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## Behavior Problems and Executive Function Impairments in Preterm Compared to Full Term Preschoolers

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### Abstract

**Background:** Children born preterm (PT) are at high risk for behavior problems and deficits in executive function (EF), a set of cognitive processes that guide goal-directed behaviors. Behavior differences have been found as early as 2 years in PT children; EF differences have been found in infancy. Whether behavior problems and EF deficits co-occur at young ages has not been fully investigated.

**Aims:** To determine whether (1) PT children have more behavior problems and EF impairment than full term (FT) children and (2) larger proportions of PT children show behavior problems or EF impairments

**Design/Methods:** PT (34 wks, n=82) and FT (n=79) preschoolers (mean age 4.4 years) completed an EF battery. Parents completed rating scales of behavior problems and EF skills. Mean scores and proportions with impairment were compared between groups. Logistic regression predicting to impairment defined odds ratios for PT/FT groups.

**Results:** PT compared to FT had more problems on most behavior and EF scales and poorer EF scores on all tasks and greater proportion with impairments on most behavior scales, all EF ratings, and all EF tasks,  $p < .05$ . PT had elevated odds for impaired performance-based EF, parent-rated EF and CBCL scores compared to FT,  $p < .05$ . Within the PT group, EF impairments were twice as common as behavior impairment.

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None declared.

**Conclusions:** We recommend early identification of EF impairments in PT children. Future research should evaluate whether EF impairments serve as better early markers for later functional difficulties compared to behavior problems, as well as targets for intervention.

## Keywords

executive function; preterm birth; premature birth; behavior problems; preschool

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## 1. Introduction

Children born preterm (PT) are at high risk for behavior problems and deficits in executive function (EF), a set of cognitive processes that guide goal-directed behaviors. Behavior problems in children born PT have been documented throughout the lifespan (1, 2), with higher internalizing and dysregulation scores found as early as two years of age (3). Common behavior problems from school age through young adulthood include internalizing problems such as withdrawal, depression, and anxiety; social problems; and inattention (4, 5); a meta-analysis also identified externalizing problems (6). Follow-up studies show that PT children are at increased risk for mental health or behavioral disorders, such as anxiety disorders and Attention Deficit Hyperactivity Disorder (ADHD) (4, 7). Disorders such as ADHD, anxiety, and depression are characterized by EF impairments (8, 9). Although PT children may demonstrate symptoms of behavior disorders, many studies often do not include diagnostic measures due to practical considerations (i.e., length of diagnostic interview) or the symptoms may not reach the diagnostic threshold for a disorder (5, 10).

Deficits in EF are also highly prevalent, occurring with learning problems and other less severe disabilities, in up to half of children born PT (11). EF skills are often subdivided into component skills of response inhibition, working memory and cognitive flexibility or set-shifting (12), and include higher level skills such as initiation of activity, planning and organization, selection of efficient problem-solving strategies, and monitoring of performance (11). EF skills have been linked to important functional outcomes, including academic achievement, social competence, and adaptive function in cross-sectional (13–15) and longitudinal studies of PT and typical development across childhood and the lifespan (16–20). While EF impairments can be identified through parent and teacher report or measured directly, there is no specific diagnosis in the Diagnostic and Statistical Manual-5 (DSM 5) or special education eligibility category for executive dysfunction. The impact of co-occurring behavior problems coupled with EF impairments may pose added risk to the poor academic, educational, and functional outcomes in children born PT. A few studies have found EF differences in PT children as early as infancy and the toddler years (21–23), although EF impairments are more readily identified at preschool through kindergarten age (11, 24). Early identification of both behavior and EF impairments could facilitate earlier monitoring and intervention to improve outcomes for preterm children.

The co-occurrence of behavior problems and EF deficits at young ages has not been fully investigated in PT children, as many studies either report on the domains of behavior problems and EF separately, or as part of an extensive battery that includes several outcomes of PT birth (25, 26). The linkages between EF and behavior disorders are also more difficult

to interpret at young ages due to lack of diagnostic certainty, regardless of PT or FT birth status. General pediatricians are often reluctant to diagnose behavioral conditions such as ADHD at preschool and kindergarten age, and parents may also wait before pursuing evaluation for behavior concerns. One study of PT children at kindergarten age included diagnostic interview for behavioral disorders and examined EF concurrently through both parent-report and direct measures (27). The study found that rates of ADHD combined were twice as high for the PT compared to FT group; ADHD was also associated with deficits on ratings and tests of EF but not with global cognitive impairment (27). A longitudinal study of extremely PT children (less than 26 weeks gestational age) found that attention and EF at age 6 years were associated with mathematics and reading attainment in the PT group at age 11 years (28), providing additional evidence that executive dysfunction at young ages might serve as markers for later adverse educational outcome. However, the study did not describe the concurrent association of EF deficits with behavior problems or disorders.

Given the increased risk of ADHD in the PT population, results from cross-sectional and longitudinal studies of children with ADHD or ADHD symptoms might also inform the use of EF impairments as markers for later adverse outcomes. A study of neuropsychological deficits in preschool ADHD found that the ADHD group differed from controls on all EF measures; however, a substantial subgroup (23%) of children with ADHD did not have an EF deficit in any domain (29). A cross-sectional study of neuropsychological subtypes of ADHD in school-age children found that children with and without EF deficits had comparable ADHD symptomatology and school function, but differed in other aspects of cognitive function, including IQ and response variability (30). In these two studies, behavior impairments rather than EF served as a more consistent finding for children with ADHD—not surprising given that the diagnosis is clinically defined by behavior symptoms rather than EF impairments. A longitudinal study of children with typical development examined whether neuropsychological functioning in preschool can predict ADHD symptoms in late adolescence; the study also examined neuropsychological deficits in relation to academic achievement in late adolescence when controlling for early ADHD symptom levels (31). In addition to measures of EF, emotional reactivity and emotion regulation were also measured at preschool ages. Controlling for early ADHD symptoms, preschool measures of EF, specifically working memory and reaction time variability, as well as emotion regulation were significantly related to inattention and academic achievement at late adolescence (31). These results suggest that screening for early EF deficits may be an effective approach to identify children at risk for later adverse outcomes, including both behavioral and EF impairments.

How best to apply the results from research studies that report significant differences at the group level to clinical practice at a pragmatic, individual level remains unclear. Studies often report on variable-oriented analyses, or the differences between groups on mean values from behavior or EF measures. Given the heterogeneity in behavior and EF within a clinically defined group, it has been argued that the proportion of individuals with impairment should be reported since a minority of participants may lead to group differences. Such a person-oriented approach might allow for categorization of participants into subgroups that are more clinically relevant and guide both identification and interventions (29, 32). Although PT children are at increased risk of behavioral disorders, not all may meet criteria for

disorder. A “preterm behavioral phenotype” characterized by symptoms of inattention, anxiety and social difficulties has been proposed (5).

Recognizing that many biological, environmental, and child factors contribute to development of EF skills and behavior problems (2), we also considered these factors in conjunction with PT birth status. Some studies have shown that neonatal complications do not confer additional risk on outcomes beyond those indexed by gestational age or birth weight (33, 34). In one study family factors were stronger predictors of school outcomes than perinatal complications (35), although other studies show contributions of both biological risk and social factors, such as brain injury related to PT birth and low socioeconomic status (SES) (36). Socioeconomic disadvantage has been associated with poor EF skills (37–39) and adverse cognitive and neurodevelopmental outcomes in PT birth (1). Studies on the influence of sex on EF and neurodevelopmental outcomes in PT birth are mixed (27, 40). Age and IQ also influence EF, behavior, and developmental outcomes (41, 42). Although considered separate, but related constructs, EF and IQ are not used interchangeably, and justification has been provided for not controlling for IQ in studies of neurodevelopmental conditions, including PT birth (43).

In our study we sought to examine behavior symptoms and EF skills, both parent-rated and directly measured, in PT children and specifically compare whether behavior or EF impairments were more common. We examined a wide gestational age range and used PT versus FT birth group status as our main variable representing biological risk. Our study is strengthened by use of both parent-rated and performance-based EF. Our objectives were to determine (1) if PT children have more EF impairment and parent-rated behavior problems than full term (FT) children based on both variable-oriented (i.e., means and group differences) and person-oriented (i.e., proportion of individuals with impairment) analyses; (2) within the PT group, to determine whether a larger proportion of PT children show behavior problems or EF impairments; and (3) the odds of behavior or EF impairment based on PT birth status, controlling for important variables associated with poorer EF and behavior outcomes in PT children, including SES and sex. We hypothesized that: (1) PT preschoolers have more EF impairments and behavior problems than FT children, consistent with past literature, using both variable- and person-oriented approaches; (2) within the PT group, we hypothesized that EF impairments are more common than behavior problems; and (3) the PT group would have increased odds of behavior and EF impairment.

## 2. Methods

### 2.1 Participants

The study population consisted of a convenience sample of 3- to 5-year old children born from 2004 to 2009 and recruited from Palo Alto, CA, and surrounding counties. PT subjects were recruited by letters sent to families of children who were evaluated at High Risk Infant Follow-up Services at Lucile Packard Children’s Hospital at Stanford Children’s Health and by postings on local parent message boards. Comparison group children born FT were recruited by postings on parent message boards, by flyers in general pediatric clinics and community daycares and preschools, and by word of mouth. Study subjects had a history of PT birth (< 34 weeks gestation) and birth weight (BW) < 2500 g (n = 82). A comparison

group was comprised of children born FT ( 37 weeks) and had no major medical complications (n = 79).

Exclusion criteria for all participants included sensory impairments (i.e., blind or deaf), identified genetic syndrome or congenital heart disease, and inability to comprehend task instructions. Comprehension was not formally assessed with language or intelligence tests prior to enrollment; however, ability to participate was estimated during an IRB-approved phone screening. Parents were asked questions to assess parent perception of the child's overall development (i.e., "How is your child doing compared to other children his or her age? Has your child had a recent developmental or IQ test?") No parents reported IQ scores, but some children had developmental evaluations completed in high-risk infant follow-up clinics or through early intervention. Parents who described mild or moderate delays received follow-up questions to determine if they thought the child could participate. This step did not result in the exclusion of any participants. We attempted to group-match children born FT to children born PT for age, gender, ethnicity, race, and maternal education. The study was approved by the Stanford Institutional Review Board. A parent or legal guardian provided informed consent. Participants were compensated with one \$50 payment for participation.

## 2.2 Procedures

Potential participants were initially screened for eligibility using an IRB-approved waiver as described above. Parents completed a Family Demographics and Child Health Questionnaire and well-known standardized parent rating scales (described below) while children completed an EF battery of tasks. The battery was administered in fixed order by trained research assistants over approximately 1 to 1.25 hours. Breaks were provided as needed.

## 2.3 Measures and Variables

**2.3.1 Family Demographics and Child Health Questionnaire**—Participant characteristics, including GA, BW, and medical complications, were gathered from parent report using a questionnaire developed and used in several IRB-approved studies at Stanford University (13, 44). Neonatal history and complications were also confirmed from review of medical records. Demographic information included race, dichotomized as white versus nonwhite; ethnicity, defined as Nonhispanic/Nonlatino versus Hispanic/Latino or mixed Hispanic/Latino; maternal education as a proxy for SES; and parent report of services. Maternal education was gathered in 5 categories: less than high school, high school graduate or GED, AA/2-year degree or less than 4 years of college, college degree, and MA or greater.

**2.3.2 IQ**—Full scale IQ was estimated using the two-subtest format of the Stanford-Binet Intelligence Scales, 5<sup>th</sup> edition, an assessment of intelligence and cognitive abilities in individuals age 2-85+ years. Vocabulary and object-series/matrices subtests are combined to provide the Abbreviated Battery IQ (ABIQ) (45).

**2.3.3 Performance EF Battery**—Tasks were selected to represent core EF constructs based on the developmental literature in typical and PT preschoolers (24, 26, 46–48). Tasks

included: (1) 3- and 6- Boxes Task measures self-ordered working memory and planning (49). Three, and then six, stationary boxes with different color lids are baited with a treat in view of the child. The child's task is to find all treats in the least number of reaches by keeping track of the boxes that have already been searched. (2) Verbal Fluency measures idea generation with language and organizational components (i.e., the use of subcategories as a strategy results in increased productivity) (50). The task requires the child to generate as many words as possible within specific categories (i.e., animals, foods) in one minute. (3) Day/Night measures complex response inhibition, defined as response inhibition coupled with working memory (51). The child must hold a rule in mind and respond while inhibiting a prepotent response, suppressing competing visual information when responding. The child should respond "night" when shown a picture of the sun and "day" when shown a picture of moon and stars (52). (4) Bird/Dragon also measures complex response inhibition, defined as response inhibition and working memory (53). A modified "Simon Says" task, the child should follow verbal instructions of one puppet (bird), but not the other puppet (dragon). (5) Dimensional Change Card Sort, measures cognitive flexibility/task switching and attention shifting (54). The child is shown cards depicting colored shapes that can be sorted according to color or shape. The child must sort according to one dimension and then shift to sort according to the other dimension. Additional details of task administration and dependent variables were previously described (13, 44). We analyzed results for each individual task and also calculated z-scores for each task; the z-scores were averaged to create a summary/composite EF score.

#### **2.3.4 Behavior Rating Inventory of Executive Function-Preschool version**

**(BRIEF-P)**—This is a standardized parent-rating scale of behavioral manifestations of EF in children 2.0-5.11 years (55). Sixty-three items measure aspects of EF: Inhibit, Shift, Emotional Control, Working Memory, and Plan/Organize. Three broad indexes (Inhibitory Self-Control, Flexibility, Emergent Metacognition) and a composite score (Global Executive Composite, GEC) are also reported. Items are rated on a 3-point scale of "never," "sometimes," or "often." Scores are reported as t-scores (mean of 50, SD of 10) in which higher scores indicate greater executive dysfunction. Scores at or above 65 are considered clinically significant. The measure is normed for gender and age by two groupings: 2:0 to 3:11 and 4:0 to 5:11. Content validity is based on factor analysis of clinical and normative samples, convergence/discriminance with preschool rating scale measures, and on the ability to detect EF deficits in children with risk factors or disorder (56, 57). We analyzed the GEC, subscales, and indexes.

**2.3.5 Child Behavior Checklist for Ages 1½-5 (CBCL)**—Parents completed the CBCL, a well-validated behavior rating questionnaire (58). The CBCL asks parents to rate 100 items on a 3-point Likert scale (0 = not true; 1 = somewhat/sometimes true; 2 = very/often true). The items describe specific kinds of behavioral, emotional, and social problems that characterize preschool children. Items are grouped into 7 subscales—emotional reactivity, anxious/depressed, somatic complaints, withdrawn, sleep problems, attention, and aggression—as well as three summary scales of Total Problems, Internalizing and Externalizing Problems scores. Scores are reported as t-scores with mean of 50 and SD of 10. For the subscales, scores of 65-69 are considered borderline clinically significant and



scores of 70 and above are considered clinically significant. For the Internalizing, Externalizing, and Total Problems scales, scores of 60 to 63 (approximately 83<sup>rd</sup> to 90<sup>th</sup> percentiles) are considered borderline clinically significant, and scores of  $\geq 64$  are clinically significant.

## 2.4 Statistical Analyses

To compare demographic variables between groups, we used t-tests for continuous outcomes and Pearson chi-square for dichotomous outcomes. To compare group means of normally distributed IQ, EF battery test scores, BRIEF GEC and index scores, and CBCL summary scales total scores between groups, we used ANCOVA with maternal education as a covariate; non-normally distributed EF battery, BRIEF and CBCL scale scores were compared with nonparametric Mann-Whitney tests. Group differences were further described by calculating effect size for ANCOVA analyses using partial  $\eta^2$ , with small effect = .01, medium = .06, and large = .14, and for Mann-Whitney analyses using absolute  $r$ , with small effect = .1, medium = .3, and large = .5 (59).

Based on other studies of PT children that sought to identify children at risk for later adverse outcomes (60, 61), we similarly chose a cutoff for impairment of 1 SD from the mean in the unfavorable direction for the outcome measures. We defined impairment in parent-rated behavior problems (CBCL) or EF (BRIEF-P) as t-scores  $\geq 60$ . For EF performance, z-scores for tasks with continuous outcomes were derived from performance (mean, SD) of FT subjects in the 3 age groups of 3, 4, and 5 years. We also calculated an average z-score for the 5 EF tasks as a summary indicator of performance based EF. Impairment for the z-score was also defined as z score  $\geq 1$  SD from the mean (i.e., in the unfavorable direction). Chi-square was used to compare proportions with impairment between groups. Differences in proportions with impairment were further described by calculating effects sizes using  $\phi$ , defined as small effect = .1, medium = .3, and large = .5 (59).

Hierarchical logistic regression models predicting to impairment in CBCL Total Behavior Problems, BRIEF GEC, and average EF z-score examined the following factors stepwise: (1) maternal education, given group differences and the association of SES with outcomes in other studies of EF and PT children (MA or higher served as the reference group), (2) sex, given past literature indicating effects of sex for EF and PT outcomes with generally poorer outcomes for male compared to female children (females as the reference group), and (3) group status (PT vs. FT; FT served as the reference group). We did not include age in the models as the groups did not differ by age and outcomes were normed for age or standardized using a z-score. Given the concerns that IQ has overlap with EF and has been argued against as a covariate in cognitive studies of neurodevelopmental disorders (43), we did not include IQ in the models.

Within the PT group, we identified the percent with behavior vs. EF impairments overall. Pearson correlation was used to examine the association between summary EF scores (GEC or average z-score) and overall behavior problems score (CBCL Total Problems). Using person-oriented analyses, we examined the number of children within the PT group with EF impairment alone, behavior impairment alone, both, and none. Significance level was set at  $p < .05$  for the analyses.

### 3. Results

#### 3.1 Missing data

For the BRIEF-P, data were incomplete for 4 PT participants. Data were missing from the EF battery as follows: 1 PT and 1 FT child for the bird/dragon task (would not play); 2 PT and 1 FT child for the day/night task (technical failure—loss of data recording due to power failure or running out of digital memory); 14 PT and 6 FT for the verbal fluency task (change in testing protocol with task added after the first 18 participants were tested; 2 refused). There were no significant differences in demographic variables for PT and FT groups completing the verbal fluency task compared to the larger study sample. For analyses with missing data, degrees of freedom were adjusted accordingly.

#### 3.2 Participant Characteristics (Table 1)

PT and FT groups did not differ in terms of age, race, ethnicity, or sex. By design, PT and FT groups differed in GA and BW, with the PT group having a range of GA of 23 to 34 weeks. Compared to the PT group, a larger proportion of the FT group had mothers with higher education. Given the smaller number of mothers with lower education, numbers were combined for categories less than 4 years of college to balance the education categories in this relatively high SES sample. Fifty-one PT children (62%) received early intervention or rehabilitation services, such as speech-language services, compared to 7 FT children (9%). Group differences for ABIQ scores are also shown in Table 1; similar to other studies of PT children (11, 62), IQ scores were in the average range, but lower than scores of FT children.

Results from the parent-completed Demographics/Health Questionnaire and review of the medical records showed that more severe neonatal complications were associated with lower GA. Medical complications at birth in the PT group included: 11 had abnormal findings on head ultrasound or magnetic resonance imaging (at least grade 2 intraventricular hemorrhage or IVH, echodensities, or cystic lesions) and 13 had mildly abnormal findings (grade 1 IVH or choroid plexus cyst); 49 had respiratory distress syndrome (RDS) and 8 developed chronic lung disease; 6 had necrotizing enterocolitis; and 8 were small for GA (defined as lying at or below the 3<sup>rd</sup> percentile in birth weight for GA). RDS was associated with GA.

#### 3.3 Performance-based EF, parent-rated EF, and parent reported behavior problems (Table 2)

For performance-based EF, the PT group had significantly poorer performance compared to the FT group on all individual EF tasks and the average z-score, controlling for age and maternal education. Maternal education was significant only in the model for verbal fluency. On parent-rated EF, the PT group had significantly higher scores and standard deviations for the BRIEF GEC, all indexes, and subscales, indicating more executive dysfunction than the FT group. Although the means were within the average range, the PT group had a wider range of scores. Similarly, for parent-rated behavior problems on the CBCL, the PT group had significantly higher scores, indicating more problems, for all summary scales and all subscales except for the anxious/depressed and sleep problems subscales. Again, the means were within the average range, but the PT group had a wider range of scores. Effect sizes were large for the performance-based EF average z-score, parent-rated BRIEF emergent



metacognition index, and approached a large effect for the parent-rated GEC and parent-rated CBCL Total Problems scores. Most individual EF tasks, other BRIEF indexes, and BRIEF and CBCL subscales had effect sizes in the small to medium range.

### **3.4 Proportions with impairment in performance-based EF, parent-rated EF and parent-rated behavior problems (Table 3)**

The PT group compared to the FT group had significantly higher proportions of children with performance-based EF in the impaired range on all individual EF tasks and the average z-score. For parent-rated EF on the BRIEF, the PT group had greater proportions with impairment on the GEC, all indexes and subscales except for the shift subscale. For behavior problems on the CBCL, the PT compared to FT group had greater proportions with impairment on the Total, Internalizing, and Externalizing summary scales, and all subscales, except for emotional reactivity and anxious-depressed subscales. The PT compared to FT group had five to six times as many children impaired on overall performance-based (32 vs. 6%) and parent-rated EF (28 vs. 5%), respectively. The PT compared to FT group had three times as many children impaired on overall parent-rated behavior problems (15 vs. 5%). The effect size for both performance-based and parent-rated EF was medium, greater than the effect size for behavior problems.

### **3.5 Odds ratios predicting impairment in overall performance-based EF, parent-rated EF and parent-rated behavior problems (Table 4)**

For all three outcomes, the overall models were significant. Male sex was significant only for performance-based EF with males 2.6 times more likely to have impairment. SES based on maternal education was not significant in any of the models. The PT group was 6.1 and 6.8 times more likely to have impaired performance-based or parent-rated EF. The PT group was 12.8 times more likely to have impaired parent-rated behavior problems compared to the FT group.

### **3.6 Proportions with impairment within the PT group**

Within the PT group, EF impairments were approximately twice as common (31% for performance-based EF, 28% for parent-rated EF) as CBCL/behavior impairment (15%). Pearson correlations showed that only parent-rated measures (GEC and CBCL Total Problems scores) were significantly correlated,  $r = .728$ ,  $p < .001$ . The average z-score was not significantly correlated with the GEC,  $r = -.178$ ,  $p = .12$ , or the CBCL Total Problems score,  $r = -.073$ ,  $p = .52$ . Using a person-oriented approach, for the children with complete data for average z-score and CBCL Total Problems within the PT group ( $n = 80$ ), 59% were not impaired, 26% had performance-based EF impairment alone, 10% had behavior impairment alone, and only 5% had both. Using the GEC and CBCL Total Problems scores for children with complete data in the PT group ( $n = 77$ ), 68% were not impaired, 17% had parent-rated EF impairment alone, 4% had behavior impairment alone, and 12% had both.

## **4. Discussion**

In summary, consistent with our hypotheses and past literature, we found that the PT compared to FT group had more impaired EF and behavior on both variable- and person-

oriented analyses for all summary measures and most subscales. The regression models showed similarly elevated risk for performance and parent-rated EF impairment (OR of 6.1 and 6.8 respectively) in PT compared to FT children, with even higher odds for behavior impairment (OR of 12.8). Within the PT group, EF impairments occurred twice as often as behavior impairments.

#### 4.1 Variable-oriented Analyses

As expected, the PT group had more EF impairment on both performance-based and parent-rated measures. For the EF battery, the PT group had poorer performance on each individual task and overall as captured by the average z-score, collectively capturing impairments in the core components of EF, including working memory, response inhibition, and cognitive flexibility. Although other studies may find different patterns of impairment in EF based on the sample and EF tasks used (26, 63), our findings are consistent with a meta-analysis of EF studies in PT children that showed decrements with combined small to medium effect sizes of .57 SD for verbal fluency, 0.36 SD for working memory, and 0.49 SD for cognitive flexibility (47). Similarly, the PT group had significantly higher scores on all parent-rated EF subscales, summary indexes, and the overall GEC on the BRIEF consistent with other geographic cohort studies of PT children (64). For behavior problems on the CBCL, similar to other studies (25), the PT group had significantly higher scores or more problems for all scales, except sleep and anxious/depressed. Despite group differences in mean scores for both parent-rated EF and behavior problems, the means for the PT group were in the average range, indicating that person-oriented analyses could provide meaningful information beyond the differences at the group level.

#### 4.2 Person-oriented Analyses

Consistent with the variable oriented analyses, the proportion of PT children impaired was significantly higher for summary measures of EF and behavior as well as all individual EF tasks and most BRIEF and CBCL subscales. A person-oriented approach goes beyond the general knowledge that group means are different and provides additional information to identify individuals who could be targeted for intervention (29, 32). For the CBCL Total Problems, Internalizing, and Externalizing scores, a t-score of 60 or above is in the borderline clinically significant range. For the BRIEF-P GEC, a t-score of 65 is considered clinically significant; a borderline clinically significant cutoff is not designated. Using more stringent cutoffs identified fewer children with impairment (results available on request). While our cutoff of one standard deviation captures a wider range of children than the clinically significant cutoff scores designated by standardized measures such as the BRIEF or CBCL, at these young ages behavior and EF problems are likely still emerging. Given that early identification and intervention might serve to prevent or lessen adverse outcomes, use of a less stringent cutoff might miss fewer children at risk.

#### 4.3 Differences in EF vs. Behavior Impairments within the PT Group

Despite the PT compared to FT group having increased odds for behavior impairments that were approximately twice that of EF impairments (aOR of 12.8 for behavior vs. approximately 6 for EF), person-oriented analyses within the PT group showed that EF impairments, whether measured directly (31%) or by parent ratings (28%) were twice as

common as behavior problems (15%). Although the performance-based and parent-rated scores captured similar percentages of children with EF impairments, there are findings that suggest that overlapping or different constructs of EF may be captured by performance-based vs. parent-rated measures of EF (44, 65, 66). Despite having face validity for EF constructs, parent ratings and performance tasks tapping the same EF construct may or may not significantly correlate with each other and sometimes correlate with a different EF construct. For example, a study of PT children at school age found that parent ratings of working memory were significantly associated only with performance measures of working memory and shifting; parent ratings of inhibition and shifting were not associated with any EF performance measures (67). Similarly, studies of typical and other clinical populations using both parent-rated EF and performance-based EF showed correlations between some, but not all EF constructs, or correlations between one parent-rated EF construct and a different performance-based EF construct (66, 68, 69). Similarly, the correlations in our study between performance-based and parent-rated EF were not significant; in addition, behavior was only significantly correlated with parent-rated EF, likely due to shared method variance.

The discrepancies between parent reports and performance-based EF measures are often attributed to the differences in ecological validity between the two approaches. Parent ratings are designed to capture a global view of children's behaviors in everyday environments, placing the use of EF skills in the context of naturalistic home, school, and community settings (55). Performance-based measures often attempt to isolate and measure a single EF construct by administering a task in a controlled, one-on-one setting that may be free of distractions. From a practical standpoint, administration of a parent-report measure for EF is much less time and labor intensive for busy families and clinicians than performance-based EF measures. The person-oriented approach using either performance-based EF with behavior impairment or parent-rated EF with behavior impairment captured approximately 41 and 32%, respectively, of PT children with either EF or behavior impairment.

#### 4.4 Limitations

The study consisted of a convenience sample, and PT and FT groups differed in SES with the PT group having lower SES, similar to other studies of PT children. Overall, the high mean SES in the study was consistent with the geographic area; however, the results may not be representative of both PT and FT populations with lower SES. In addition, there was a wide range of GA in the PT group. While PT research often focuses on children born extremely PT (< 28 weeks GA), the literature on late PT birth (34 to < 37 weeks GA) also shows increased risk for adverse neuropsychological outcomes (70). Future work with larger samples would have increased ability to examine gradient effects of GA on behavior and EF impairments. There were more children missing data on the verbal fluency task, although there were no demographic differences between participants with and without data. Although we had both performance-based and parent-rated measures of EF, we only had parent report of child behavior problems. Future work that includes direct observation of behavior and longitudinal assessments would provide additional information to clarify the

relationship between EF and behavior problems and progression to developmental or psychiatric disorders.

#### 4.5 Clinical Implications and Future Directions

Behavior symptoms and EF skills are still emerging and developing in the preschool years and may not be at a threshold for clinical diagnosis or disorder. Our findings have potential clinical and public health/policy implications. Our findings suggest that EF impairments may be more common and readily identified than behavior problems at this age in PT children. Pediatricians are more likely to utilize general surveillance for behavior problems and developmental delays rather than specific standardized screens, despite professional pediatric organization recommendations (71). Pediatricians should be educated on the importance of EF skills and educated on how to screen for EF problems and when to refer. Given the important links between EF and later functional outcomes, EF should be further studied longitudinally to determine if it serves as a better marker or predictor of later adverse outcomes than behavior symptoms.

The evidence for EF as a contributor to the development of academic skills and subsequent academic achievement is strong (28, 31, 72). A recent longitudinal study of children with high rates of poverty found that EF at age 5 years prior to school entry strongly predicted 5<sup>th</sup> grade academic skills; interestingly, the study found an interaction between early math ability and EF such that the magnitude of association between early math and later math varied as a function of early EF (72). Children with high levels of EF were able to “catch up” to peers who performed better on assessments of early math ability (72). Whether interventions targeting EF at young ages could result in improved EF and subsequent academic skills and achievement warrants further research.

Many high-risk or neonatal follow-up programs only follow children from infancy, through the toddler years, and often stop at the early preschool years. Early identification has the potential to allow for prevention strategies rather than waiting for the emergence of disorder level symptoms and the need for remediation. Currently in the US there are 13 categories for special education eligibility with no specific category for executive dysfunction (73). Although specific learning disability (SLD) accounted for the largest group of children receiving special education in 2015-16 at almost 39% (73), PT children may demonstrate EF difficulties but remain subthreshold for SLD or a behavioral diagnosis such as ADHD that might qualify the child for an individualized education plan. On a policy level, further research is warranted to evaluate whether executive dysfunction could be considered within the realm of specific learning disability or as a separate category. This type of policy change could increase access to special education for children born preterm. Additional research on identification and interventions for EF impairments not only in PT children, but all children, is needed (63, 74, 75).

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## Abbreviations:

|                 |   |
|-----------------|---|
| <b>ADHD</b>     | Attention Deficit Hyperactivity Disorder                  |
| <b>BRFEEF-P</b> | Behavior Rating Inventory of Executive Function-Preschool |
| <b>BW</b>       | birth weight  |
| <b>CBCL</b>     | Child Behavior Checklist                                  |
| <b>DSM-5</b>    | Diagnostic and Statistical Manual-5                       |
| <b>EF</b>       | executive function  |
| <b>FT</b>       | full term   |
| <b>GA</b>       | gestational age   |
| <b>GEC</b>      | Global Executive Composite                                |
| <b>IVH</b>      | intraventricular hemorrhage                               |
| <b>PT</b>       | preterm   |
| <b>RDS</b>      | respiratory distress syndrome                             |
| <b>SES</b>      | socioeconomic status                                      |
| <b>SLD</b>      | specific learning disability                              |

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### Highlights

- Children born preterm are at high risk for behavior problems and deficits in executive function.
- The co-occurrence of behavior problems and executive function deficits at young ages in preterm children has not been fully investigated.
- Impairments in executive function, both performance-based and parent-rated, were twice as common as behavior problems/impairments in preterm preschoolers.
- We recommend early identification of executive function impairments in preterm children. Future longitudinal and intervention research should evaluate whether executive function impairments serve as better early markers for later functional difficulties in preterm children compared to behavior problems, as well as targets for intervention.

**Table 1.**

Participant characteristics, demographics, and IQ scores

| Participant Characteristics <sup>a</sup> | Preterm (n = 82) |          | Full Term (n = 79) |           | t or X <sup>2</sup> | p      |
|--|------------------|----------|--------------------|-----------|---------------------|--------|
|  | Mean (SD)        | Range    | Mean (SD)          | Range     |                     |        |
| Age (years)                              | 4.5 (.77)        | 3.0-5.9  | 4.5 (.81)          | 3.1-5.9   | -1.3                | .19    |
| Perinatal Data                           |                  |          |                    |           |                     |        |
| GA (weeks)                               | 29.7 (2.7)       | 23-34    | 39.3 (1.4)         | 37-42     | 28.8                | <.001* |
| Birthweight (g)                          | 1369 (450)       | 468-1369 | 3334 (507)         | 2239-3334 | 26.0                | <.001* |
| Demographics <sup>b</sup>                | Preterm          |          | Full Term          |           | t or X <sup>2</sup> | p      |
| Race, n (%)                              |                  |          |                    |           |                     |        |
| White                                    | 45 (55)          |          | 49 (62)            |           |                     |        |
| Nonwhite                                 | 37 (45)          |          | 30 (38)            |           |                     |        |
| Ethnicity, n (%)                         |                  |          |                    |           | .39                 | .53    |
| Nonhispanic/Nonlatino                    | 62 (76)          |          | 63 (80)            |           |                     |        |
| Hispanic/Latino or Mixed Hispanic/Latino | 20 (24)          |          | 16 (20)            |           |                     |        |
| Sex, n (%)                               |                  |          |                    |           | 2.7                 | .10    |
| Male                                     | 47 (57)          |          | 35 (44)            |           |                     |        |
| Female                                   | 35 (43)          |          | 44 (56)            |           |                     |        |
| Maternal Education, n (%)                |                  |          |                    |           | 7.9                 | .02*   |
| < 4 year college                         | 21 (26)          |          | 7 (9)              |           |                     |        |
| > 4 year college                         | 24 (29)          |          | 27 (34)            |           |                     |        |
| MA or higher                             | 37 (45)          |          | 45 (57)            |           |                     |        |
| Cognitive Scores                         | Mean (SD)        | Range    | Mean (SD)          | Range     | t                   | P      |
| IQ <sup>a</sup>                          | 101 (14)         | 67-127   | 110 (13)           | 82-139    | 4.3                 | <.001* |

<sup>a</sup>Data analyzed by t-test<sup>b</sup>Data analyzed by chi-square (asymptotic significance: 2-sided)

Abbreviations: GA—gestational age; MA—Masters degree

**Table 2.**

Group differences in performance-based executive function (EF), parent-rated EF, and parent-rated behavior problems

|   | Preterm (n=82) | Full Term (n=79) |      |        |          |
|---|----------------|------------------|------|--------|----------|
| <b>Performance-Based Executive Function</b> |                |                  |      |        |          |
| <b>EF Battery<sup>a</sup></b>               | Mean (SD)      | Mean (SD)        | F    | P      | $\eta^2$ |
| Average Z-score                             | -.57 (1.1)     | 0.16 (.57)       | 28.7 | <.001* | .049     |
| 6-boxes                                     | 7.0 (1.8)      | 6.5 (1.0)        | 8.1  | .005*  | .063     |
| Verbal Fluency                              | 8.2 (2.8)      | 9.8 (2.6)        | 9.3  | .003*  | .051     |
| Bird/Dragon                                 | 10.4 (4.9)     | 12.2 (3.7)       | 8.3  | .004*  | .026     |
| Day/Night                                   | 7.3 (6.2)      | 9.3 (5.0)        | 4.2  | .043*  | .080     |
| Card Sort                                   | 3.6 (2.6)      | 5.0 (1.9)        | 13.7 | <.001* | .154     |
| <b>Parent-Rated EF</b>                      |                |                  |      |        |          |
|   | n=78           | n=79             |      |        |          |
| <b>BRIEF Indexes,<sup>a</sup> t-score</b>   |                |                  |      |        |          |
|   | Mean (SD)      | Mean (SD)        | F    | P      | $\eta^2$ |
| Global Executive Composite (GEC)            | 52.6 (14.7)    | 43.6 (7.6)       | 19.9 | <.001* | .114     |
| Inhibitory Self-Control Index (ISCI)        | 51.7 (14.1)    | 45.0 (8.4)       | 11.0 | .001*  | .067     |
| Flexibility Index (FI)                      | 50.3 (11.4)    | 45.6 (7.9)       | 8.2  | .005*  | .050     |
| Emergent Metacognition (EMI)                | 54.1 (14.8)    | 43.7 (7.8)       | 26.4 | <.001* | .146     |
| <b>BRIEF Scales,<sup>b</sup> t-score</b>    |                |                  |      |        |          |
|   |                |                  | Z    | P      | r        |
| Inhibit                                     | 51.9 (14.5)    | 45.5 (8.4)       | -2.5 | .012*  | .200     |
| Shift                                       | 49.3 (10.2)    | 45.8 (7.4)       | -2.1 | .035*  | .168     |
| Emotional Control                           | 51.3 (11.7)    | 45.5 (7.9)       | -3.2 | .001*  | .255     |
| Working Memory                              | 55.2 (14.1)    | 44.2 (7.7)       | -5.3 | <.001* | .423     |
| Plan/Organize                               | 51.5 (14.7)    | 43.7 (8.1)       | -3.3 | .001*  | .263     |
| <b>Parent-Rated Behavior Problems</b>       |                |                  |      |        |          |
| <b>Child Behavior Checklist (CBCL)</b>      |                |                  |      |        |          |
|   | n=80           | n=79             |      |        |          |
| <b>Broadband Scales<sup>a</sup></b>         |                |                  |      |        |          |
|   |                |                  | F    | P      | $\eta^2$ |
| Total                                       | 47.5 (11.1)    | 40.5 (7.2)       | 19.7 | <.001  | .112     |
| Internalizing                               | 47.6 (11.2)    | 42.2 (8.3)       | 10.6 | .001*  | .064     |
| Externalizing                               | 47.1 (10.9)    | 40.5 (8.2)       | 16.2 | <.001* | .094     |
| <b>Subscales<sup>b</sup></b>                |                |                  |      |        |          |
|   |                |                  | Z    | P      | r        |
| Emotional Reactivity                        | 53.0 (4.7)     | 51.7 (3.5)       | -2.2 | .028*  | .174     |
| Anxious/Depressed                           | 52.3 (4.4)     | 51.3 (3.2)       | -1.4 | .165   | .111     |
| Somatic Complaints                          | 54.4 (7.0)     | 51.2 (2.9)       | -3.8 | <.001* | .301     |
| Withdrawn                                   | 55.1 (7.1)     | 51.2 (3.2)       | -2.6 | .010*  | .206     |
| Sleep Problems                              | 54.0 (6.8)     | 52.2 (3.5)       | -1.2 | .244   | .095     |
| Attention                                   | 53.3 (5.6)     | 50.8 (2.6)       | -4.1 | <.001* | .325     |
| Aggression                                  | 53.3 (6.1)     | 50.8 (2.3)       | -3.6 | <.001* | .285     |

Abbreviations: EF—executive function; BRIEF—Behavior Rating Inventory of Executive Function; CBCL—Child Behavior Checklist



<sup>a</sup>Data analyzed by ANCOVA, covarying by maternal education

<sup>b</sup>Data analyzed by Mann-Whitney U test for nonparametric data

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**Table 3.**

Proportions of preterm compared to full term children with impairment in executive function or behavior problems, defined as 1 SD below (performance EF) or above the mean (parent-rated EF or behavior problems).

|                                      | Preterm (n=82)        | Full Term (n=79)      |                      |          |          |
|--------------------------------------|-----------------------|-----------------------|----------------------|----------|----------|
| <b>Performance EF</b>                |                       |                       | <b>X<sup>2</sup></b> | <b>p</b> | <b>φ</b> |
| <b>EF battery<sup>a</sup></b>        | <b>n (%) impaired</b> | <b>n (%) impaired</b> |                      |          |          |
| Average z-score                      | 26 (32)               | 5 (6)                 | 16.7                 | <.001*   | .19      |
| Six Boxes                            | 27 (33)               | 13 (17)               | 5.8                  | .016*    | .25      |
| Verbal Fluency                       | 26 (38)               | 11 (15)               | 9.8                  | .002*    | .22      |
| Bird/Dragon                          | 27 (33)               | 11 (14)               | 8.1                  | .004*    | .18      |
| Day/Night                            | 36 (44)               | 21 (27)               | 5.3                  | .021*    | .24      |
| Card Sort                            | 32 (39)               | 14 (18)               | 8.9                  | .003*    | .32      |
| <b>Parent-rated EF<sup>a</sup></b>   | <b>n=78</b>           | <b>n=79</b>           |                      |          |          |
| <b>BRIEF</b>                         | <b>n (%) impaired</b> | <b>n (%) impaired</b> |                      |          |          |
| Indexes                              |                       |                       |                      |          |          |
| GEC                                  | 22 (28)               | 4 (5)                 | 15.2                 | <.001*   | .31      |
| ISCI                                 | 18 (23)               | 5 (6)                 | 8.8                  | .003*    | .23      |
| FI                                   | 12 (15)               | 4 (5)                 | 4.6                  | .033*    | .17      |
| EMI                                  | 27 (35)               | 5 (6)                 | 19.4                 | <.001*   | .35      |
| Scales                               |                       |                       |                      |          |          |
| Inhibition                           | 19 (24)               | 4 (5)                 | 11.7                 | .001*    | .27      |
| Shift                                | 10 (13)               | 6 (8)                 | 1.2                  | .279     | .09      |
| Emotional Control                    | 15 (19)               | 6 (8)                 | 4.6                  | .032*    | .17      |
| Working Memory                       | 29 (37)               | 4 (5)                 | 24.4                 | <.001*   | .39      |
| Plan/Organize                        | 22 (28)               | 5 (6)                 | 13.2                 | <.001*   | .29      |
| <b>Behavior Problems<sup>a</sup></b> | <b>n=80</b>           | <b>n=79</b>           |                      |          |          |
| <b>CBCL</b>                          | <b>n (%) impaired</b> | <b>n (%) impaired</b> |                      |          |          |
| Broadband Scales                     |                       |                       |                      |          |          |
| Total                                | 12 (15)               | 4 (5)                 | 10.0                 | .002*    | .25      |
| Internalizing                        | 12 (15)               | 4 (5)                 | 4.3                  | .037*    | .16      |
| Externalizing                        | 9 (11)                | 1 (1)                 | 6.7                  | .010*    | .20      |
| Subscales                            |                       |                       |                      |          |          |
| Emotional Reactivity                 | 9 (11)                | 4 (5)                 | 2.0                  | .155     | .11      |
| Anxious/Depressed                    | 5 (6)                 | 3 (4)                 | .5                   | .479     | .06      |
| Somatic Complaints                   | 15 (19)               | 3 (4)                 | 8.9                  | .003*    | .24      |
| Withdrawn                            | 23 (29)               | 3 (4)                 | 18.1                 | <.001*   | .34      |
| Sleep Problems                       | 12 (8)                | 4 (5)                 | 4.3                  | .037*    | .16      |
| Attention                            | 12 (15)               | 1 (1)                 | 10.0                 | .002*    | .25      |
| Aggression                           | 8 (10)                | 1 (1)                 | 5.7                  | .017*    | .19      |

<sup>a</sup>Data analyzed by chi-square (asymptotic or exact significance: 2-sided)

Abbreviations: EF—executive function; BRIEF—Behavior Rating Inventory of Executive Function; CBCL—Child Behavior Checklist

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**Table 4.**

Logistic Regression (final models) predicting to impairment in performance-based EF (average z-score), parent-rated EF (BRIEF GEC score), and parent-rated behavior problems (CBCL Total Problems score)

| Outcome                             |  |           |             |             |               |          |
|-------------------------------------|--|-----------|-------------|-------------|---------------|----------|
| Predictors                          |  |           |             |             |               |          |
| <b>EF Z-score</b>                   | <b>Overall R<sup>2</sup> = 21.5%, model p &lt; .001*</b> |           |             |             |               |          |
|                                     | <b>β</b>   | <b>SE</b> | <b>Wald</b> | <b>OR</b>   | <b>95% CI</b> | <b>p</b> |
| Maternal Education                  | -.23   | .27       | .71         | .79         | .47-1.4       | .4       |
| Sex                                 | .96  | .46       | 4.4         | 2.6         | 1.1-6.4       | .04*     |
| Group                               | 1.81   | .53       | 11.7        | <b>6.1</b>  | 2.2-17.2      | .001*    |
| Constant                            | -2.9   | .65       | 19.9        | .06         |               | <.001*   |
| <b>BRIEF GEC</b>                    | <b>Overall R<sup>2</sup> = 19.6%, p &lt; .001*</b>       |           |             |             |               |          |
|                                     | <b>β</b>   | <b>SE</b> | <b>Wald</b> | <b>OR</b>   | <b>95% CI</b> | <b>p</b> |
| Maternal Education                  | -.44   | .28       | 2.4         | .65         | .37-1.12      | .12      |
| Sex                                 | .24  | .46       | .27         | 1.3         | .51-3.2       | .6       |
| Group                               | 1.92   | .58       | 10.9        | <b>6.8</b>  | 2.2-21.4      | .001*    |
| Constant                            | -2.46  | .70       | 12.3        | .09         |               | <.001*   |
| <b>CBCL Total Behavior Problems</b> | <b>Overall R<sup>2</sup> = 16.9%, p = .007*</b>          |           |             |             |               |          |
|                                     | <b>β</b>   | <b>SE</b> | <b>Wald</b> | <b>OR</b>   | <b>95% CI</b> | <b>p</b> |
| Maternal Education                  | -.17   | .37       | .20         | .8          | .41-1.8       | .66      |
| Sex                                 | .33  | .62       | .29         | 1.39        | .41-4.7       | .59      |
| Group                               | 2.55   | 1.06      | 5.76        | <b>12.8</b> | 1.6-102       | .016*    |
| Constant                            | -4.28  | 1.16      | 13.6        | .014        |               | <.001*   |

Abbreviations: EF—executive function; BRIEF—Behavior Rating Inventory of Executive Function; GEC—Global Executive Composite; CBCL—Child Behavior Checklist.

Significant odds ratios in bold.