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Neurocognitive, Social-Behavioral, and Adaptive Functioning in Preschool Children with Mild to Moderate Kidney Disease

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Abstract

Objective—The negative impact of End Stage Kidney Disease on cognitive function in children is well established, but no studies have examined the neurocognitive, social-behavioral, and adaptive behavior skills of preschool children with mild to moderate chronic kidney disease (CKD).

Methods—Participants included 124 preschool children with mild to moderate CKD, ages 12-68 months (median=3.7 years), and an associated mean glomerular filtration rate (GFR) of 50.0 ml/min per 1.73m^2. In addition to level of function and percent of participants scoring≥1SD below the test mean, regression models examined the associations between biomarkers of CKD (GFR, anemia, hypertension, seizures, abnormal birth history), and Developmental Level/IQ, attention regulation, and parent ratings of executive functions, social-behavior, and adaptive behaviors.

Results—Median scores for all measures were in the average range; however, 27% were deemed at-risk for a Developmental Level/IQ<85, 20% were at-risk for attention variability, and parent ratings indicated 30% and 37% to be at-risk for executive dysfunction and adaptive behavior problems, respectively. Approximately 43% were deemed at-risk on two or more measures. None of the disease-related variables were significantly associated with these outcomes, although the presence of hypertension approached significance for attention variability ($p<.09$). Abnormal birth history and lower maternal education were significantly related to lower Developmental Level/IQ; seizures were related to lower parental ratings of executive function and adaptive behavior; and abnormal birth history was significantly related to lower ratings of adaptive behavior. When predicting risk status, the logistic regression did evidence both higher GFR and the lack of anemia to be associated with more intact Developmental Level/IQ.

Conclusions—These findings suggest relatively intact functioning for preschool children with mild to moderate CKD, but the need for ongoing developmental surveillance in this population remains warranted, particularly for those with abnormal birth histories, seizures, and heightened disease severity.

Keywords

Chronic kidney disease; CKD; Mild to moderate CKD; CKiD; Preschool CKD; Neurocognitive function in CKD; Social-behavioral function in CKD; Adaptive behavior function in CKD; Neurobehavioral performance in early childhood CKD

Neurocognitive, Social-Behavioral, and Adaptive Functioning in Preschoolers with Mild to Moderate Chronic Kidney Disease

While the importance of chronic kidney disease (CKD) to development has been recognized for decades, recent research has refined our understanding.[1] Severity of CKD, duration, early age of onset, and proteinuria have been shown to increase the extent of neurocognitive and social-behavioral problems, yet few studies have examined the neurocognitive, social-behavioral, and adaptive behavior (i.e., activities of daily living) of preschool children with mild to moderate CKD. Awareness of the risk of disruption of brain development during

formative early years has led us to focus research on infants, toddlers, and preschoolers. [2]. Additionally, identifying developmental concerns early in life may direct early intervention services that have been shown to improve developmental progress and outcomes in otherdisorders [3].

Neurocognitive and Social-Behavioral Findings in Preschoolers with CKD

To date, there are a number of studies that have provided key information pertaining to developmental functioning during the preschool years, with a particular emphasis on preschoolers with more severe disease severity. Earlier work noted that many young children were severely impaired, with rates of developmental delay ranging as high as 85% [4-11]. Long-term follow-up of children treated for more severe CKD during their preschool years has documented the presence of persistent neurocognitive deficits, particularly for children diagnosed with end stage renal disease during the first two years of life [12]. Across the earlier studies, developmental difficulties in preschool children with CKD tended to be related to other neurologically-based conditions such as seizures, microcephaly, slowed rates of physical growth, and intellectual disabilities [13-14], comorbidities typically not as prevalent in mild to moderate CKD.

Subsequent research examining CKD during the preschool years has revealed findings of a much more positive nature, with the rates of developmental delays being much lower than earlier estimates, with rates hovering around 25% [15]; however, more precise estimates of Developmental Level/IQ in this population remain unclear. Further, while studies examining specific cognitive abilities, such as executive functions, have begun in both typical [16] and atypical preschool populations [17], there are no studies exploring such functions in preschoolers with mild to moderate CKD. Further, estimates of social-behavioral difficulties remain unknown in this young population, although adaptive behavior functions have begun to be examined..In their small sample of preschool children of mixed CKD severity, Duquette et al. [18] found significant differences between the CKD and typically developing groups, with lower developmental level and adaptive behavior in the CKD group. Disease severity was associated with both developmental level and adaptive behavior outcomes. In general, preschoolers with CKD were 8 times more likely than their typically developing peers to have at least one score on the Mullen Scales of Early Learning or the Vineland Adaptive Behavior Scale that was greater than two standard deviations below the normative mean.

Current Study

The available literature clearly indicates the presence of developmental deficits in young children with advanced CKD; however, whether these findings apply to young children with mild to moderate CKD remains an ongoing question. This study was conducted to address this void in the literature using the largest sample of preschool children with mild to moderate CKD to date. The study posed three major research questions. First, what are the level and pattern of neurocognitive abilities, social-emotional functioning, and adaptive behavior in preschool children with CKD? Consistent with the recent findings for our older school-age cohort [19], we suspect that the preschool sample will place within the low average to average range on all tasks and ratings. Second, what is the percentage of

preschoolers who meet an at-risk designation, defined as at least one standard deviation below the normative mean for the tasks and rating scales administered? Similar to findings in our older cohort[19], we anticipate that higher than expected rates of impairment will be present in the preschool children, with rates perhaps being commensurate with the rates uncovered for school-age children with mild to moderate CKD. Finally, what are the disease-related factors that are associated with neurocognitive, social-behavioral, and adaptive behavior for preschool children with mild to moderate CKD? With this younger age group, we suspect that disease severity, as defined by GFR, and the presence of proteinuria, will be associated with preschool children being at risk for problems in neurocognition, social-behavioral skills, and adaptive behavior.

Method

Participants

The sample comprised 124 preschoolers enrolled in The Chronic Kidney Disease in Children (CKiD) prospective cohort study. The CKiD Study is a multisite study funded by the National Institutes of Health to examine various facets of mild to moderate kidney disease, including the manifestation of neurocognitive deficits. Eligibility criteria for enrollment in CKiD included an estimated GFR as calculated by the Schwartz formula of 30 to 90 ml/min per $1.73m^2$, and exclusion criteria included solid organ, bone marrow, or stem cell transplant, cancer/leukemia, or HIV [20]. Participants for this report were between the ages of 12 and 68 months of age, and many had completed neurocognitive testing at study entry. Although there were missing data points scattered across all of the measures, largely secondary to behavioral compliance and age-bands for specific measures (e.g., K-CPT), this sample represents the youngest subset of subjects enrolled in the CKiD study. This study protocol was approved by the institutional review boards of all 48 sites, and informed consent was obtained from all caregivers.

Measures

The neurocognitive, social-behavioral, and adaptive behavior measures were selected to be age-appropriate, applicable to a preschool population with chronic conditions and developmental disabilities, to have good psychometric properties, and to have good administrative reliability across sites. Within the neurocognitive domain, measures of Developmental Level/IQ (Mullen Scales of Early Learning for ages 12 to 30 months, MSEL; Wechsler Preschool and Primary Scale of Intelligence-III for ages 30 months to 71 months, WPPSI-III) and attention regulation (Kiddie Conners' Continuous Performance Test for ages 48 to 71 months, K-CPT) were administered directly to the child. With both tests having a mean of 100 and a standard deviation of 15, the overall scores from the measures of general development (i.e., Mullen Early Learning Composite) and intelligence (WPPSI-III Full Scale IQ) were combined across cases to produce a single estimate of Developmental Level/IQ. For our sample, 17 subjects received the MSEL and 87 subjects received the WPPSI-III. For both the Mullen and WPPSI-III, the reliability and validity of these measures were deemed strong, with reliability estimates ranging across age groups from .91 to .96 for the WPPSI-III Full Scale IQ, and being .91 for the Mullen Early Learning Composite. For the K-CPT, reliability ranged from .72 to .83.

Parents completed ratings of their children's executive functioning (Behavior Rating Inventory of Executive Functioning-Preschool, BRIEF-P), social-emotional behavior (Behavior Assessment System for Children-2, BASC-2), and adaptive behavior (Adaptive Behavior Assessment Scale-II, ABAS II). For all of the rating scales, if parents required assistance in the reading or understanding of the items, it was provided by project staff at the site. All three rating scales utilize a Likert Scale format. For the BRIEF-P, parents are asked to respond to various items addressing their child's day-to-day functioning with respect to organization, planning, working memory, affective control, and problem solving. Reliability and validity estimates of the BRIEF-P are satisfactory, with an internal consistency estimate of the Global Executive Composite of .91. For the BASC-2, parents are asked to describe their child's social and affective functioning by responding to questions about social functioning, anxiety symptoms, depression symptoms, aggression, and related conduct problems. Reliability and validity of the BASC-2 Total Behavior Symptoms Index are adequate, with reliability estimates being greater than .90 across the age bands represented. The ABAS-II is a parent rating scale that asked parents to respond to various questions about their activities of daily living, including social, communication, and general adaptive behaviors. Reliability and validity estimates for the ABAS-II General Adaptive Composite are satisfactory, with reliability estimates ranging from .98 to .99.

For all of the measures, the overall summary variables were extracted for data analyses. “At-risk” status was defined as placing one standard deviation or more below the normative mean for each of the summary variables.

Additionally, key sociodemographic (chronological age, gender, race, maternal education) and CKD-related variables (GFR, glomerular diagnosis or non-glomerular, CKD duration, CKD age of onset, elevated proteinuria, hypertension, anemia, seizures) were selected to serve as predictors of at-risk status for each of the outcome variables. Here, hypertension was defined as casual systolic or diastolic blood pressure ≥ 95^{th} percentile for age, gender, and height, current use of any antihypertensive medication, or parent report of hypertension, while anemia was operationalized as hemoglobin < 5^{th} percentile of normal for age and gender, or taking an erythropoiesis stimulating agent. Elevated proteinuria was defined as urine protein-to-creatinine ratio > 2. Given the higher than average rate of abnormal birth histories in our sample (i.e., low birth weight, small for gestational age, premature birth) [21], and the overlap of these variables in our sample, we created a combined variable, abnormal birth history, to control for this CKD-related variable in our analyses.

Kidney Function

The CKiD study includes measurement of GFR by iohexol clearance [22], but it was decided to separate neurocognitive testing from the clearance study to avoid the distraction of a time consuming medical procedure on the same day. Analysis of the iohexol data has allowed calculation of an estimated GFR (eGFR) [23], and this was utilized for children who did not provide a valid iohexol clearance study. GFR was used to define severity of kidney disease in this population.

Data Analyses

To address the first research question, basic descriptive statistics were derived to determine the overall level and pattern of function across the various outcome measures. To address the second research question, the percentage of participants placing at least one standard deviation or more below the normative mean for each variable was calculated. Finally, for the third research question, multiple linear regression was used to assess the effects of sociodemographic and disease-specific variables on neurocognitive, social-behavior, and adaptive behavior functions. Additionally, a logistic regression model was examined to determine these variables were related to at-risk status for each of the developmental outcomes.

Results

Sample Description

Table 1 provides a description of the sociodemographic and disease-related variables for the preschool sample. The children ranged in age from 12 months to 68 months of age, with a median age of 3.7 years. The sample was 69% male and 39% had mothers with a high school degree or less. The median GFR was 50.0 ml/min per $1.73m^2$ and only 6% of the sample had a glomerular diagnosis. All of the participants were diagnosed with CKD at birth. Additionally, the sample was characterized by 56% having hypertension, 21% with anemia, and 8% with elevated proteinuria. For the combined variable of abnormal birth histories, 20% had low birth weight, 19% were premature, and 16% were small for gestational age. Seizures were present in 11% of the sample. Additionally, at this young age, only two parents reported the presence of a learning disability and no parents reported the presence of ADHD.

Although 124 preschool children were enrolled in the CKiD Study, sample sizes varied across all of the outcomes measures, largely secondary to behavioral compliance and the applicability of measures to a specific age range. Completed measures of Developmental Level/IQ, executive functioning, and social-behavior were available for the majority of participants (104, 106, and 114, respectively). The measure of adaptive behavior (a parent report measure) was discontinued in CKiD after 2008, and there were 75 participants for which this tool was available. Largely because participants had to be at least 48 months of age to complete the K-CPT, only 30 cases were available. Despite the variability in sample size across measures, there were no differences in sociodemographic or CKD-related variables between those without or without data for any of the outcome measures.

Neurocognitive Performance, Social-Emotional Behavior, and Adaptive Behavior Ratings

The median performances of the preschool participants on the various outcome variables are presented in Table 2. Although the sample did not show extreme outliers on any of the tests, medians were employed given that the obtained scores were skewed to the left. When examining the overall group performance, it is clear that the sample placed within the average range on development/intelligence. Attention regulation also placed within the average range, with errors of omission, errors of commission, and variability being consistently within the average range. Parent ratings of executive functioning were within

the average range as well, with estimates of Emergent Metacognition, Inhibitory Self-Control, and Flexibility being evenly developed within that range.

Similarly, parent ratings of social-behavioral functioning placed within the average range. Specifically, no problems were noted for internalizing, externalizing, or overall behavioral symptoms. These ratings for the overall group indicated few concerns at this developmental time point for the presence of symptoms suggestive of anxiety, depression, or other affective or social-behavioral difficulties.

In contrast, the summary scores for the ABAS-II were somewhat lower, placing within the low average to average range. On the ABAS-II, specific concerns were noted by parents in the Practical Composite Score, which placed one standard deviation below the normative average for the test. Items on this scale reflect capabilities in age-appropriate community functions (e.g., adequately moving around environment), home living (e.g., cleaning, chores), health and safety (following safety rules), and self-care (e.g., eating, dressing, toileting), functions that could be negatively affected by CKD.

Percentage of Participants Defined as At-Risk

Although the majority of the scores for the neurocognitive, social-behavior, and adaptive behavior measures placed within an age-appropriate range, when the percentage of preschool children placing more than one standard deviation below the mean was examined, rates were uniformly higher (indicating more are at-risk) than would be expected from normative standards (approximately 16%). Specifically, as seen in Table 2, within the Developmental Level/IQ domain, 27% of the children were deemed at-risk. Within the attention regulation domain, 23% of the children were at least one standard deviation below the mean on errors of commission, suggesting a heightened rate of impulsive responding in this sample. Parent ratings of executive functioning placed about 30% of the students at-risk for their overall executive capabilities, with rates ranging from 23% on the Flexibility Index to 34% on the Emergent Metacognition Index.

Parent ratings of social-behavior functioning did not place many subjects in the at-risk category. Only 13% of the sample received ratings that were at least one standard deviation below the mean, with reports of internalizing problems (i.e., symptoms of depression, anxiety) and externalizing problems (i.e., conduct problems, aggression) reflecting 20% and 14%, respectively, of the sample being described as at-risk. These rates are well within normal curve expectations.

Finally, the adaptive behavior domain revealed the most concerns, with parents reporting 37% of the preschoolers to be at-risk for their general adaptive behavior capabilities. The number of preschoolers at-risk for adaptive behavior problems ranged from 32% on the Conceptual Composite Score to 51% on the Practical Composite Score, suggesting that many of these children were at risk for not developing age-appropriate activities of daily living.

With respect to the percentage of preschoolers who were at-risk, one question pertains to how many preschoolers were reflected as at-risk across multiple measures. Specifically,

approximately 43.5% of the preschool children (n=54) manifested at-risk status on two or more of the measures, indicating that most of the participants were not at-risk or only at-risk on one of the measures.

Predictors of Neurocognition, Social-Emotional Behavior, and Adaptive Behavior

As can be seen in Table 3, when CKD disease-related variables were entered into the multiple linear regression models, none were significant for any of the targeted outcome variables after adjusting for other key sociodemographic variables, although the presence of hypertension approached significance for attention variability ($p < .09$) in the expected direction. Abnormal birth history and lower maternal education were significantly related to lower Developmental Level/IQ; seizures were related to lower parental ratings of executive function and adaptive behavior; and abnormal birth history was significantly related to lower ratings of adaptive behavior.

When entering the CKD disease-related variables into a logistic regression to examine their association with at-risk status on the various measures, a few new findings were noted. Specifically, after adjusting for sociodemographic variables, disease severity, as defined by GFR ($p<.04$) and anemia ($p<.05$) were significant predictors of Developmental Level/IQ risk status, with Odds Ratios of .96 and .13, respectively. This indicates that lower GFR and a non-anemic presentation are associated with a higher Developmental Level/IQ in this sample. The findings were unchanged for the other preschool outcomes when compared to the linear regression results.

Discussion

This study was conducted to address several key questions pertaining to the developmental/cognitive, social-behavior, and adaptive function capabilities of preschool children with precisely measured mild to moderate CKD. In the largest examination of this population to date, results from this study provide some of the first large scale neurocognitive, social-behavioral, and adaptive behavior findings on preschool children with mild to moderate CKD. As suspected, and consistent with their school-age peers [19], the overall median for all of the variables placed the CKD group within the average range of functioning. As hypothesized, however, a disproportionate number of preschoolers were at-risk for lower Developmental Level/IQ, executive dysfunction, and adaptive behavior problems, with rates ranging from a low of 13% for overall social-behavioral symptoms to 51% for selected adaptive behavior problems. These rates were present even in attention regulation and inhibitory control (K-CPT Errors of Commission) where there was a relatively smaller sample (n=30) due to the age restriction of the K-CPT. Some of the highest percentages were reached on parent rating scales (e.g., ABAS-II), and these findings should receive follow-up as it remains uncertain if these ratings are reflecting the impact of CKD on the preschool child, parental perceptions and associated worries for a young child with a chronic illness, or perhaps use of a measurement developed for typically developing children.

Further, as might be expected, a large percentage of preschoolers were at-risk on multiple measures, with approximately 43.5% of the preschool children manifesting at-risk status on two or more of the measures. This is important in that some of these children may be

eligible for special education services in the preschool setting through their public school systems due to a developmental delay. The term “developmental delay” conveys a particular meaning in special education and implies that the child is delayed in one of five areas of development. To receive special education services, a preschool child should have a developmental delay in one or more of the following domains: physical, cognitive, communication, social/emotional, and self-help. While operational definitions of those who do and do not quality for special education services vary from state to state (see http://www.nectac.org/~pdfs/topics/earlyid/partc_elig_table.pdf), knowing that a large percentage of preschool children with CKD may be at-risk in a number of key developmental domains will be critical for their parents and professionals to consider when pursuing special education services.

In contrast to expectations, particularly given the suspected neurological vulnerability of this sample, none of the disease-related variables were predictive of risk for neurocongitive, social-behavioral, or adaptive behavior problems at this developmental time point. This may not be surprising, given the relatively short duration of illness and, perhaps, reduced precision of measurement in the preschool years. Further, proteinuria was not associated with decreased cognition in the preschool subjects, although this has been shown to be a significant predictor of lower neurocognitive performance in the older children in the CKiD cohort. In that regard, only a small number of the preschool subjects had elevated proteinuria, which was likely a consequence of the low number of subjects with glomerular disease compared with the older cohort and concerns that the CKiD sample may be biased in favor of a healthier group of preschool children. Although not significant, the presence of hypertension did show a trend in the expected direction for an association with lower attention variability, and this would be consistent with emergent literature showing this connection in older children [24]. When risk status was included in a logic regression model, both disease severity, as defined by GFR, and anemia were significant predictors of Developmental Level/IQ risk status, with the findings indicating that lower GFR and a non-anemic presentation are associated with a higher Developmental Level/IQ in this sample. Again, not surprisingly, better kidney functioning and overall health during the infant/toddler and preschool years portends a higher level of performance on measures of development and intelligence.

When compared to available early childhood findings in CKD, these findings are gratifying in that they reflect little in the way of major concerns or severe developmental challenges for this population as a whole at this time point in their development and associated disease status. While previous studies have demonstrated high rates of developmental delays [11], with deficient developmental and adaptive behavior levels being reported [16], nearly all of these studies have been conducted with small samples comprising more severe CKD. In their mixed sample, Duquette et al. [18] did show that less disease severity was associated with higher cognitive and adaptive functioning, and this finding would be consistent with our data on preschool children with mild to moderate CKD showing that higher GFR was associated with higher Developmental Level/IQ. Additionally, the rates of individual cases being at-risk for developmental difficulties ranged widely in the current study but, in general, would be lower than rates documented in earlier studies; again, largely due to the CKiD sample having less renal disease severity, fewer cases of glomerular disease, and consequently less

associated disease burden. Further, when compared to school-age children and adolescents with mild to moderate CKD [19], these results are remarkably similar in their scope and manifestation, and the current data extend those findings to include parental ratings of social-behavior, adaptive behavior, and executive functions, along with direct assessment of attention regulation abilities. Finally, when compared to other preschool populations with chronic conditions, such as congental heart disease [25], Type 1 Diabetes [26], Liver Disease [27], and absence epilepsy [28], the level and subtle diffuse nature of the current findings are remarkably similar across preschool samples. At this developmental epoch, the generalized nature of these findings may be associated with the risk for greater difficulties over the course of development, particularly as the chid enters into the formal school-age years, and implicates the need for early identification of such concerns and early intervention.

This is one of the first studies to examine the cognitive, social-behavioral, and adaptive behavior functioning in preschool children with mild to moderate CKD and, at present, is the largest study to date in this regard. The sample is well-characterized with accompanying standardized measures of the domains of interest. Despite these strengths, there are several limitations that require mention. First, given the performance inconsistencies that can be seen in the preschool child, the sample size for each of the measures varies. This issue is particularly noteworthy in the K-CPT where the numbers are relatively smaller due to the age constraints on this measure (i.e., applicable for ages 4-5 years) and, to some extent for the ABAS-II. Taken together, this may have contributed to inconsistency of our findings. Second, given our sample size limitations and the different measures needed to assessment development and IQ across the ages 12 to 71 months, we adopted the strategy of combining our developmental and IQ variables into a single variable representing development/IQ. We recognize that there is an assumption of developmental continuity in deploying this strategy, but we had little recourse given our sample size. Having a larger sample of infants (birth to 24 months), toddlers (24 to 36 months), and preschooler (36 to 60 months) would permit closer examination of these developmental age bands using single measures, thus reducing the potential error variance associated with a combined test strategy. Finally, we obtained significantly divergent findings on the parent rating scales reporting social-behavior and adaptive behavior functions. In future studies it would be important to collect teacher ratings on these behaviors in an effort to determine the cross-setting similarities and differences in observations of preschoolers with CKD.

Despite these relatively positive findings, ongoing developmental surveillance of this population remains prudent, particularly given their potential neurological and psychosocial vulnerability secondary to the early age of diagnosis and eventual chronicity of disease, and the number of children who fall into at-risk performance in different domains. Having CKD at an early age should enable frequent discussions regarding both medical and developmental needs, along with the possibility of specialized preschool services. Further, long-term follow-up of children treated for CKD during their preschool years has documented the presence of persistent neurocognitive deficits, particularly with respect to the presence of more severe kidney disease [12]. Indeed, this developmental epoch may be an optimal time point in which to begin monitoring developmental status via formal and informal assessments over the course of disease progression, and more frequent contacts with primary care providers and school personnel may be necessary. In fact, working with

the family and the local educational system will be essential in in order to determine the type and amount of early intervention services required for some cases where encroachment on developmental status is suspect or observed. Early intervention efforts may be important with respect to lessening the developmental risk for targeted preschool children, and possibly to decreasing the future developmental risk that may be associated with CKD disease progression.

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Table 1
Description of the CKiD Preschool Sample (N = 124) at Study Entry

Sample Characteristic	*% (n)* or *median [iqr]*
Age	3.7 [2.4, 4.6]
Male Gender	69% (87)
Maternal Education (N=123)	
High School or less	39% (48)
Some College	33% (40)
College or more	28% (35)
Glomerular Diagnosis	6% (8)
Percent of Life with CKD	100 [100, 100]
GFR *	50.1 [38.3, 61.2]
Elevated Proteinuria (N=113)	8% (9)
Hypertension **	56% (71)
Anemia ***	21% (26)
Low birth weight (N=124)	20% (25)
Small for Gestational Age (N=121)	16% (19)
Premature birth (N=122)	19% (23)
Presence of Seizures (N=125)	11% (14)

* iohexol GFR if available (N=108), eGFR if not (N=16)

** defined as casual systolic or diastolic blood pressure ≥95th percentile for age, gender and height; current use of any antihypertensive medication; or self-report of hypertension.

*** defined as hemoglobin <5th percentile of normal for age and gender or taking an erythropoiesis-stimulating agent.

Table 2

Medians, Means, Interquartile Ranges, and Percentages of Preschool Children Placing One Standard Deviation or More Below Normative Standards at Study Entry

Measure	*N*	*Median [IQR]*	*Mean [IQR]*	*% (n) at risk**
Developmental Level/ IQ	104	96 [85, 104]	95.4 ± 15.5	27% (28)
BRIEF-P				
Emergent Metacognition	105	54 [46, 62]	55.2 ± 11.9	34% (36)
Inhibitory Self-Control	106	51 [44, 61]	52.4 ± 11.4	28% (30)
Flexibility	106	48.5 [42, 58]	50.2 ± 10.2	23% (24)
Global Executive Composite	105	53 [45, 60]	53.3 ± 11.7	30% (31)
K-CPT				
Omissions	30	50.5 [46, 58]	51.6 ± 7.9	20% (6)
Commissions	30	53 [46, 58]	52.7 ± 7.7	23% (7)
Variability	30	55.5 [48, 59]	54.3 ± 7.6	20% (6)
BASC-2				
Internalizing Problems	114	50 [44, 58]	51.7 ± 10.4	20% (23)
Externalizing Problems	114	50.5 [43, 58]	50.9 ± 9.0	14% (16)
Adaptive	114	47 [41, 54]	47.3 ± 9.3	24% (27)
Behavioral Symptoms	114	50 [44, 56]	50.7 ± 9.4	13% (15)
ABAS-II				
Practical Composite	63	84 [77, 94]	86.1 ± 15.0	51% (32)
Conceptual Composite	74	93 [82, 103]	91.5 ± 16.2	32% (24)
Social Composite	75	93 [80, 102]	92.2 ± 17.0	37% (28)
General Adaptive Composite	65	89 [76, 102]	89.5 ± 16.3	37% (24)

Note. Developmental Level/IQ and ABAS-II scores have a mean = 100 and a Standard Deviation = 15, with higher scores reflecting a more intact performance. The K-CPT, BRIEF-P, and BASC-2 scores have a mean = 50 and a Standard Deviation = 10. For th K-CPT and BRIEF-P, higher scores reflect more impaired performance. For the BASC-2 scores, higher scores reflect more impaired performance accept for the Adaptive Composite where higher scores reflect more intact performance.

* at risk" defined as ≥ 1 standard deviation below mean performance.

Table 3

Results of the Multiple Linear Regression Models Showing the Relationship between Targeted Predictors and the Neurocognitive, Social-Behavioral, and Adaptive Behavior Outcomes

Predictor	Developmental Level/IQ (n=92)			CPT-II Attention Variability (n=29)			Global Executive Composite (n=94)			BASC-2 Behavioral Symptom (n=103)			ABAS-II Adaptive Behavior (n=59)		
	Estimate	*Std. Err.*	*p-value*	*Estimate*	*Std. Err.*	*p-value*	*Estimate*	*Std. Err.*	*p-value*	*Estimate*	*Std. Err.*	*p-value*	*Estimate*	*Std. Err.*	*p-value*
Age	1.71	1.38	0.22	5.37	3.51	0.14	0.84	1.19	0.48	0.97	0.91	0.29	1.44	1.87	0.44
Male	-4.68	3.48	0.18	3.27	3.43	0.35	1.62	2.92	0.58	0.28	2.25	0.90	-1.57	4.25	0.71
Maternal Education															
Some college	6.67	3.58	*0.07*	-7.02	4.02	*0.10*	1.35	3.02	0.66	0.55	2.36	0.82	4.29	4.74	0.37
College or more	14.11	3.60	**0.0002**	-0.88	3.73	0.82	-3.84	3.07	0.22	-2.83	2.46	0.25	5.39	5.24	0.31
GFR	0.10	0.09	0.25	0.07	0.09	0.43	0.07	0.07	0.37	0.05	0.06	0.43	0.01	0.13	0.94
Proteinuria	0.97	6.32	0.88	-1.17	6.02	0.85	3.78	5.53	0.50	-1.74	4.54	0.70	5.80	9.36	0.54
Hypertension	2.05	3.21	0.53	5.82	3.23	*0.09*	-0.37	2.62	0.89	-2.12	2.06	0.31	0.01	4.07	>0.99
Anemia	5.66	4.07	0.17	0.71	3.74	0.85	2.09	3.39	0.54	1.20	2.62	0.65	-2.02	5.41	0.71
Seizures	-2.31	5.22	0.66	-4.87	5.17	0.36	8.69	4.03	**0.03**	2.02	3.33	0.55	-17.00	6.69	**0.01**
Abnormal Birth Hx[+]	-7.16	3.41	**0.04**	2.25	3.28	0.50	3.72	2.70	0.17	0.50	2.13	0.82	-11.96	4.43	**0.01**

[+] Low birth weight, small for gestational age, or premature birth