language development increasing with age (Stolt et al., 2014; Stolt et al., 2014). In a longitudinal study of infants born PLBW, Stolt and colleagues (2014) found that weak language ability at age 2 years was a significant predictor of weak language skills at age 3 years. After excluding children with neurological impairment, these differences persisted though age 5 years (Stolt et al., 2014).

When examining executive dysfunction in PLBW children, Anderson and Doyle (2004) reported that these children exhibited global impairment rather than deficits in specific executive domains compared to full term children. Further, PBLW children displayed more behavioral problems indicative of executive dysfunction (Anderson & Doyle, 2004). Aarnoudse-Moens et al (2009) conducted a quantitative meta-analysis of studies published between 1998 and 2008 on academic achievement, behavioral functioning, and executive functioning outcomes in PLBW children. Combined effect sizes demonstrated that PLBW children scored 0.60 *SD* lower on mathematics, 0.48 *SD* on reading, and 0.76 *SD* on spelling than their full term peers. With regard to measures of behavior problems, attention problems were most common in PLBW children, with PLBW children scoring 0.43 to 0.59 *SD* higher than children born full term. These findings suggest bleaker outcomes for children born PLBW; suggesting, although not proving, early and targeted intervention may mitigate some of the risks associated with PLBW.

CHAPTER 5: ASSESSING DEVELOPMENT

Developmental Milestones

Developmental milestones are skills that a child is expected to exhibit by a predefined age. Major developmental milestones include sitting up, crawling, walking, speaking, and toileting. Developmental milestones are commonly used to determine if a child is progressing at an age appropriate rate and possess the skills necessary to function in their environment at an age appropriate level (Masten & Coatsworth, 1998). Though rate of development is variable, developmental milestones are used as general guidelines to characterize typical development among children (Petermann & Macha, 2008; Rydz, Shevell, Majnemer, & Oskoui, 2005). Delay in meeting developmental milestones often ignites concerns for caregivers and clinicians.

Developmental delays may become apparent to caregivers and clinicians in different ways: a child may be slower than expected in developing skills necessary to reach established developmental milestones, a child may present with a splintered pattern of skill development in various domains, or a child may not follow the expected developmental course and exhibit behaviors that are different from those of a typical child of any age (Accardo, 2007). In some cases, delays in development may be indicative of a long-term developmental disability, but in other cases, a child may have some delays in the short-term but eventually catch up to their peers. As such, developmental concerns should be addressed through a comprehensive evaluation.

Method of Assessment

Assessing development in young children most commonly involves an unstructured interview with the caregiver(s) and formal in person assessment of the child. The goal of the unstructured interview with the child's caregiver(s) is to obtain a detailed developmental history.

This approach includes information on presenting concerns, the child's pre and postnatal periods, developmental milestones, medical history, communication and social development, adaptive functioning, psychological function, and family history. Gathering information on past diagnoses as well as interventions and evaluations is also important.

Following the interview, a formal developmental assessment of the child is recommended. Two of the most widely used measures in young children are the Battelle Developmental Inventory, Second Edition (BDI-2) and the Bayley Scales of Infant Development-Third Edition. Both measures are administered directly to the child by a trained professional to evaluate multiple areas of cognitive function, including language, motor skills, social skills, and adaptive behaviors. Using these measures, a young child is diagnosed with DD if they perform 1.5 to 2.0 standard deviations below the mean of typically developing peers in two or more domains (Shevell, Majnemer, Platt, Webster, & Birnbaum, 2005). Developmental assessments such as the BDI-2 are also designed to gather information from multiple sources. Over one-third of the BDI-2 items can be administered using multiple sources of information (Newborg, 2005). Interview items of the BDI-2 are structured as open-ended questions allowing for consistency of administration but also providing the examiner with an opportunity to query if deemed necessary. These measures of development are preferable to IQ tests because they assess a broader range of development domains that are more stable at young ages (Fombonne, 1999). Further, IQ does not provide a picture of a child's developmental strengths and weaknesses compared to same-aged typically developing peers.

Measuring developmental quotient (DQ) is often a better method for assessing the presence or absence of developmentally appropriate behaviors than IQ. DQ is used to assess how a child compares to typically developing children their age across domains that contribute to overall developmental growth (Berk, 2007; Newborg, 2005). Considering developmental growth in an assessment can assist in differential diagnosis; determining the overall level of impairment, developing a treatment plan, and informing prognosis.

Challenges of Assessing Young Children

Standardized testing of young children, both typically and atypically developing, can present many challenges. Tests that only measures one area of development, such as intelligence, often have difficulty establishing norms and evaluating individual differences because variability in other domains is not taken into consideration. The performance of young children (e.g., 24 months) on standardized intelligence tests may be strongly affected by individual differences in areas of communication, motor skills, and social skills. Factors such as experience with unfamiliar adults or comfort level in new environments, along with deficits in communication skills or noncompliance, can impact performance (Feldman et al., 2005). Many tests rely on good expressive and receptive communication skills, which is one of the most common areas of impairment in young children at risk for DD (Lichtenberger, 2005). Therefore, commonly used standardized intelligence tests may provide more information on attention or motivation than information on cognitive or language ability (Koegel, Koegel, & Smith, 1997). The consequence of these limitations is that the measures may underestimate the child's true capabilities (Courchesne, Meilleur, Poulin-Lord, Dawson, & Soulières, 2015).

Measures that provide a normed DQ (e.g., BDI-2) and incorporate information from multiple sources are often better suited to assess children with DD (Newborg, 2005). Such measures allow for a flexible administration, present untimed items, are less dependent on expressive and receptive language for items for which assessing language is not the goal, and provide more concrete and interesting materials for the child (Lichtenberger, 2005).

Implementation of the most appropriate and effective treatment is critically dependent on reliable assessment. Therefore strengthens and limitation of assessment tools must be recognized when selecting a measure to assess a child with DD.

CHAPTER 6: PURPOSE

Research on the independent effects of LBW and premature birth on development is limited, as most studies combine these populations into one group or do not clearly distinguish between the two. Identifying different developmental profiles, with regard to areas of impairment, can have significant implications on the design of interventions and area of most intensive services. This type of research is essential given the well documented positive effects of early intervention, especially highly targeted and individualized treatment plans (Dawson, 2008; Harris & Handleman, 2000; Perry, Blacklock, & Dunn Geier, 2013). This approach in turn has a positive effect on long term developmental outcomes and quality of life for both the caregivers and child. Therefore, the first aim of this study was to compare the developmental outcomes of children born premature to those born LBW. Additionally, the study aimed to examine developmental outcomes of children who were born PLBW. That is, children who are born prematurely and are LBW for the number of weeks they gestated. These children have been largely ignored and little research exists comparing their developmental outcomes to their peers who are either full term but LBW, premature but the correct weight for the number of weeks gestated, and peers born full term and normal birthweight.

The second aim of this study was to examine the predictive value of age, gender, race, birthweight, and weeks of gestation on impairment in developmental outcomes. Understanding which factors predict impairment and the degree of impairment has many important implications. Findings may be critical in informing type and intensity of early interventions and prognosis, as they relate to the support services required. Overall development was examined in addition to specific areas of development including adaptive skills, personal-social skills, communication skills, motor skills and cognitive skills. Developmental delays are not always global. By investigating how these factors predict impairment in specific areas of development provides valuable information when planning and coordinating intervention services. Especially when there are barriers to service (e.g., insurance coverage, time available), resources can be better allocated when more information is available for highest risk areas. Finally, prevention is the best treatment. With clear evidence of how development is influenced by factors such as birthweight, weeks of gestation, children born premature and/or LBW early intervention supportive services can be initiated. This in turn may prevent developmental delays or reduce the degree of impairment.

CHAPTER 7: METHOD

Participants

Participants in this study were recipients of services from EarlySteps, Louisiana's Early Intervention System administered under the Individuals with Disabilities Education Act, Part C. This program provides screening and intervention services to infants and toddlers, and their families, from birth to 36 months. Children qualify for services if they have a medical condition likely to result in a developmental delay, or have developmental delays. Qualifying conditions include prematurity and LBW; other diagnoses represented in the sample include CP, genetic and chromosomal disorders or deletion syndromes, epilepsy, neurofibromatosis, asthma, vision or hearing problems, and other diagnoses that may impact one or more areas of development. As the EarlySteps screening program and related services are provided statewide, this sample is thought to be representative of infants and toddlers in the state of Louisiana.

Participants were 17 to 37 (*M* = 25.59, *SD* = 4.76) months of age and selected from a pre-existing database which contains demographic, diagnostic, and evaluation information gathered through the EarlySteps program (e.g., Baby and Infant Screen for Children with aUtIsm Traits, BDI-2). Participants (N = 7863) were divided into four groups; premature (PRE; n = 285), full term gestation with low birthweight (LBW; n = 1286) premature with low birthweight (PLBW; n = 198), and full term (FT; n = 6094). The PRE group consisted of children born at a gestational age < 37 weeks who had a birthweight consistent with current standards for length of gestation. The LBW group was comprised of children with gestational age ≥ 37 weeks and birthweight ≤ 5.5 lbs. The PLBW group consists of children born at a gestational age < 37 weeks whose birthweight was considered low for the number of weeks they gestate. The FT group consists of children with gestational age ≥ 37 weeks and birthweight > 5.5 lbs.

Since group sizes differs so that the largest groups are more than 1.5 times greater (N = 283) than the smallest group, participants were randomly deleted from the FT, PRE, and LBW groups until the size of the groups was within acceptable limits (Nimon, 2012; Pituch, Whittaker, & Stevens, 2013). Hence, statistical analyses were conducted on n = 283 for each group except PLBW which was n = 189. This resulted in a sample size of 1038 (Figure 1). Approximately 39% were female and 61% were male, with a racial distribution of 42% Caucasian, 49% African American, 3% Hispanic, and 6% other or unspecified. The demographic information is presented within Table 1.

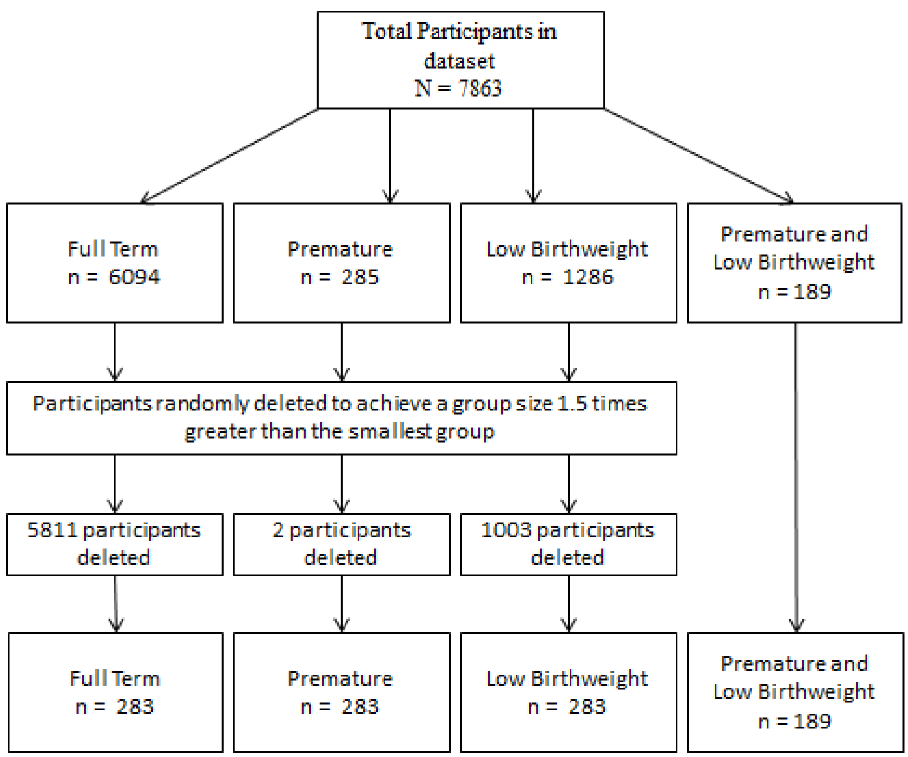


Figure 1. Participant randomization

Table 1. Demographic Information (N = 1038).

Demographic Characteristics	Diagnostic Group FT (*n* = 283)	PRE (*n* = 283)	LBW (*n* = 283)	PLBW (*n* = 189)	Total (N = 1038)
Age (in months)					
Mean (SD)	25.47 (4.93)	24.91 (4.44)	25.72 (5.08)	25.72 (4.97)	25.43 (4.86)
Range	17-35	17-35	17-36	17-35	17-36
Gender %					
Male	70.67%	65.02%	55.48%	49.74%	61.18%
Female	29.33%	34.98%	44.52%	50.26%	38.82%
Race/Ethnicity %					
Caucasian	58.99%	53.54%	42.39%	35.83%	42.13%
African-American	30.22%	40.78%	47.83%	53.48%	48.78%
Hispanic	2.52%	2.84%	4.71%	3.74%	3.42%
Other/Unspecified	8.27%	2.84%	5.07%	6.95%	5.67%

Measures

Battelle Developmental Inventory, Second Edition (BDI-2; Newborg, 2005). The purpose of the BDI-2 is to assess developmental skills in children from birth to 7 years 11 months (Newborg, 2005). The BDI-2 is one of the most widely used tests in the United States to measure multiple domains of development (Brassard & Boehm, 2007). This scale is designed to be used with children with, without, and at risk for DD. Administration includes structured, observation, and interview components in response to 450 questions addressing issues related to the child's skills using a Likert scale of 0 (no ability), 1 (emerging ability), or 2 (ability in this skill). Answers correspond to one of the five domains comprising the overall score: adaptive, personal-social, communication, motor, and cognitive. Each of these domains includes two or more subdomains (e.g., "Communication" is comprised of both "Receptive" and "Expressive" subscales). These subdomains are given scaled scores ($M = 10$; $SD = 3$), which are combined into the domain scores, which are then integrated into an overall DQ ($M = 100$, $SD = 15$).

The BDI-2 exhibits robust psychometric properties. Test-retest reliability is above .80 for the total score and all domain scores, with internal consistency coefficients ranging from .98 to .99 (Newborg, 2005). Test-retest reliability for individuals with or at risk for developmental delays, based on 2 to 25 day intervals between first and second assessment in a group of four-year-old and a group of two year old children, was above .80 for all domain and total scores (Alfonso, Rentz, & Chung, 2010). Overall test-retest reliability for the two year old group was .93 (Bliss, 2007). Internal consistency coefficients range from .98 to .99 (Newborg, 2005).

Baby and Infant Screen for Children with aUtIsm Traits - Demographics Form (BISCUIT). The BISCUIT is an informant rated diagnostic tool designed to assess for ASD in children 17-37 months of age (Matson et al., 2009). The BISCUIT consists of a demographic form and three parts, which assess symptoms of ASD, comorbid psychopathology, and challenging behaviors. The section of interest for this analysis, the BISCUIT - Demographic Form, contains questions about the child's history. For example, the form includes questions regarding the child's date of birth, birthweight, current measurements (i.e., height/weight), ethnicity, medical history, and developmental milestones. For the purposes of this study, the child's birthweight and medical history (i.e., weeks of gestation) were used to determine group membership.

Procedure

The Louisiana State University Institutional Review Board and the State of Louisiana's Office for Citizens with Developmental Disabilities approved the study before test administration and continually throughout the years of data collection as part of statewide screening and early service provision efforts. Personal identifiers of EarlySteps participants, including name and date of birth, were removed from the database by the Department of Health and Hospitals before receipt. Prior to December 2013, informed consent was collected from all participants; however, as data was obtained from a deidentified database provided for research purposes, it was determined upon re-approval by the institutional review boards that informed consent was not required from participants. Therefore, informed consent was not collected for EarlySteps participants evaluated after December 2013. Each of the approximately 175 test administrators held an appropriate degree and certification or licensure to qualify to provide services in the State of Louisiana's EarlySteps program. Assessors had licensures or certifications in a variety of fields, including psychology, occupational therapy, speech and language pathology, physical therapy, special education and social work. Obtained degrees earned by administrators ranged from bachelor's degrees in early childhood education to doctoral degrees in psychology. All providers were deemed proficient in assessment of and intervention for young children, and also had experience administering the BDI-2 and collecting relevant demographic and medical information.

CHAPTER 8: PART 1

Statistical Analysis

A power analysis was conducted to establish appropriate sample sizes, *a priori* (Faul, Erdfelder, Lang, & Buchner, 2007). A power of 0.80 and an alpha of 0.05 were used along with an effect size of 0.25 as these are considered adequate and reasonable levels accepted within the research field (Cohen, 2008). The power analysis for the analysis of variance (ANOVA) using these settings indicated a minimum sample size of 180 participants. Since the dataset exceeds this amount, all participants meeting the study inclusion/exclusion criteria (i.e., within appropriate age limits) and those without missing data were initially included. Chi-square analyses were conducted to determine if the groups (i.e., PRE, LBW, PLBW, FT) differ on the demographic variables of ethnicity and/or gender. An ANOVA was performed to detect any differences in age at time of assessment between the four groups.

Initial analyses involved conducting an ANOVA, with DQ total score as the dependent variable and group membership (i.e., LBW, PRE, PLBW, FT) as the independent variable. This analysis was used to determine whether there were main differences among the diagnostic groups. A Bonferroni post hoc test was used to determine where these differences rest. To confirm the ANOVA, assumption of normal distribution, a Kolmogrov-Smirnov test of normality was performed to test for significant differences between this distribution of scores and a normal distribution (Field, 2009).

After the preliminary assessment was completed, a multiple analysis of variance (MANOVA) was used to determine potential relationships among the five scales of the BDI-2 (i.e., adaptive, personal-social, communication, motor, cognitive skills), using group membership as an independent variable and total scale score as a dependent variable. GPower was used to determine the appropriate number of participants in the sample. Based on a power of 0.80, alpha of 0.05, a medium effect size of 0.25, and five response variables, it was determined that a total of 32 participants would be needed. Significant findings were further assessed using a discriminant function analysis to identify which developmental domains contributed most to differences among the groups. All statistical analyses were carried out using SPSS 23.0.

Hypotheses

It was hypothesized that the FT group would have the highest overall DQ score and domain scores, indicating the least impairment in areas of development. This assumption was based on literature indicating that compared to their FT peers, children born at a premature age, LBW, and PLBW exhibit greater impairments in cognitive functioning, motor skills, and language and experienced higher rates of behavioral problems, CP, and internalizing problems (Aarnoudse-Moens et al., 2009; Abbott, 2015; Allen, 2002; Goldenberg et al., 1996; Hack & Fanaroff, 1999; Larroque et al., 2008; Shah & Kingdom, 2011; Stolt et al., 2014). It was hypothesized that the PLBW group would exhibit the overall lowest DQ score and lowest cognitive domain score compared to the other groups. Support for this assumption comes from the limited literature suggesting that greater impairments in functioning as a result of the combined effects of premature birth and LBW, specifically in the area of intellectual functioning (Aarnoudse-Moens et al., 2009; Goldenberg et al., 1996).

Results

Preliminary Analysis. Two chi-square tests for association were conducted between gender and group assignment and ethnicity and group assignment (i.e., FT, PRE, LBW, PLBW). All expected cell frequencies were greater than five for both tests. There was a statistically significant association between gender and group assignment, $\chi^2(3) = 12.714$, $p < .001$ and a significant associate between ethnicity and group assignment $\chi^2(9) = 46.210$, $p < .001$. Differences in gender were expected for this sample because males are at higher risk than females for preterm birth (Brettell, Yeh, & Impey, 2008; Jongbloet, 2005; Zeitlin, Ancel, Larroque, Kaminski, & the EPIPAGE group, 2004) due to a greater vulnerability to complications (e.g., infection), greater body weight, and an association between male sex hormones and preterm labor (Cooperstock & Campbell, 1996; Zeitlin et al., 2004). Differences in ethnicity were also expected for this sample with non-Hispanic black women having the highest rate of low birthweight and preterm births, around 16% (Martin, Hamilton, & Osterman, 2014; Martin et al., 2015; Tucker et al., 2015). A one-way ANOVA was conducted to determine if between groups differences existed in age at time of the assessment. Age at time of assessment was not statistically different among the groups, $F(3, 997) = 1.647$, $p = 0.177$.

Preliminary assumption checking for the initial ANOVA revealed that were no outliers in the data, as assessed by inspection of a boxplot for values greater than 1.5 box-lengths from the edge of the box. DQ score was normally distributed, as assessed by Kolmogrov-Smirnov test of normality ($p > .05$). The assumption of homogeneity of variances was met, as assessed by Levene's Test of Homogeneity of Variance ($p = 0.969$).

Preliminary assumption checking for the MANOVA revealed that the first three assumptions of a MANOVA were met; 1) there was a continuous dependent variable, 2) the independent variable was categorical with two or more independent groups, and 3) there was independence of observations. Next, the data was inspected for univariate outliers and normality. Several outliers were found (Figure 2). Outliers were reviewed for possible data entry mistakes. As none were found, and their exclusion was not found to impact the model, the decision was made to include all outliers in the sample (Tabachnick & Fidell, 2007).

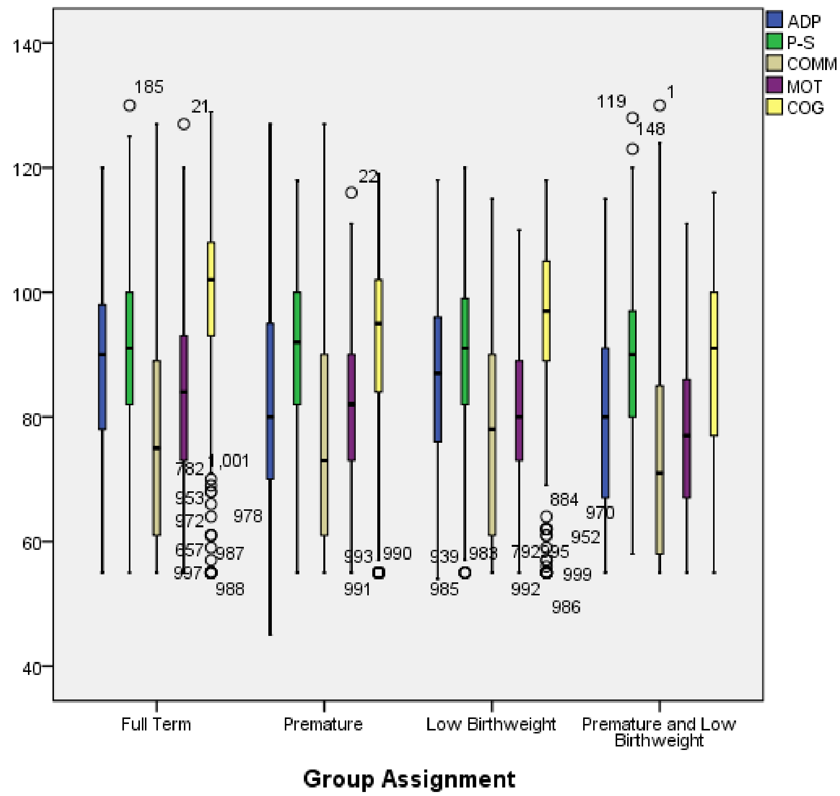
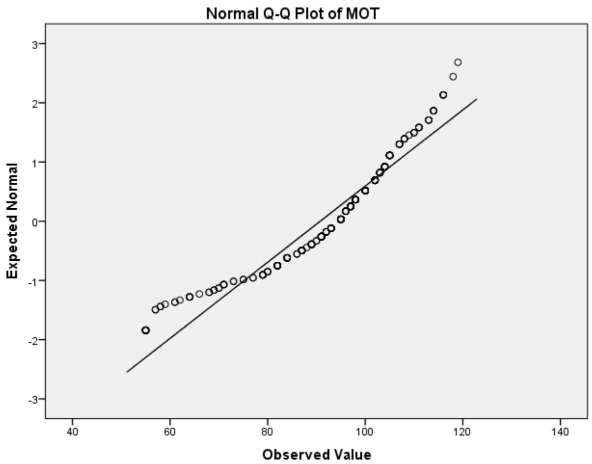
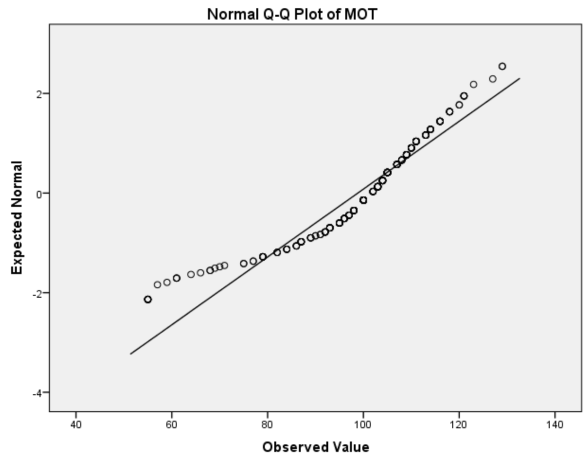


Figure 2. Boxplot from untransformed data

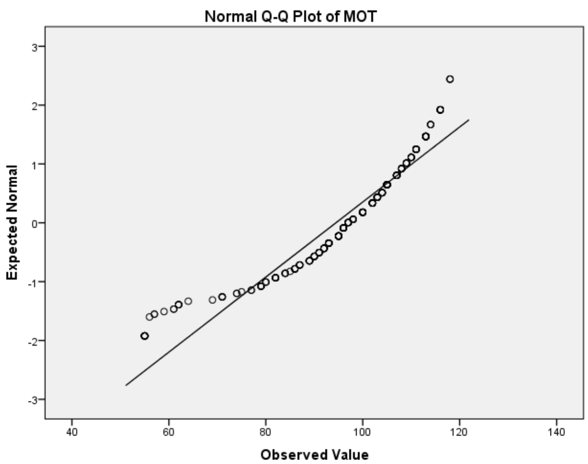
With regard to normality, the MOT domain scores were not normally distributed for each group, as assessed by examining normal Q-Q plots (Figure 3) and the Shapiro-Wilk's test. Therefore, the MOT variable was transformed using a square root transformation. The transformation was found to impact the model and therefore all data analysis was conducted using the transformed data (Figure 4).



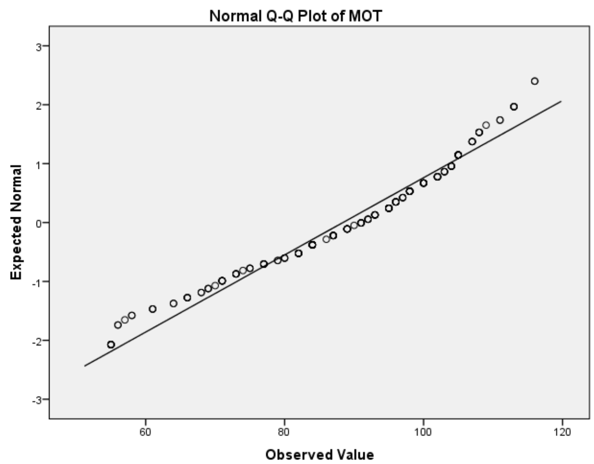
1. Full Term



2. Premature

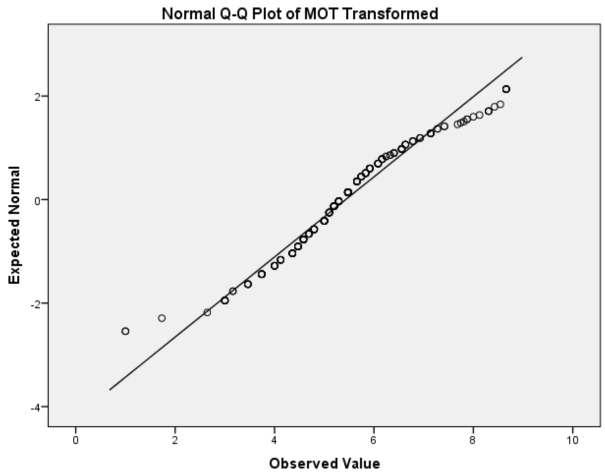


3. Low Birthweight

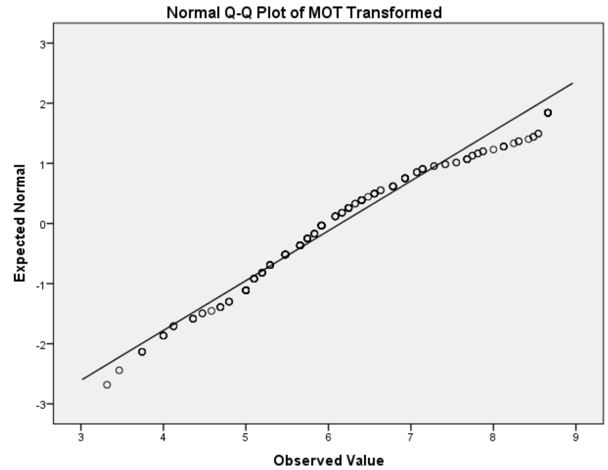


4. Premature and Low Birthweight

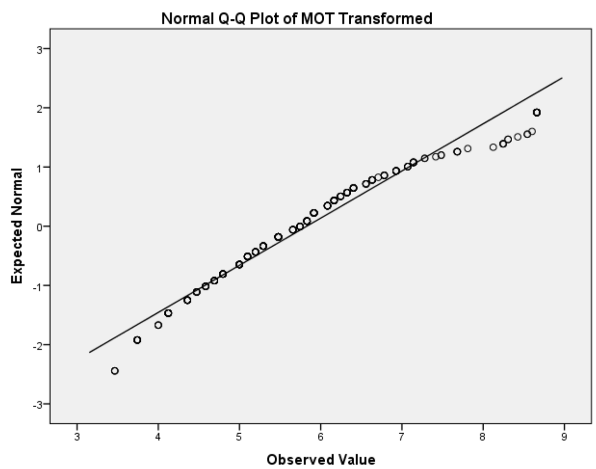
Figure 3. Normal Q-Q Plots of MOT from the untransformed data



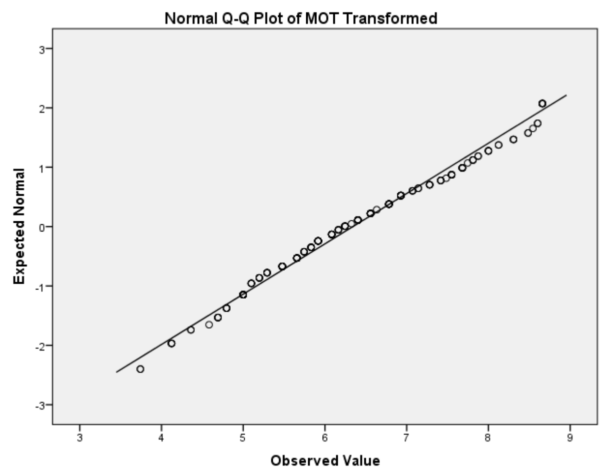
1. Full Term



2. Premature



3. Low Birthweight



4. Premature and Low Birthweight

Figure 4. Normal Q-Q Plots of MOT from the transformed data

Next, it was found that the assumptions of multicollinearity and linearity were met. There was no multicollinearity, as assessed by Pearson correlation. There was a linear relationship between domain scores for each group, as assessed by scatterplot. Finally, the assumptions for homogeneity of variance-covariance matrices and homogeneity of variances were checked. The assumption of homogeneity of variance-covariance matrices was violated, as assessed by Box's M test of equality of covariance matrices ($p < .001$). However, when sample sizes are equal or close to, it is recommended that the Box's M statistics be interpreted cautiously because it is a highly sensitive test of the violation of the multivariate normality assumption, particularly with large sample sizes (Tabachnick & Fidell, 2007). The assumption of homogeneity of variances was met, as assessed by Levene's Test of Homogeneity of Variance (ADP, $p = 0.089$; P-S, $p = 0.293$; COMM, $p = 0.858$; MOT, $p = 0.159$; COG, $p = 0.083$).

Main Analysis. Descriptive statistics revealed that participants in the PLBW groups scored the lowest on all areas of development compared to the FT, PRE and LBW groups. The FT group scored the highest on all areas of development, with the exception of the COMM domain, in which the LBW group scored the highest. Complete descriptive statistics are presented in Table 2.

Table 2. Means and Standard Deviations for BDI-2 total and domain scores for participant groups

	Group Assignments									
	FT (*n* = 283)		PRE (*n* = 283)		LBW (*n* = 283)		PLBW (*n* = 189)		Total	
BDI-2 Domains	M	*SD*	M	*SD*	M	*SD*	M	*SD*	M	*SD*
Total Developmental Quotient	84.65	*15.10*	80.96	*14.75*	82.48	*14.93*	77.51	*14.60*	81.75	*14.60*
Adaptive	87.58	*14.11*	81.74	*15.50*	85.38	*14.67*	79.14	*14.71*	83.85	*15.06*
Personal-Social	90.92	*14.35*	90.84	*12.69*	90.22	*12.78*	89.15	*13.26*	90.38	*13.28*
Communication	76.29	*16.62*	76.08	*16.76*	77.17	*16.21*	73.33	*16.82*	75.93	*16.61*
Motor	98.84	*14.68*	90.77	*15.55*	94.46	*15.68*	88.39	*15.27*	93.54	*15.76*
Cognitive	82.63	*13.82*	81.26	*12.32*	80.27	*12.30*	77.32	*11.76*	80.65	*12.76*

A one-way ANOVA was first run to determine the effect of premature and/or LBW on general developmental level. There was a statistically significant difference among the groups on the DQ variable, $F(3, 997) = 8.87$, $p < .001$; partial $\eta^2 = 0.026$. A post hoc test using the Bonferroni correction indicated that the FT group had significantly higher total DQ score than the PRE and PLBW groups ($p = 0.023$ and $p < .001$, respectively) but not the LBW group ($p = 0.526$). The LBW group had a significantly higher total DQ score than the PLBW group ($p <$

.001) but not the PRE group (p = 1.00). Children in the PLBW group did not have a significantly lower total DQ score from their peers in the PRE group (p = .093). See Table 3 for significant group comparisons.

Table 3. Significant post-hoc group comparisons.

	Group comparison
Developmental Quotient	FT - PRE*, FT - PLBW***, LBW - PLBW**

Note: FT = Full Term, PRE = Premature, LBW = Low Birthweight, PLBW = Premature and Low Birthweight; * $p < .05$, ** $p < .01$, ***$p < .001$.

Next, a one-way MANOVA was used to determine the effect of PRE and/or LBW on distinct developmental outcomes. Five areas of development were assessed: adaptive skills, personal-social skills, communication skills, motor skills, and cognitive skills. There was a statistically significant difference among the groups on the combined dependent variables, $F(15, 2742) = 8.43$, $p < .001$; Wilks' $\Lambda = 0.883$; partial $\eta^2 = 0.041$. A discriminant analysis was performed where the 5 distinct BID-2 development domains served as predictors of group membership. Three discriminant functions were revealed. The first function explained 85.3% of the variance, canonical $R^2 = 0.10$, whereas the second and third explained 10%, canonical $R^2 = .01$ and 4.7%, canonical $R^2 = 0.01$, respectively. In combination, the first three discriminant functions significantly differentiated the groups, $\Lambda = 0.88$, $\chi^2(15) = 129.72$, $p < .001$, as did the second and third, $\Lambda = 0.98$, $\chi^2(8) = 19.87$, $p < .01$; however, removing the second function indicated that the third function did not significantly differentiate the groups, $\Lambda = 0.99$, $\chi^2(3) = 6.36$, $p > .05$. Therefore, only functions 1 and 2 were interpreted.

The correlations between outcomes and the discriminant functions revealed the ADP loaded more highly with function 1 than function 2 (r = 0.607, r = -0.019, respectively); P-S loaded more strongly with function 2 (r = 0.304) than function 1 (r = 0.083); COMM loaded fairly evenly on functions 1and 2 (r = 0.141, r = 0.064, respectively). MOT loaded more highly with functions 1 than function 2 (*r* = 0.736, *r* = 0.103, respectively); COG loaded more highly on functions 2 (*r* = 0.743) than function 1 (*r* = 0.314; Table 4).

Table 4. Pooled within-groups correlations between discriminating variables and standardized canonical discriminant functions.

	Functions		
Predictors	1	2	3
MOT	0.736*	0.103	0.053
ADP	0.607*	-0.019	0.492
COG	0.314	0.743*	0.439
P-S	0.083	0.304	0.222
COMM	0.141	0.064	0.771

Note: MOT = Motor Skills; ADP = Adaptive Skills; COG = Cognitive Skills; P-S = Personal Social Skills; COMM = Communication Skills; * = correlations above 0.33

Using 0.33 to constitute a large enough loading to define a function (Tabachnick & Fidell, 2007), the structure (loading) matrix of correlations between predictors and discriminate functions, suggested that the best predictors for distinguishing among the groups (function 1) are motor skills (MOT domain) and adaptive skills (ADP domain). Motor skills and adaptive skills are closely related and are often interconnected in that specific motor abilities are a prerequisite for carrying out certain adaptive behaviors (e.g., fine motor skills necessary for zippering a jacket). The mean of the discriminant function scores for function 1 was highest for participants in the FT group (*M* = 0.467) and lowest for participants in the PLBW group (*M* = -0.435).

For function 2, the structure (loading) matrix of correlations between predictors and discriminate functions, suggested that the best predictors for distinguishing between the groups is cognitive skills (COG domain). None of the other factors had a large enough loading to define function 2. The COG domain reflects skills that are less observable in the natural environment and often require contriving situations to measure. Skills related to the COG domain are also often taught and are less likely to be acquired through observation compared to the skills characterized by the other domains. For function 2, participants in the PRE group had the highest mean (*M* = 0.151) and participants in the LBW group had the lowest (*M* = -0.133); however, the means for all 4 groups are very close for function 2 (Table 5).

Table 5. The means of the discriminant function scores by group for each function calculated

Group Assignment	Functions		
	1	2	3
Full Term	0.467	0.050	-0.062
Premature	-0.271	0.151	0.048
Low Birthweight	0.093	-0.133	0.091
Premature and Low Birthweight	-0.435	-0.102	-0.116

Function 1 did most of the work in separating the groups; however, the error rate for classification is relatively high (Figure 5). The model does a fairly good job at classifying children born FT (59%), but is not as effective as classifying children born PRE (26%), LBW (25%), or PLBW (43%; Table 6).

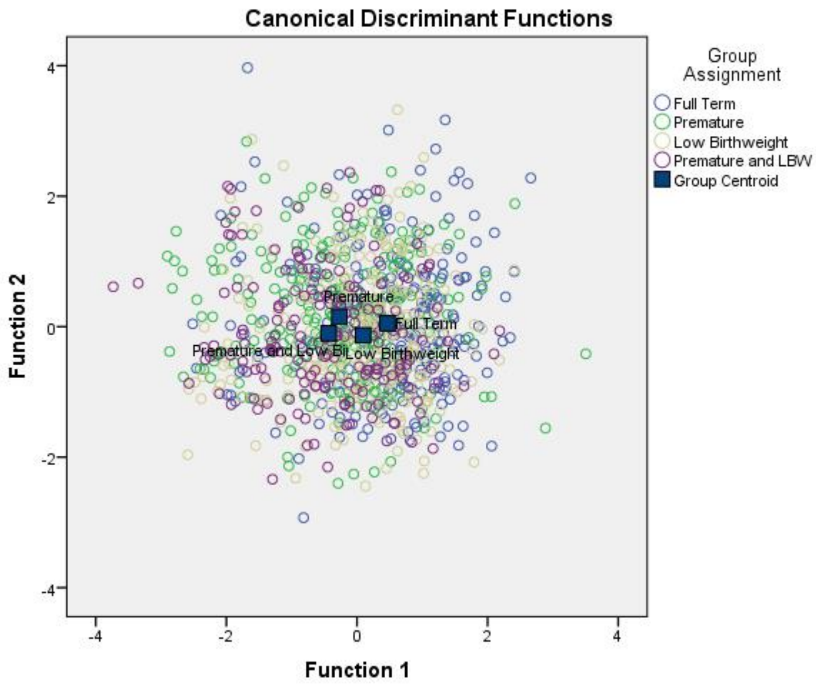


Figure 5. Combined groups plot

Table 6. Classification Results.

Group Assignment	Predicted Group Membership: Full Term	Premature	Low Birthweight	Premature and Low Birthweight
Full Term	59.0%	11.0%	15.8%	14.3%
Premature	24.2%	26.4%	19.4%	30.0%
Low Birthweight	38.5%	13.6%	25.5%	22.3%
Premature and Low Birthweight	20.3%	23.1%	13.7%	42.9%

Note: 38.1% of original grouped cases correctly classified.

Discussion

There is a strong association between premature birth and/or LBW and risk for impairment in areas of development (Aarnoudse-Moens et al., 2009; Abbott, 2015; Allen, 2002; Goldenberg et al., 1996; Hack & Fanaroff, 1999; Larroque et al., 2008; Shah & Kingdom, 2011; Suvi Stolt et al., 2014). Few studies have investigated the independent effects of being born either premature, LBW, or PLBW on developmental outcomes. Descriptive statistics of this sample suggested that children born premature and/or LBW exhibit different developmental profiles. As such, it is important that these populations be distinguished early in life and treatment strategies be tailored to each population.

Participants in the PLBW group scored the lowest in all domains of development examined. Lower scores are associated with greater impairment. This finding was not surprising as it was hypothesized that the combined effect of being born premature would be associated with a disruption in the pattern of brain development, and LBW, associated with fetal malnutrition, would have the largest impact of developmental outcomes (Aarnoudse-Moens et al., 2009; Anderson & Doyle, 2004; Goldenberg et al., 1996; Hall & Wolke, 2012; Kapellou et al., 2006; Rees et al., 2008). Not unanticipated, the FT group scored the highest in the areas of motor skills, adaptive skills, personal-social skills, and cognitive skills. Unexpectedly, the LBW group scored the highest for communication skills, indicating the least impairment in this area of development. However, the difference between mean scores for the FT group and the LBW group on the COMM domain was modest, less than a point. Thus, the participants in the LBW group had communications skills on par with those in the FT group, suggesting no apparent impairment in this area.

The discriminant function analysis suggested that the group separation can best be explained in terms of two underlying functions. Discriminant function analysis is useful for building a predictive model of group membership based on observed characteristics of each group. For function 1, which explains most of the variance, the predictors that best separate the groups were the MOT domain and the ADP domain. These data indicate that these groups can be best distinguished by their level of impairment of motor skills and adaptive skills. Communication, personal-social, and cognitive skills were not loaded on function 1, i.e., these skills are the weakest predictors which suggests that these developmental areas are not associated with group membership but are rather/instead a function of other unassessed factors. For function 2, which explained a significant but much smaller amount of the variance, the predictor that best separated the groups was participants' score on the COG domain. Therefore, level of impairment of cognitive abilities can distinguish among the groups.

Motor skills and adaptive skills are easily observable and interrelated which may explain why they both loaded highly on the first function. For example, a child needs fine motor abilities to grasp a zipper and zip up a jacket. Without the fine motor ability, the child would not be able to dress themselves, which is considered an adaptive skill. Children that are born LBW, either premature or not, more often experience medical complications which may limit their mobility. These limitations may manifest early in their life, prior to hospital discharge, and persist thereafter. The delays may also be a result of the medical condition itself (e.g., gastrostomy tube, braces) which limit mobility and thus slow down development of motor skills. Additionally, brain injury as a result of preterm birth has been associated with motor impairments (Allen, 2002; Staudt et al., 2003). Children born full term are less likely to experience limited mobility in early development or have medical conditions that are likely to lead to limited mobility and thus, are less at risk for motor skill delays.

In regard to classification, the discriminant function analysis was best, however not excellent, at correctly classifying participants that were FT. The model was fair at correctly classifying children born PLBW, but poor at classifying children born premature or LBW. The overall poor classification ability of the model may be attributed to characteristics of the study cohort. The study participants were selected from a clinical sample that was referred for a host of neurodevelopmental concerns. The impact of prematurity and LBW compared to the FT participants may be less apparent in a sample of children referred because of developmental concerns.

The composition of the premature and LBW groups may have also contributed to the unexpected findings. For example, in this study, the LBW group contained children whose birthweights ranged from 453g to 2500g. Forty-eight percent of the participants in the LBW group fell into the 2500-1500gs range, 22% fell into the 1500-1001g, and 30% weighed <1000g. Much of the research to date has found that as birthweight decreases, level of impairment increases (Hack et al., 1995). With the majority of participants falling into the highest weight range, it could have skewed upward toward the average score within this group. The designation LBW encompasses a wide range of birthweights. Hence, this finding, in light of previous research, suggests that to best understand the developmental outcomes of these children, researchers should separate children deemed premature or LBW into subgroups (i.e., LBW, VLBW, ELBW, LPT, VPT, EPT). Studying the groups as a whole is informative, but the degree of prematurity or LBW likely contributes to complications associated with their developmental outcomes.

CHAPTER 9: PART 2

Statistical Analyses

Utilizing GPower with the prespecified power of 0.80, an effect size of at least 0.15 (f2), and error probability of $\alpha = 0.05$, the total sample size required for Part 2 to complete the multiple regression was 131 participants. Univariate analysis was conducted to describe the sample and perform variable diagnostics. Before the regression models were built, bivariate relationships between the dependent and independent variables were examined (e.g., chi square, t-test, simple linear regression). All significant variables were included in the regression model.

Six multiple regression analyses were conducted to examine factors influencing the BDI-2 DQ and domain total scores. BDI-2 DQ and domain total scores (i.e., adaptive, personal-social, communication, motor, cognitive skills) served as a dependent variable for each of the multiple regression models. The independent variables included birthweight, weeks of gestation, age, gender, and race. The assumptions of multiple regressions were analyzed for any violations that required correction before the six multiple regressions were run. Checking that no violations occurred ensured the accuracy of the predictions, assessed how well the regression model fits the data, determined the variation in the dependent variable explained by the independent variables, and tested the hypotheses on the regression equation.

Measurement of Variables

Five independent variables were examined in this study: birthweight, weeks of gestation, age, gender, and race. All five independent variables were used in each of the six multiple regression models. The dependent variables examined were total BDI-2 DQ score in model 1, total Adaptive domain (ADP) score in model 2, total Personal-Social domain (P-S) score in model 3, total Communication domain (COMM) score in model 4, total Motor domain (MOT) score in model 5, and total Cognitive domain (COG) score in model 6 (Figure 6).

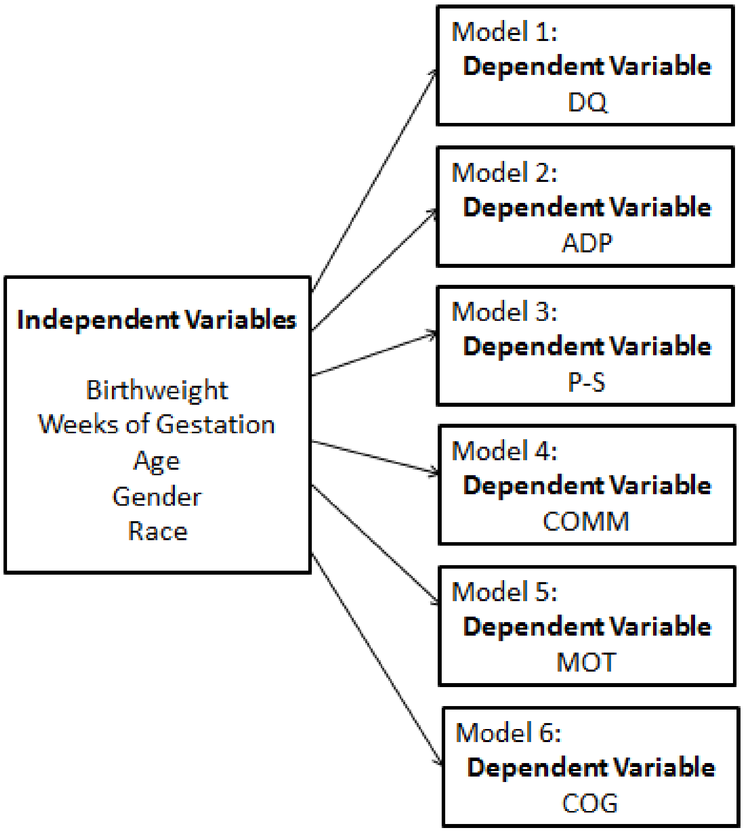


Figure 6. Full multiple regression models

Operationalization of variables

Dependent Variables

Developmental Quotient. DQ total score was calculated by summing the scaled score from the five developmental domains. The DQ represents a child's general level of development, and where the child is in the process of developing age appropriate abilities. DQ was a continuous variable.

Adaptive Domain. The ADP assesses ability to use information and skills in daily living. The ADP contains two subdomains: self-care and personal responsibility. Subdomain scores are summed and the raw scores are converted into scaled scores (*M* = 10, *SD* = 3), age equivalents, and percentile ranks. The scaled scores for each subdomain are added together to obtain the domain sum. ADP was a continuous variable.

Personal-Social Domain. The P-S assesses positive social interactions and social skills. The P-S is made up of three subdomains: adult interaction, peer interaction, and self-concept and social role. Subdomain scores are summed and the raw scores are converted into scaled scores (M = 10, SD = 3), age equivalents, and percentile ranks. The scaled scores for each subdomain are added together to obtain the domain sum. P-S was a continuous variable.

Communication Domain. The COMM domain assesses how effectively a child expresses and receives information verbally and nonverbally. The COMM contains two subdomains: receptive communication and expressive communication. Subdomain scores are summed and the raw scores are converted into scaled scores (M = 10, SD = 3), age equivalents, and percentile ranks. The scaled scores for each subdomain are added together to obtain the domain sum. COMM was a continuous variable.

Motor Domain. The MOT assesses ability to use and control small and large movements. The MOT contains three subdomains: gross motor, fine motor, and perceptual motor. Subdomain scores are summed and the raw scores are converted into scaled scores (M = 10, SD = 3), age equivalents, and percentile ranks. The scaled scores for each subdomain are added together to obtain the domain sum. MOT was a continuous variable.

Cognitive Domain. The COG assesses mental and intellectual abilities. The COG contains three subdomains: attention and memory, reasoning and academic skills, and perception and concepts. Subdomain scores are summed and the raw scores are converted into scaled scores (M = 10, SD = 3), age equivalents, and percentile ranks. The scaled scores for each subdomain are added together to obtain the domain sum. COG was a continuous variable.

Independent Variables

Birthweight. Birthweight is obtained from the BISCUIT - Demographic Form based on caregiver report. Birthweight is a continuous variable but for this study it was recoded into categorical dummy variables representing weights below 2,500 grams: normal birthweight served as the reference, ELBW (<1000g; = 1, else = 0), VLBW (1001 - 1500g; = 1, else = 0), LBW (1501 - 2500g; = 1, else = 0).

Weeks of Gestation. Weeks of gestation was collected on the BISCUIT-Demographic Form if a caregiver reported that the child was born prematurely. Weeks of gestation is a continuous variable but for this study it was recoded into categorical dummy variables representing degree of premature birth: FT (≥37 weeks) served as the reference, EPT (<26weeks; = 1, else = 0), VPT (26-33 weeks; =1, else = 0), and LPT (34-36 weeks; = 1, else = 0).

Age. Age in months at time of the evaluation was collected prior to administration of the BDI-2 from the child's caregiver to determine where to begin test administration. This variable was continuous.

Gender. Gender is based on caregiver report was collected at the beginning of the administration of the BDI-2. Gender was coded dichotomously (male = 0, female = 1).

Race. Race was obtained through the caregiver report as part of the BISCUIT – Demographic From. Response categories included Caucasian, African American, Hispanic, and other. Race was recoded into categorical dummy variables, other served as the reference.

Hypotheses

After reviewing the literature, it was hypothesized that weeks of gestation and birthweight would serve as significant predictors of DQ score and domain scores. It was further hypothesized that weeks of gestation and birthweight would have independent effects on developmental outcomes such that as weeks of gestation decreases, developmental delays increase. Studies looking at both weeks of gestation and birthweight have found that in several areas of development, decreasing weeks of gestation and birthweight negatively, affect development (Allen et al., 2011; Bhutta et al., 2002; Hack et al., 1995; Petersen et al., 1990; Saigal et al., 1991). Therefore, it was expected that the children born EPT and ELBW would serve as the best predictors of developmental delays. For example, Larroque and colleagues reported that cognitive impairments were found in 12% of children born FT compared to 26% of children born at 32 weeks of gestation and 44% of children born between 24 and 25 weeks of gestation. Those born EPT had significantly higher rates of cognitive impairment compared to both their

FT term peers and VPT peers. This same trend is observed in children born ELBW (Hack et al., 1995).

Results

Model 1 (DQ). The same sample from Part 1 was utilized for Part 2; therefore, univariate findings remained the same. A multiple regression was run to predict DQ from birthweight, weeks of gestation, age, gender, and race. All assumptions of a multiple regression were checked. There was one dependent variable (i.e., DQ), that was measured at the continuous level and two or more independent variables that were measured either at the continuous or nominal level. There was linearity as assessed by partial regression plots and a plot of studentized residuals against the predicted values. Independence of residuals was also established, as assessed by a Durbin-Watson statistic of 2.081. There was homoscedasticity, as assessed by visual inspection of a plot of studentized residuals versus unstandardized predicted values. No evidence of multicollinearity was noted, as assessed by tolerance values greater than

0.1. There were no studentized deleted residuals greater than ±3 standard deviations, no leverage values less than 0.2, and no values for Cook's distance above 1.

Birthweight, weeks of gestation, age, gender, and race significantly predicted DQ, $F(11,973) = 9.528$, $p < .001$, adj. $R^2 = 0.087$. Three of the variables added significantly to the prediction, $p < .05$. Birthweight was found to be a significant predictor of DQ, indicating that children born ELBW scored 6.30 points lower ($t = -3.62$; $p < .001$) on the DQ than children born more than 2500g. Weeks of gestation was a significant predictor of DQ, with results indicating that children born EPT scored 5.26 points lower ($t = -2.40$; $p < .05$) on the DQ than children born more than 26 weeks of gestation. Gender was found to be a significant predictor of DQ, with female gender associated with a 2.97 point increase ($t = 3.14$; $p < .01$) in the DQ scores. Regression coefficients and standard errors for Model 1 can be found in Table 7.

Table 7. Summary multiple regression analysis for Model 1 (DQ).

Variable	*B*	SE_B	β
Age	-0.032	0.096	-0.010
Gender			
Male (reference)	-	-	-
Female	2.97	0.946	0.096*
Race			
African American	-1.33	2.26	-0.044
Caucasian	3.80	2.25	0.126
Hispanic	-2.28	3.47	-0.025
Other (reference)	-	-	-
Birthweight			
Normal (reference)	-	-	-
Low Birthweight	0.137	1.20	0.004
Very Low Birthweight	-1.55	1.65	-0.037
Extremely Low Birthweight	-6.30	1.74	-0.169*
Weeks of Gestation			
Full Term (reference)	-	-	-
Late Preterm	-2.93	1.51	-0.062
Very Preterm	-0.756	1.32	-0.022
Extremely Preterm	-5.26	2.20	-0.095*

Note. * $p < .05$; *B* = unstandardized regression coefficient; SE_B = standard error of the coefficient; β = standardized coefficient

Model 2 (ADP). The assumptions of a multiple regression were again checked as was done for Model 1. All assumptions were met. Of note, there was independence of residuals, as assessed by a Durbin-Watson statistic of 2.054. Birthweight, weeks of gestation, age, gender, and race significantly predicted ADP, $F(11,973) = 10.961$, $p < .001$, adj. $R^2 = 0.100$. Six of the variables added significantly to the prediction, $p < .05$. Birthweight was found to be a significant predictor of ADP, with results indicating that children born ELBW scored 6.22 points lower (t = -3.61; $p < .001$) on the ADP than children born more than 2500g. Weeks of gestation was found to be a significant predictor of ADP, with results indicating that children born LPT scored 4.51 points lower (t = -3.01; $p < .05$), children born VPT scored 3.54 points lower (t = -2.71; $p < .05$), and children born EPT scored 5.00 points lower (t = -2.29; $p < .05$) on the ADP than children born more than 37 weeks of gestation. Age was found to be a significant predictor of ADP, indicating that each additional year of age was associated with a .463 point increase (t = -2.29; $p < .001$) in ADP score. Finally, gender was found to be a significant predictor of ADP, with female gender associated with a 3.14 point (t = 3.34; p = .001) increase in the ADP scores. Regression coefficients and standard errors for Model 2 can be found in Table 8.

Table 8. Summary multiple regression analysis for Model 2 (ADP).

Variable	*B*	SE_B	β
Age	0.463	0.095	0.149*
Gender			
Male (reference)	-	-	-
Female	3.14	0.940	0.102*
Race			
African American	-1.13	2.25	-0.037
Caucasian	2.49	2.24	0.083
Hispanic	-0.048	3.44	-0.001
Other (reference)	-	-	-
Birthweight			
Normal (reference)	-	-	-
Low Birthweight	0.167	1.19	0.005
Very Low Birthweight	-0.442	1.64	-0.011
Extremely Low Birthweight	-6.23	1.73	-.167*
Weeks of Gestation			
Full Term (reference)	-	-	-
Late Preterm	-4.51	1.50	-0.096*
Very Preterm	-3.54	1.31	-0.104*
Extremely Preterm	-5.00	2.18	-0.090*

Note. * $p < .05$; *B* = unstandardized regression coefficient; SE_B = standard error of the coefficient; β = standardized coefficient

Model 3 (P-S). The assumptions of a multiple regression were again checked as was done for Model 1. All assumptions were met. Of note, there was independence of residuals, as assessed by a Durbin-Watson statistic of 1.907. Birthweight, weeks of gestation, age, gender, and race significantly predicted P-S, $F(11,973) = 7.557$, $p < .001$, adj. $R^2 = 0.068$. Two of the variables added significantly to the prediction, $p < .05$. The first, age, was found to be a significant predictor of P-S, indicating that each additional year of age associated with a 0.388 point decrease ($t = -4.54$; $p < .001$) in P-S score. The second, gender, was found to be a significant predictor of P-S, with female gender associated with a 3.19 point ($t = 3.77$; $p < .001$) increase in the P-S scores. Regression coefficients and standard errors for Model 3 can be found in Table 9.

Table 9. Summary multiple regression analysis for Model 3 (P-S).

Variable	*B*	SE_B	β
Age	-0.388	0.085	-0.141*
Gender			
Male (reference)	-	-	-
Female	3.19	0.846	0.117*
Race			
African American	-1.37	2.02	-0.052
Caucasian	2.50	2.01	0.094
Hispanic	-2.32	3.10	-0.029
Other (reference)	-	-	-
Birthweight			
Normal (reference)	-	-	-
Low Birthweight	0.809	1.07	0.029
Very Low Birthweight	0.594	1.47	0.016
Extremely Low Birthweight	-2.34	1.56	-0.071
Weeks of Gestation			
Full Term (reference)	-	-	-
Late Preterm	-1.05	1.35	-0.025
Very Preterm	1.47	1.18	0.038
Extremely Preterm	-2.94	1.96	-0.060

Note. * $p < .05$; *B* = unstandardized regression coefficient; SE_B = standard error of the coefficient; β = standardized coefficient

Model 4 (COMM). The assumptions of a multiple regression were again checked as was done for Model 1. All assumptions were met. Of note, there was independence of residuals, as assessed by a Durbin-Watson statistic of 1.981. Birthweight, weeks of gestation, age, gender, and race significantly predicted COMM, $F(11,973) = 5.939$, $p < .001$, adj. $R^2 = 0.052$. Three of the variables added significantly to the prediction, $p < .05$. Birthweight was found to be a significant predictor of COMM, with results indicating that children born ELBW scored 4.09 points lower on the COMM than children born more than 2500g ($t = -2.09$; $p < .05$). Age was found to be a significant predictor of COMM, indicating that each additional year of age was associated with a 0.321 point increase ($t = 2.98$; $p < .01$) in COMM score. Gender was found to be a significant predictor of COMM, with female gender associated with a 4.55 point ($t = 4.27$; *p*

< .001) increase in the COMM scores. Regression coefficients and standard errors for Model 4 can be found in Table 10.

Table 10. Summary multiple regression analysis for Model 4 (COMM).

Variable	*B*	SE_B	β
Age	0.321	0.108	0.093*
Gender			
Male (reference)	-	-	-
Female	4.55	1.07	0.133*
Race			
African American	0.249	2.55	0.007
Caucasian	4.08	2.54	0.123
Hispanic	-3.57	3.90	-0.036
Other (reference)	-	-	-
Birthweight			
Normal (reference)	-	-	-
Low Birthweight	2.07	1.35	0.058
Very Low Birthweight	0.725	1.86	0.016
Extremely Low Birthweight	-4.08	1.96	-0.099*
Weeks of Gestation			
Full Term (reference)	-	-	-
Late Preterm	-1.77	1.70	-0.034
Very Preterm	0.497	1.48	0.013
Extremely Preterm	-2.36	2.47	-0.039

Note. * $p < .05$; *B* = unstandardized regression coefficient; SE_B = standard error of the coefficient; β = standardized coefficient

Model 5 (MOT). The assumptions of a multiple regression were again checked as was done for Model 1. All assumptions were met. Of note, there was independence of residuals, as assessed by a Durbin-Watson statistic of 1.906. Birthweight, weeks of gestation, age, gender, and race significantly predicted MOT, $F(11,973) = 11.964$, $p < .001$, adj. $R^2 = 0.109$. Five of the variables added significantly to the prediction, $p < .05$. Birthweight was found to be a significant predictor of MOT, with results indicating that children born LBW scored 2.57 points lower ($t = -2.07$; $p < .05$), children born VLBW scored 5.26 points lower ($t = -3.08$; $p < .01$), and children born ELBW scored 8.99 points lower ($t = -5.00$; $p < .001$) on the MOT than children born more than 2500g. Weeks of gestation was found to be a significant predictor of MOT, with results indicating that children born LPT scored 3.50 points lower (t = -2.24; p < .05) and children born EPT scored 8.28 points lower (t = -3.65; p < .001) on the MOT than children born more than 37 weeks of gestation. Regression coefficients and standard errors for Model 5 can be found in Table 11.

Table 11. Summary multiple regression analysis for Model 5 (MOT).

Variable	*B*	SE_B	β
Age	0.181	0.099	0.056
Gender			
Male (reference)	-	-	-
Female	-0.174	0.978	-0.005
Race			
African American	0.203	2.34	0.006
Caucasian	2.91	2.33	0.092
Hispanic	-0.102	3.58	-0.011
Other (reference)	-	-	-
Birthweight			
Normal (reference)	-	-	-
Low Birthweight	-2.57	1.24	-0.077*
Very Low Birthweight	-5.26	1.70	-0.121*
Extremely Low Birthweight	-8.99	1.80	-0.230*
Weeks of Gestation			
Full Term (reference)	-	-	-
Late Preterm	-3.50	1.56	-0.071*
Very Preterm	-2.27	1.36	-0.063
Extremely Preterm	-8.28	2.27	-0.143*

Note. * p < .05; *B* = unstandardized regression coefficient; SE_B = standard error of the coefficient; β = standardized coefficient

Model 6 (COG). The assumptions of a multiple regression were again checked as was done for Model 1. All assumptions were met. Of note, there was independence of residuals, as assessed by a Durbin-Watson statistic of 1.935. Birthweight, weeks of gestation, age, gender, and race significantly predicted COG, $F(11,973) = 12.666$, $p < .001$, adj. $R^2 = 0.115$. Three of the variables added significantly to the prediction, $p < .05$. Birthweight was found to be a significant predictor of COG, with results indicating that children born ELBW scored 4.35 points lower on the COG domain than children born more than 2500g (t = -2.99; p < .01). Age was found to be a significant predictor of COG, indicating that each additional year of age associated with a .403 point decrease (t = -5.04; p < .001) in COMM score. Gender was found to be a significant predictor of COG, with female gender associated with a 1.96 point (t = 2.48; p < .05) increase in the COG scores. Regression coefficients and standard errors for Model 6 can be found in Table 12.

Table 12. Summary multiple regression analysis for Model 6 (COG).

Variable	*B*	SE_B	β
Age	-0.403	0.080	-0.152*
Gender			
Male (reference)	-	-	-
Female	1.96	0.791	0.075*
Race			
African American	-2.17	1.89	-0.085
Caucasian	3.65	1.88	0.143
Hispanic	-1.37	2.89	-0.018
Other (reference)	-	-	-
Birthweight			
Normal (reference)	-	-	-
Low Birthweight	-0.098	1.00	-0.004
Very Low Birthweight	-1.81	1.38	-0.051
Extremely Low Birthweight	-4.35	1.45	-0.137*
Weeks of Gestation			
Full Term (reference)	-	-	-
Late Preterm	0.483	1.26	0.012
Very Preterm	0.246	1.10	0.008
Extremely Preterm	-3.23	1.84	-0.069

Note. * p < .05; *B* = unstandardized regression coefficient; SE_B = standard error of the coefficient; β = standardized coefficient

Discussion

There is a paucity of research on the independent effects of being born either premature or LBW on developmental outcomes. It is well established that being born one or the other leads to poorer developmental outcomes; however, not much is known about if either impacts development differentially or if the presence of both alters outcomes. Most research to date on this population combines children born premature and LBW into one group; however, this may be misleading if the effects of premature birth and LBW on the brain are not the same. If the effect on the brain is different, the impact on development may also be different. As such, the aim of this part of the study was to assess the independent effects of weeks of gestation, birthweight, age, race, and gender on developmental outcomes.

In our sample, birthweight, weeks of gestation, age, gender, and race significantly predicted all six of the domains examined (i.e., DQ, ADP, P-S, COMM, MOT, COG). In each model, different variables added significantly to the prediction and with different degrees of influence (Table 13). This finding is important because it informs best practices for treating children, considering their specific characteristics. For example, sex was a significant predictor of DQ, ADP, P-S, and COG scores, with male gender associated with greater impairment in those domains. Within those domains, males scored 4.5 points lower with regard to communication skills and almost 2 points lower with regard to cognitive skills compared to females. This tells us that not only are males more likely to have poorer developmental outcomes, but also that communication skills are a particular area of weakness. Another point to underscore is that males are more likely to be affected by a host of genetic/chromosol disorders also impacting their development.

Age was also a significant predictor of ADP, P-S, COMM, and COG domains, with increasing age associated with higher scores (less impairment). This finding may indicate that as children age, they begin to play developmental catch up. Thus, intervening when a child is still young and while their intellectual functioning is still considered unstable, may positively influence their developmental trajectory, moving them closer to that of a typically developing peer. In this cohort, race was not a significant outcome modifier.

Table 13. Dependent variables significantly predicted by each independent variable.

	Independent Variables							
	Age	Gender	LPT	VPT	EPT	LBW	VLBW	ELBW
Dependent Variables	ADP P-S COMM COG	DQ ADP P-S COG	ADP MOT	ADP	DQ ADP MOT	MOT	MOT	DQ ADP COMM MOT COG

Note: DQ = Developmental Quotient; APD = Adaptive domain; P-S = Personal-Social domain; COMM = Communication domain; MOT = Motor domain; COG = Cognitive domain

Weeks of gestation was a significant predictor of level of impairment in many domains, but like sex, the influence of weeks of gestation varied from domain to domain. Being born LPT was associated with impairment in the ADP and MOT domains; though, to a lesser degree compared to their counterpart born VPT or EPT. Being born EPT was associated with impairment in the greatest number of domains (i.e., DQ, ADP, MOT) and exerted a stronger influence on level of impairment than LPT and VPT. Thus, the fewer weeks a child gestated, the greater their level of impairment. A similar trend was observed when examining the findings for birthweight. Being born LBW, VLBW, or ELBW was associated with impairment in the MOT domain, with decreasing weight related to greater impairment. These findings confirm previous research indicating that as weeks of gestation and birthweight decrease, level of impairment increases (Allen et al., 2011; Hack et al., 1995). Children classified as extreme for both prematurity and birthweight overall, were more impaired compared to their peers who were less premature or had greater birthweights.

Interestingly, ELBW significantly predicted impairment in the most domains (i.e., DQ, ADP, COMM, MOT, COG) and the greatest level of impairment in each of those domains. Children born ELBW appear to have the poorest developmental outcomes. Hack and colleagues (1995) suggested that greater incidence of medical complications associated with increasingly lower birthweights may explain the poorer outcomes observed in children born ELBW. The greater the birthweight (up to a certain point), the more likely the child experienced an optimal intrauterine environment. An optimal intrauterine environment promotes better physical and neurological development (Dombrowski, Noonan, & Martin, 2007).

Of note, certain areas of development were significantly predicted by more of the independent variables (Table 14). For example, ELBW, EPT, VPT, LPT, gender, and age all predicted a degree of impairment in adaptive skills. ELBW predicted the greatest amount of impairment in adaptive skills, closely followed by EPT. Adaptive skills are practical skills required for everyday functioning. BDI-2 items from the ADP domain include "feeds self bite-size food," "attends to one activity for 3 or more minutes," "helps with dressing by holding out arms or legs," "demonstrates caution and avoids common dangers," and "expresses need to go to the bathroom." Motor skills were the other area of development significantly predicated by the most independent variables (i.e., ELBW, VLBW, LBW, EPT, LPT). Again, ELBW predicted the greatest amount of impairment, closely followed by EPT. BDI-2 items for the MOT domain include "stands in the upright position without support for 30 or more seconds," "kicks ball forward without falling," "throws ball forward at least 3 feet," "moves from sitting to standing without support from object or person," and "opens door by turning knob." One hypothesis for why these two areas of development are more sensitive to impairment is that children born preterm or LBW experience more health problems than FT and normal birthweight children. Health problems such as medical and surgical conditions may limit mobility and activities of daily living (Hack et al., 1995; Overpeck, Moss, & Hoffman, 1989).

The P-S domain was not significantly predicted by weeks of gestation or birthweight, which is consistent with previous findings suggesting that weeks of gestation and birthweight are not associated with social skills deficits (Klein et al., 1989; Ross, Lipper, & Auld, 1990).

Personal-social skills are evaluated on positive social interactions and social skills. BDI-2 items for the P-S domain include " responds to adult praise, rewards, or promise of reward," "enjoys having simple stories read," "shows affection towards or liking for peers," "identifies self in mirror," "participates in group play," and "generally follows directions related to daily routine." Prior observations suggested that behavioral problems occur at a higher rate in premature and LBW children compared to FT and normal weight peers. Common behavior problems associated with LBW include conduct disorder and ADHD (Aarnoudse-Moens et al., 2009; Hack et al., 1995; McCormick et al., 1990; Ross et al., 1990). Behavioral problems may be interpreted as poor social skills, when in reality the child may have the ability to engage in appropriate social skills, but behavioral problems are interfering with this ability. Once the behavior problems are addressed, the child's social skills often appear improved. Therefore, it is important when assessing personal-social skills to differentiate between behavior problems and actual deficits in social abilities.

In general, as behavioral problems occur at a higher rate in children born premature and/or LBW, before treating any deficits in development, behavioral problems must first be addressed. Without such intervention, behavioral problems, compliance, and engagement with treatment procedures will be difficult. Problems with compliance and engagement may also lead providers to believe that deficits exist where they do not. Refusal to perform a skill is different than not having the ability to perform the skill. Treating/reducing behavioral problems first will lead to better treatment outcomes.

Table 14. Independent variables that significantly predicted specific dependent variables.

	Dependent Variables					
	DQ	ADP	P-S	COMM	MOT	COG
Independent Variables	ELBW EPT Gender	ELBW EPT VPT LPT Gender Age	Gender Age	ELBW Age Gender	ELBW VLBW LBW EPT LPT	ELBW Age Gender

Note: LBW = Low birthweight; VLBW = Very low birthweight; ELBW = Extremely low birthweight; LPT = Late premature; VPT = Very premature; EPT = Extremely premature

CHAPTER 10: CONCLUSION

Prior to the 1960s, very few infants born less than 28 weeks of gestation and/or with a birthweight of less than 1000g survived. Those who did survive tended to be more physiologically mature and healthier. Through advances in neonatal care, infants born extremely premature and at lower and lower birthweights have been given a greater likelihood of surviving. Though such medical advances have decreased the rate of mortality, what has become a concern is how these children will develop and progress through life. Many infants born premature and/or LBW display no developmental concerns; however, a large portion do and at a higher incidence than in the general population (Abbott, 2015; Bhutta et al., 2002). Increased risk of impairment has been reported in most areas of development, including cognitive functioning, motor skills, adaptive skills, and later school performance (Bhutta et al., 2002; Hack & Fanaroff, 1999).

One limitation of these reported findings is that often children born prematurely and those who are born LBW are studied as a homogenous group. However, LBW is not necessarily a result of preterm birth and there is a subset of infants born LBW who gestate more than 37 weeks. Additionally, there are children born preterm who are LBW even taking into account expected weight for weeks of gestation. As the cause of preterm birth and LBW are not necessarily the same, it is important that the outcomes of these children be differentiated. Further, even within each group (i.e., PRE, LBW, PLBW), differences in developmental outcomes exist due to different levels of prematurity and birthweight. At this time, it is well established that as weeks of gestation and birthweight decrease, risk of developmental delays increases (Allen et al., 2011; Hack et al., 1995).

The purpose of this study was twofold. The first aim was to gain an understanding of the independent effects of LBW and/or prematurity on development. More specifically, this study aimed to determine if particular developmental profiles exist. The second aim was to determine whether weeks of gestation, birthweight, age, race, and gender significantly predicted impairment in general developmental level, adaptive skills, personal-social skills, communication skills, motor skills, and cognitive skills. These findings indicate that children born PLBW had the greatest level of impairment in all areas of development compared to their peers born PRE, LBW, and FT. Children born FT were found to be the least impaired even in this sample of children referred specifically for developmental concerns. Additionally, weeks of gestation, birthweight, age, race, and gender significantly predicted impairment. ELBW and EPT were the most common factors that predicted impairment. Additionally, ELBW and EPT predicted the greatest degree of impairment compared to the other factors.

When conceptualizing study findings, it is clear that children born PRE, LBW, and PLBW have poorer developmental outcomes than their FT peers. It is likely that early intervention will improve outcomes and reduce their risk of long term developmental impairment (Crossman, 2016; Dawson, 2008). Specifically, children born PLBW should be closely monitored as this group exhibited the greatest degree of impairment and may require the most comprehensive and intensive intervention services. Further, it is apparent that motor skills and adaptive skills should be a component of assessment for treatment planning in every early intervention program for PRE, LBW, and PLBW children. This approach is based on the fact that impairment in motor and adaptive skills are strongly influenced by weeks of gestation, birthweight, gender, and age and are the best predictors of group membership.

Children born LPT and LBW may experience more developmental advantages compared to their EPT and ELBW peers and thus may benefit from more targeted interventions; whereas children born EPT or ELBW would likely benefit from intensive and comprehensive intervention as they appear to experience the greatest degree of impairment, and have impairment in the most areas of development. Gender is also an important factor to consider as our findings indicated that male gender is a predictor for increased likelihood of impairment in almost all areas of development. Race, however, was not found to predict impairment in any areas of development.

These findings highlight the need for early and frequent screening for developmental delays in children born premature and/or LBW. Health care professionals should pay particular attention to the children at the greatest risk (i.e., males and those born ELBW, EPT) and provide early parent education. For example, though a delay may not be apparent, there is strong evidence demonstrating that impairment in motor skills is common in children born ELBW, indicating that preventative services should be implemented. Health care providers should not necessarily wait until a parent notices a delay to begin assessing development, as it is clear there is an increased risk for delays. These findings may also be helpful in determining amount of support required and where emphasis of treatment should be focused. The earlier and more individualized the intervention, the better the outcomes (Cooper, Heron, & Heward, 2007). Early intervention has been demonstrated to be especially important for circumventing the need for intensive treatment later in life. The most successful treatment plans often involve therapies that include multiple domains; behavioral therapy, occupational therapy, physical therapy, and special academic instruction (Katz & Lazcano-Ponce, 2008).

Children presenting with developmental delays frequently improve with the implementation of therapeutic services; however, they may require long-term support to maintain gains (Shevell, Majnemer, Platt, Webster, & Birnbaum, 2005). Ongoing reassessment is critical for children born premature and/or LBW as these children often experience residual delays (Hack et al., 1995; Lubchenco et al., 1963). This involves periodic systematic reassessment at key points in the lifespan to assess the effectiveness of current intervention, identify ongoing difficulties, and determine if new supports and resources are required as the individual progresses through different life stages are recommended(e.g., dating, independent living). This periodic reassessment is also useful for maintaining progress made through previous therapeutic services and build on current skills (Shevell et al., 2005). Through this approach, functional and developmental capabilities can be enhanced and individual, family, and societal burdens minimized (Rydz et al., 2005; Shevell et al., 2005).

Future Directions

As noted above, providing early intervention services when a child presents with developmental delays improves long-term developmental outcomes. At this point there is little disagreement that children born preterm and/or LBW are at an increased risk for developmental delays. Therefore, providing preventative services, which has been accepted by the medical community and practiced for many years, has the potential for providing even better outcomes for this population. The benefit of this model is that medical problems can be caught in the very early stages, thus decreasing the amount of damage/impairment and decreasing the need for more expensive and invasive treatments. Prematurity and/or LBW are easy to identify and known immediately upon delivery, and in many cases prior to birth. Therefore, applying this same model to identify not just medical but also more comprehensively identify developmental risks for children born premature and/or LBW would be beneficial on many levels. A well-documented and significant gap exists between the identification of concerns and the delivery of developmental services to children and their families (Dworkin, 2015; Raspa et al., 2015). There is no need for this gap to exist. Parents of children at risk for developmental delays should be provided with education very early on in development regarding expected developmental milestones, the importance of periodic and routine screening and/or assessment of developmental skills as their children develop, and how to connect with early assessment and early intervention services. Delays may be avoided or the severity reduced if preventative services are implemented early. Additionally, preventative services will likely reduce the amount of services required as the child ages. Since there is such a clear link between premature and/or LBW and developmental delays, the "wait and see" method that is currently in practice is not acceptable. Preventative services are the best practice and will lead to the best developmental outcomes for these children.

Limitations

There are a few notable limitations to this study. First, caregivers self-reported their child's weeks of gestation and birthweight. Weeks gestated and birthweight were not independently verified. Second, additional maternal and environmental factors that have been linked to preterm birth and LBW, such as maternal age, maternal substance use, maternal pregnancy weight gain, maternal infection, and socioeconomic status (Chomitz, Cheung, & Lieberman, 1995) were not available, hence, could not be factored into the analyses with the data. Collecting and analyzing this kind of information would be beneficial for follow-up or similar studies. The participants in this study were derived from a clinical sample that was referred for being at risk for a host of neurodevelopmental concerns, which should be considered when interpreting the findings. Lastly, to create equal group sizes participants were randomly deleted; matching participants by demographic characteristics may have also been an appropriate approach and could be considered in follow-up studies.

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APPENDIX: IRB DOCUMENTATION

Bobby Jindal
GOVERNOR

Kathy Kliebert
SECRETARY

State of Louisiana

Department of Health and Hospitals

December 4, 2013

Dr. Johnny L. Matson
Department of Psychology
Louisiana State University
324 Audubon Hall
Baton Rouge, LA 70803

Via email: johnmatson@aol.com

Re: Autism in Early Childhood

Dear Dr. Matson:

Thank you for submitting the above-referenced proposal. We have taken into advisement information provided in the proposal package. We find that all areas of concerns were clarified and the project has been approved by Expedited Review.

The IRB approves the project for the purposes of investigating developmental patterns and differences in atypically developing children with and without autism spectrum disorders. If you should desire to conduct additional research using the data collected under this project, that proposal much be submitted separately to the IRB for review.

I am requesting that the Principal investigator report to the DHH IRB any emergent problems, serious adverse reactions, or changes to protocol that may affect the status of the investigation and that no such changes be instituted prior to DHH IRB review, except where necessary in order to eliminate immediate hazards. The investigator also agrees to periodic review of this project by the DHH IRB at intervals appropriate to the degree of risk to assure that the project is being conducted in compliance with the DHH IRB's understanding and recommendations.

If I can be of any further assistance to you, please feel free to contact me.

Sincerely,

Nell W. Allbritton, MPA
Director, Institutional Review Board
Department of Health and Hospitals
628 North 4th Street, Third Floor
Baton Rouge, Louisiana 70802
(225) 342-4169
nell.allbritton@la.gov

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"An Equal Opportunity Employer"

Application for Exemption from Institutional Oversight

LSU

Institutional Review Board
Dr. Robert Mathews, Chair
131 David Boyd Hall
Baton Rouge, LA 70803
P: 225.578.8692
F: 225.578.5983
irb@lsu.edu
lsu.edu/irb

Unless qualified as meeting the specific criteria for exemption from Institutional Review Board (IRB) oversight, ALL LSU research/projects using living humans as subjects, or samples, or data obtained from humans, directly or indirectly, with or without their consent, must be approved or exempted in advance by the LSU IRB. This Form helps the PI determine if a project may be exempted, and is used to request an exemption.

– Applicant,Please fill out the application in its entirety and include the completed application as well as parts A-F, listed below, when submitting to the IRB. Once the application is completed, please submit two copies of the completed application to the IRB Office or to a member of the Human Subjects Screening Committee. Members of this committee can be found at http://research.lsu.edu/CompliancePoliciesProcedures/InstitutionalReviewBoard%28IRB%29/item24737.html

– A Complete Application Includes All of the Following:
- **(A)** Two copies of this completed form and two copies of parts B thru F.
- **(B)** A brief project description (adequate to evaluate risks to subjects and to explain your responses to Parts 1&2)
- **(C)** Copies of all instruments to be used.
  - *If this proposal is part of a grant proposal, include a copy of the proposal and all recruitment material.
- **(D)** The consent form that you will use in the study (see part 3 for more information.)
- **(E)** Certificate of Completion of Human Subjects Protection Training for all personnel involved in the project, including students who are involved with testing or handling data, unless already on file with the IRB. Training link: (http://phrp.nihtraining.com/users/login.php)
- **(F)** IRB Security of Data Agreement: (http://research.lsu.edu/files/item26774.pdf)

1) Principal Investigator: Dr. Johnny L. Matson **Rank:** Clinical Director

Dept: Clinical Psychology **Ph:** (225) 578-8745 **E-mail:** johnmatson@aol.com

2) Co Investigator(s): please include department, rank, phone and e-mail for each
*If student, please identify and name supervising professor in this space

IRB# E8292 LSU Proposal #
✓ Complete Application
✓ Human Subjects Training

3) Project Title: Autism in Early Childhood

Study Exempted By:
Dr. Robert C. Mathews, Chairman
Institutional Review Board
Louisiana State University
203 B-1 David Boyd Hall
225-578-8692 | www.lsu.edu/irb
Exemption Expires: 4/30/2016

4) Proposal? (yes or no) no **If Yes, LSU Proposal Number**

Also, if YES, either ◯ **This application completely matches the scope of work in the grant**
OR ◯ **More IRB Applications will be filed later**

5) Subject pool (e.g. Psychology students) Young children assessed for developmental delay via EarlySteps

*Circle any **"vulnerable populations" to be used**: (children <18; the mentally impaired, pregnant women, the ages, other). Projects with incarcerated persons cannot be exempted.

6) PI Signature [signature] **Date** 4-19-13 (no per signatures)

**** I certify my responses are accurate and complete.** If the project scope or design is later changes, I will resubmit for review. I will obtain written approval from the Authorized Representative of all non-LSU institutions in which the study is conducted. I also understand that it is my responsibility to maintain copies of all consent forms at LSU for three years after completion of the study. If I leave LSU before that time the consent forms should be preserved in the Departmental Office.

Screening Committee Action: Exempted √ Not Exempted ____ Category/Paragraph 4

Signed Consent Waived?: Yes / No

Reviewer Mathews **Signature** [signature] **Date** 5/1/13

VITA

Rachel L. Goldin was born in Boston, Massachusetts, in 1988. She received her Bachelor of Arts degree in psychology from Clark University in 2010. Following completion of her degree, she was employed Massachusetts General Hospital, Boston, Massachusetts, as a research coordinator and assistant in the department of pediatric psychopharmacology. She subsequently enrolled in Louisiana State University's Clinical Psychology Doctoral Program in 2012. Her current clinical and research interests are the assessment and treatment of individuals with Autism Spectrum Disorders and other developmental disabilities, with a particular emphasis on factors influencing the course and presentation of the disorder.