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Perinatal Medical Variables Predict Executive Function within a Sample of Preschoolers Born Very Low Birth Weight

Susanne W. Duvall, PhD[a], **Sarah J. Erickson, PhD**[b], **Peggy MacLean, PhD**[c], and **Jean R. Lowe, PhD**[d]

[a]Oregon Health & Science University Institute on Development & Disability 707 SW Gaines Street Portland, Oregon 97239-3098

[b]University of New Mexico Department of Psychology Albuquerque, NM 87131

[c]UNM HSC School of Medicine Center for Development and Disability 2300 Menaul Blvd NE Albuquerque, NM 87107

[d]University of New Mexico Department of Pediatrics Division of Neonatology Albuquerque, NM 87131

Abstract

The goal was to identify perinatal predictors of early executive dysfunction in preschoolers born very low birth weight. Fifty-seven preschoolers completed three executive function tasks (Dimensional Change Card Sort-Separated (inhibition, working memory and cognitive flexibility), Bear Dragon (inhibition and working memory) and Gift Delay Open (inhibition)). Relationships between executive function and perinatal medical severity factors (gestational age, days on ventilation, size for gestational age, maternal steroids and number of surgeries), and chronological age were investigated by multiple linear regression and logistic regression. Different perinatal medical severity factors were predictive of executive function tasks, with gestational age predicting Bear Dragon and Gift Open; and number of surgeries and maternal steroids predicting performance on Dimensional Change Card Sort-Separated. By understanding the relationship between perinatal medical severity factors and preschool executive outcomes, we may be able to identify children at highest risk for future executive dysfunction, thereby focusing targeted early intervention services.

Keywords

cognitive function; gestational age; outcome; preterm child

Corresponding Author: Susanne W. Duvall, Ph.D., Institute on Development & Disability, Oregon Health & Science University, 707 SW Gaines Street, Portland, Oregon 97239-3098, Telephone: 503-494-1557, Fax: 503-418-5203, duvall@ohsu.edu.

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INTRODUCTION

Children born very low birth weight (VLBW < 1500 g) are at increased risk for difficulties that persist over time.[1] In recent years, the importance of examining executive functioning abilities in these children has been increasingly highlighted, which include the domains of working memory, cognitive flexibility, and inhibition skills.[2–3] Additionally, degree of prematurity and increased medical complications, are risk factors for poor neurodevelopmental outcomes[2–3] including poor executive function. These executive function abilities have been emerging as important predictors of cognitive, behavioral, and academic outcomes in this population).[4–6]

To date, most studies examining executive functioning in children born preterm have focused on school-aged children and have found significant deficits in preterm children compared to those born full-term.[4,5] Fewer studies, however, have investigated executive function abilities among younger children, which is particularly important given the importance of early intervention and the growing research that precursors of executive function are emerging in the first few years of life.[7–8] The few studies that have compared executive functioning skills in toddlers and preschoolers, however, have shown that children born preterm have greater difficulties in this area[5,9], emphasizing the importance of additional research.

In addition to examining the executive functioning deficits associated with prematurity, the importance of identifying the perinatal health factors associated with these deficits has also been emphasized by others[10,11] given the prognostic value of such information for early intervention efforts. Most studies examining this area have included school-age children and adolescents and have demonstrated that executive function abilities strongly related to perinatal medical severity, with most studies finding that the more severe the medical condition, the more executive function difficulties these children encounter.[5,10,11] In particular, gestational age and birth weight frequently emerge as predictors of executive function performance in children and adolescents born very low birth weight.[5,12,13] Other health factors, such as the number and extent of medical complications at birth, neurobiological risk, being small for gestational age, longer period of oxygen requirement, and chronic lung disease have been found to predict executive function.[10–12]

Given the limited studies focusing on younger children, the purpose of the current study was to better understand the perinatal health risk factors that are associated with poorer executive function abilities in preschoolers born very low birth weight. All participants completed three executive function tasks including: Dimensional Change Card Sort-Separated[14], Bear Dragon[15] and Gift Delay Open.[4,16] An additive relationship was hypothesized such that the more perinatal health risk variables, the poorer the executive function ability among preschool children born very low birth weight. As maternal education has been found to be associated with the use of more adaptive parenting practices and may also represent wider social and economic influences that impact child outcomes[17], this variable was also included in secondary analyses.

METHODS

Patient recruitment and procedures

Recruitment was conducted by the University of New Mexico Clinical and Translational Science Center (UNM-CTSC) pediatric research nurses and a psychology graduate student affiliated with the Special Baby Clinic by review of prior admission lists from the University of New Mexico Hospital Newborn Intensive Care (UNMH-NICU) to identify infants eligible for inclusion based on birth weight. Of the 250 children who were eligible to participate through the duration of data collection, 67 (27 %) mothers could be reached. Of the 67 eligible mothers reached, 57 (85%) agreed to participate and completed the study. Based on the minimal demographic information (i.e., maternal and child ethnicity, maternal relationship status, maternal age, birth weight) available at recruitment, mothers who could not be contacted and mothers who declined participation appear comparable to those who completed the study. In addition, participants (i.e., those that completed the study) and non-participants (i.e., those that could not be contacted, that refused to participate, or that failed to keep their scheduled appointment) appeared commensurate to the larger hospital population. Once informed consent was obtained, each preschooler completed the Wechsler Preschool Primary Scale of Intelligence, Third Edition (WPPSI-III)[18] as part of a larger study and executive function performance measures were collected while the mother was asked to complete questionnaires. Perinatal medical information was obtained through hospital records. Preschoolers included in this sample were between the ages of 3 and 4.5 years (36 and 54 months) and data were collected between April 2004 and August 2009. All preschoolers born very low birth weight in this sample were admitted to the Neonatal Intensive Care Unit at the Children's Hospital of New Mexico at birth. Preschoolers were excluded from the study if they had prenatal exposure to neurotoxic substances, had sensory loss that precluded measure completion, and/or had a known genetic abnormality. Fifty-seven preschoolers born very low birth weight were included in the current study (See Table 1 for demographic information).

Measures

Perinatal Medical Severity—Based on previous literature, a set of a priori indices of perinatal medical severity was selected, including: gestational age, total days on ventilation and continuous positive airway pressure (CPAP), size for gestational age, completed course of antenatal maternal corticosteroids, and number of surgeries during initial Neonatal Intensive Care Unit hospitalization.[2,3,5,7–9,10–13]

Maternal Education—This information was collected by maternal self report of the highest level of education attained and was categorized as follows: 0 = less than High School, 1 = Completed High School, 2 = completed 1 year of college - no degree, 3 = associates degree (2 years of college), 4 = bachelors degree (4 years of college), 5= some graduate school - no degree, 6 = completed masters degree or higher.

Test Battery: Three executive function tasks from the developmental psychology literature were selected that inclusively increased in the number of executive function domain demands.

Dimensional Change Card Sort-Separated Dimensions[14]—This paradigm is the most complex task in the battery and measures the three executive function domains of cognitive flexibility, working memory and inhibitory control. A modified version of the Dimensional Change Card Sort-Separated task was used with color and size as dimensions, details for re-creating this and other similar tasks are available in the developmental literature.[14,15] The children were given sorting cards (e.g., little yellow, big blue) and were told to match the sorting cards with the target cards (e.g., little blue and big yellow) affixed to boxes in front of them. Each sorting card matched one target card on one dimension (color) and matched the other target card on the other dimension (size). In the pre-switch phase, children were told to match by color; then the child was asked to switch dimensions and sort the cards by size (the post-switch phase). This required the child to inhibit the previous sorting rule (color) and only pay attention to the relevant dimension (size). Knowledge questions and rule reminders were provided according to previously published procedures.[14] The score was the percent of correctly sorted post-switch cards out of the six total possible responses. When the dimensions are physically separated into foreground and background, typically developing children as young as 2.5 years are able to successfully complete the task. Test-retest reliability for this task falls in the 0.75–0.80 range. [14,15]

Bear Dragon[16,18]—This measure assessed two executive function domains, complex response inhibition and working memory. This measure is a simplified Go-No-Go or Simon Says task in which children inhibit certain responses in response to commands. The experimenter introduced children to a "nice" bear puppet (using a soft, high-pitched voice) and a "grumpy" dragon puppet (using a gruff, low-pitched voice). It was then explained that in this game "We will do what the nice bear says, but we will not do what grumpy dragon says." After practicing, there were 10 test trials with the bear and dragon commands in alternating order. To score this task, each response was assigned a score from 0 to 3, and the points were added to obtain a total score out of 33 possible points (3 points for each of the 10 test trials plus 3 points for passing the practice trial).[15,16] In typically developing children, the Bear Dragon task has shown high inter-rater reliability and strong consistency with other measures of inhibition.[16,19]

Gift Delay Open[15]—The Gift Delay Open task measures the executive function domain of inhibition. A wrapped present was placed in front of the child and they were told not to touch or open it while the examiner finished making them a card. The task was discontinued and the child received the gift at 2 minutes or when the child began to open the gift. This task was scored as being passed or failed based on whether the child opened the gift.

Statistical Analysis

Due to non-normal executive function variable distributions, executive function measures were transformed to lognormal distributions. The perinatal medical predictor variables (gestational age, size for gestational age, days on ventilation and continuous positive airway pressure, maternal steroids and number of surgeries, in this order) were entered simultaneously into the models with the Dimensional Change Card Sort-Separated and Bear Dragon as the two dependent variables through multiple linear regressions with a forward selection procedure that maximized R^2 given the variables already entered. The impact of perinatal medical variables was calculated while adjusting for the baseline characteristic of chronological age. For the third EF dependent variable, the likelihood of passing the Gift Delay Open task (defined as not touching the gift), a logistic regression for binomial data, was employed in relation to the perinatal medical variables and chronological age. This resulted in a likelihood ratio chi-square test and odds ratio. A secondary follow-up analysis was conducted with maternal education as an additional independent variable in all analyses, given that maternal education may be related to more adaptive parenting practices and broader influences in child outcomes.[17] As there were some significant correlations among perinatal risk factors, critical multicollinearity was examined and was not found to be impacting (all VIF values <1.97). Hypotheses tests were two-sided with a significance level of 0.05.

RESULTS

Descriptively, our sample of preschoolers born very low birth weight may have had some difficulty with executive function tasks as compared to the performance of typically developing preschoolers in the developmental literature [percent passing in typically developing, percent passing in this very low birth weight sample]:. Dimensional Change Card Sort-Separated task [62% vs. 47.5%][14,15], the Bear Dragon task [76% vs. 31.6%][15]) and Gift Delay Open task, [85% vs. 73.7%].[15]

Correlations between medical severity measures and executive function measures are provided in Table 2. When adjusting for chronological age, the number of surgeries and maternal steroids predicted performance on the Dimensional Change Card Sort-Separated task and the overall model was significant $F(53) = 6.065$, $p = .001$, $R^2 = .256$, see Table 3. Performance on the Bear Dragon task, after adjusting for chronological age, was uniquely predicted by gestational age and the overall model was significant, $F(53) = 17.496$, $p<.001$, $R^2 = .393$.

Using logistic regression, the likelihood of passing the Gift Delay Open task, adjusting for chronological age, was related to gestational age. The overall model was significant (chi squared of 7.429, $p = .024$) and the Nagelkerke R^2 indicated that the model accounted for 17.9% of the total variance and the correct prediction rate was about 78.9%. [TABLE 3 HERE] As chronological age was not significant, the regression was rerun without adjusting for age and the likelihood of passing the Gift Delay Open task continued to yield a significant model with gestational as a single predictor (chi squared of 4.582, $p=.032$).

The impact of maternal education was also examined in secondary post-hoc analyses for all executive function outcome variables and no changes were found in the models for the Dimensional Change Card Sort-Separated task, the Bear Dragon task and the Gift Delay Open task. Similarly, follow-up analyses were conducted with ventilation instead of CPAP plus ventilation and no changes were found in any of the models.

DISCUSSION

Our results align with prior research in older children and some recent studies in younger children indicating that perinatal medical severity variables correlate with executive function measures.[4–6,9–11] Specifically, in this sample of preschoolers born very low birth weight, the following medical variables were related to executive function performance: gestational age, maternal steroids, and number of surgeries. In fact, perinatal medical severity factors were solely selected into the model even when maternal education was included as a potential proxy for wider sociodemographic and parenting influences, which further implicates the importance of these medical variables. Additionally, differences were found in which particular perinatal medical variables predicted which specific executive function tasks.

Our results may be partially explained by the developmental progression of executive function abilities and how these abilities may be impacted differentially by various perinatal medical variables. The sole perinatal medical predictor variable in two out of three of our models (Bear Dragon and Gift Delay Open) was gestational age. However, gestational age was not selected in the Dimensional Change Card Sort-Separated model. Of note, gestational age seemed to be of primary importance in predicting tasks that primarily measure inhibition, such as Bear Dragon and Gift Delay Open, which tends to developmentally emerge before more complex executive function skills. Higher level executive function skills, such as improved cognitive flexibility and set shifting, tapped by measures such as Dimensional Change Card Sort-Separated, tend to emerge later in typical development[15] and are hypothesized to involve more complicated brain networks. Our findings regarding gestational age may be explained because gestational age indexes global development that would be more likely to result in diffuse difficulties with the basic building blocks of executive function, such as inhibition.[4] While number of surgeries is an illness severity marker, and maternal steroids completion serves as a preventive intervention for chronic lung disease, these are both related to efforts to mediate the impact of lung immaturity, which have been linked to neurodevelopmental outcomes.[1–3] Lung immaturity and resultant hypoperfusion may impact the still developing brain and may even result in more focal brain impairments (especially in areas with increased oxygen dependency).[2,3,20] Thus, perinatal medical severity variables related to mediation of the impact of lung immaturity may be especially important to consider in the development of executive function in the context of selective vulnerability of the brain to neonatal hypoperfusion and/or hypoxic ischemic events.[20] Although respiratory difficulties have been linked with general neurodevelopmental outcomes at 18 months of age, specific relationships with executive function have been limited in preschoolers.

Additionally, the varying patterns of perinatal medical variables related to different executive function performance measures may point to the differing underlying neuroanatomy implicated in each task. Tasks such as Gift Delay Open that are primarily reward inhibition tasks may measure orbitofrontal cortex functioning[21]; whereas tasks like Bear Dragon, which includes primary associations with inhibition but also contain a working memory component, may involve the orbitofrontal cortex as well as the anterior cingulate and lateral prefrontal cortex.[22] At an even higher executive function level, the Dimensional Change Card Sort-Separated task may tap into a more integrative "executive control network" which includes the anterior cingulate, dorsolateral prefrontal cortex, supplementary motor area, and basal ganglia,[23] given that this EF network has been postulated to underlie integrated attention and response shifting. Thus, one explanation of our findings is that different perinatal medical risk variables may have differential correlates with different areas and functions of the developing brain, which may have differential susceptibility to hypoxic events.

This study has several limitations, including the number of predictors added to the regression model. Although it may be argued that our models were underpowered due to the number of independent variables included, we were still able to find significant relationships. An additional limitation is that although our sample was ethnically diverse, we did not have the power to investigate ethnic group-specific predictive models. Also, the particular ethnic composition of our sample may limit generalizability. The rather large age range of preschool participants may also be a potential limitation; however this was addressed, in part, through the statistical analysis. An additional potential limitation is the relatively lower percentage of families who were able to be recruited from the eligible patients. It is unknown if the sample in this study is fully representative of the larger population sample, thus it is possible that the children in this study may be more healthy or less healthy than non-participants, which may have impacted these results. Future directions could include investigating these relationships in larger samples, broadening the perinatal medical severity variables included, and incorporating neuroimaging correlates. Further examination of the different patterns of predictive perinatal medical severity variables found across different executive function performance measures could help us to better understand the nature of difficulties documented in this population.

As the precursors to executive function are emerging as early as the first year of life[7–8], an improved understanding of risk factors associated with early (preschool) executive function difficulties may help identify high-risk children and inform intervention strategies. Although maternal education did not emerge as a predictor when combined with medical severity measures in the current study, higher paternal education has also been linked to improved executive function outcomes and may suggest the benefits of an enriched early environment.[24] Executive function has been postulated to be critical for success in school and life and has even been shown to be more influential than general intelligence in school readiness.[25] and researchers evaluating preschool curriculum and interventions have demonstrated that executive function can be targeted and improved[26]. Continued follow-up and intervention may be beneficial for children born very low birth weight who have the most medical complications and are therefore at greatest risk for executive function weaknesses.

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Table 1

Descriptive Participant Demographic Information, n = 57

Variables	**n (percentage of sample), or mean (SD), [range]** ***Median***
Gender, n, males	35(61.4)
Chronological Age, months	46.98(5.14) [37.3–54] *47.37*
Ethnicity, n	Caucasian: 15(26.3), Hispanic: 30(52.6), African American: 4(7.0), Native American: 8(14.0)
Income level, n	0= 7(12.3), 1= 8(14.0), 2= 14(24.6), 3= 7(12.3), 4= 3(5.3), 5= 3(5.3), 6= 2(3.5), 7= 13(22.8)
Maternal Education, n	0= 6(10.5), 1= 14(24.6), 2= 23(40.4), 3= 4(7.0), 4= 9 (15.8), 5= 1(1.8), 6= 0(0)
Medical Variables	
Gestational age, weeks	29.01(2.36) [24–35] *29.2* <28 weeks = 17, 28 to <32 weeks = 33, 32 to <37 weeks = 7
Days on ventilation plus CPAP	24.95(26.4) [0–97] *14*
Small for gestational age, n	11 (19.3) <28 weeks = 1, 28 to <32 weeks = 5, 32 to <37 weeks = 5
Maternal steroids, n	27 (47.4)
Number of surgeries, n	0= 34(56.9), 1= 11 (19.3), 2= 8 (14.0), 3= 2 (3.5), 3= 2 (3.5), 4 = 1(1.8)
Birth weight, grams	1130.19(251.55) [664–1490] *1186* <1000g = 18, <1250g = 18, <1500g = 21
Stage of ROP, stage, n	0= 20(35.1), 1= 26(45.6), 2= 7(12.3), 3+= 4 (7.0)
IVH, grade, n	None= 41(71.9), 1= 8(14.0), 2= 2(3.5), 3= 5(8.8), 4= 1(1.8)
Number of days in NICU	59.51(33.99) [0–195] *51*
PVL, n	2(3.5)
Executive Function Measures	
DCCS-Sep, correct answers	3.23(2.61), [0–6], *3*
out of 6 possible, n pass	27 (47.5) pass
Bear Dragon score, n pass	14.0(12.76), [0–33] *9* 18 (31.6) pass
Gift Delay Open, seconds, n pass	100.2(39.3), [1–120] *120* 42 (73.7) pass

Note: Income Level = Annual income, 0 = Under $10,000, 1 = $10,000–20,000, 2 = $20,000–30,000, 3 = $30,000–40,000, 4 = $40,000–50,000, 5 = $50,000–60,000, 6 = $60,000–70,000, 7 = $70,000+, Maternal Education = mother's highest level of education, 0 = less than High School, 1 = Completed High School, 2 = completed 1 year of college - no degree, 3 = associates degree (2 years of college), 4 = bachelors degree (4 years of college), 5= some graduate school - no degree, 6 = completed masters degree or higher, CPAP = continuous positive airway pressure, GA = gestational age in weeks, PVL = Periventricular leukomalacia, IVH = intraventricular hemorrhage, ROP = retinopathy of prematurity, DCCS-Sep = Dimensional Change Card Sort-Separated

Table 2

Correlations Between Executive Function Tasks and Medical Severity Variables in the Very Low Birth Weight Sample

EF measures	DCCS-Sep	Bear Dragon	Gift Open
Gestational Age	.248 (.061)	.144 (.282)	.287 (.029)*
Size for Gestational Age	−.180 (.177)	.020 (.882)	−.086 (.520)
Days on ventilation plus CPAP	−.202 (.128)	−.204 (.125)	−.207 (.120)
Number of Surgeries	−.304 (.020)*	−.195 (.141)	−.009 (.949)
Maternal Steroids	.208 (.118)	−.032 (.814)	.197 (.139)

Note:

* $p < .05$;

** $p < .01$;

*** $p < .00$;

EF= Executive function; CPAP = continuous positive airway pressure; DCCS-Sep = Dimensional Change Card Sort-Separated

Table 3

Results of Multiple Linear Regression and Logistic Regression Analyses for Medical Severity Variables and Age on Executive Function Performance.

Dependent Variable	Regression model	Standardized Beta or Odds Ratio (OR)	Model R^2 and (Δ) R^2 Change or Change in −2 Log Likelihood
Bear Dragon	***Overall Model***		***0.393 (.000)******
	Chronological age	.613 (.000)***	Δ .332 (.000)***
	Gestational Age	.250 (.023)*	Δ .061 (.023)*
Gift Open	***Overall Model***		***Nagelkerke 0.179 (.024)****
	Chronological Age	OR: 1.11 (.107)	
	Gestational age	OR: 1.411 (.025)*	Δ 5.864 (0.15)
DCCS-Sep	***Overall Model***		***0.256 (.001)******
	Chronological age	.314 (.011)*	Δ 0.096 (.019)*
	Number of surgeries	−.352 (.005)**	Δ 0.098 (.013)*
	Maternal steroids	.252 (.041)*	Δ 0.062 (.041)*

Note: exact significance values reported in parentheses, asterisks denote significance levels,

* = .05,

** = .01,

*** ≤.00;

DCCS-Sep = Dimensional Change Card Sort-Separated