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Decline in Verbal Working Memory during Treatment and Association with Achievement among Children with Acute Lymphoblastic Leukemia

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Abstract

Purpose/Objectives—To assess change in specific cognitive processes during treatment with chemotherapy-only for children with Acute Lymphoblastic Leukemia (ALL).

Design—A prospective, repeated measures design.

Setting—Pediatric oncology treatment centers at Banner University Medical Center Tucson/ University of Arizona and Texas Children's Cancer and Hematology Centers at Baylor College of Medicine in Houston, Texas.

Sample—The sample included 71 children with ALL with a mean age of 6.18 years ($SD \pm 3.07$) at the time of diagnosis.

Methods—Using mixed effect latent growth curve modeling with time since diagnosis as a fixed effect, age-adjusted standardized measures of working memory, processing speed, executive function and attention were obtained and repeated approximately one and two years later. A subsample was tested for academic achievement at the end of treatment.

Findings—There was a significant main effect for age at diagnosis on decline in verbal working memory ($F=2.98, p<.05$) during treatment. Planned contrasts revealed greater decline among children who were diagnosed when less than 5 years of age compared to those diagnosed 5 years and older ($t=2.91, p<.01$). Decline in verbal working memory and achievement in letter-word and calculation skills were associated ($r=.552, p<.01$; $r=.434, p<.05$), decline in spatial memory was associated with calculation ($r=.371, p<.05$). There was a main effect of gender on processing speed with females showing greater decline compared to males ($F=4.14, p<.05$).

Implications for Nursing—Children undergoing treatment for ALL may experience difficulties in verbal working memory and hence, increased difficulty in school. Nurses are in a position to refer parents and children to school resources for additional academic support.

Keywords

longitudinal study; child development; neuropsychology; clinical; cognitive; academic outcomes

Neurocognitive sequelae associated with treatment for childhood Acute Lymphoblastic Leukemia (ALL) are well documented when treatment included cranial radiation (see Copeland et al., 1985; Edelmann et al., 2014; Fletcher & Copeland, 1988; Krull et al., 2013). Use of intrathecal and systemic chemotherapy has now largely replaced cranial radiation for pre-symptomatic treatment of the central nervous system (Richards, Pui, & Gayon, 2013) with evidence for improvement in neurocognitive outcomes. In a systematic review of literature from 1997 to July 2008 reporting outcomes among survivors of childhood ALL treated with chemotherapy only, eight of ten studies included measures of general intelligence (IQ) and found no impairment in total IQ (Buizer, de Sonnevile, & Veerman, 2009). However, half of the studies noted problems in academic achievement suggesting more subtle effects of chemotherapy on cognitive processes that are important for success in school (see Kingma et al., 2002; Schuitema et al., 2013).

The childhood leukemia literature has evolved beyond just global IQ to include a more detailed investigation of neurocognitive effects. Even with newer ALL treatment protocols, lower performance on measures of attention (Buizer, de Sonnevile, van den Heuvel-Eibrink, & Veerman, 2005; Conklin et al., 2012; Jacola et al., 2016; Jansen et al., 2006) and processing speed (Buizer et al., 2005; Mennes et al., 2005) are noted. Consistently, chemotherapy is associated with lower than expected performance among survivors 120 weeks post-consolidation on attention, reading and math achievement, motor processing speed (Edelmann et al., 2014; Jacola et al., 2016) and working memory (Ashford et al., 2010) compared to norm reference groups, for a review see Cheung and Krull (2015). Further, age appears to moderate the effect of treatment on cognition with younger children

performing more poorly and girls more affected than boys (Campbell et al., 2007; Ciesielski, Lesnik, Benzel, Hart, & Sanders, 1999; Jain, Brouwers, Okcu, Cirino, & Krull, 2009).

Less well described are the potential effects of chemotherapy on working memory during treatment. Working memory involves temporary holding and manipulation of information and hence involves both attention and capacity (Baddeley, 2012; Gathercole, Pickering, Knight, & Stegmann, 2004). Working memory is needed for complex cognitive tasks (Baddeley, 2000, 2014) and is implicated in academic achievement such as in language comprehension, problem solving and mental arithmetic (Engle, Tuholski, Laughlin, & Conway, 1999) and with literacy and mathematics in school-aged children and achievement in science and mathematics among older children (Bull & Lee, 2014; Gathercole et al., 2004). Working memory is present even in young children with increases in the capacity of working memory through early and middle school years and adolescence (Gathercole, Pickering, Ambridge, & Wearing, 2004). Early identification of declines in working memory during treatment could improve understanding about when deficits occur, the association of these deficits with academic achievement and trigger early referral for school resources.

The purpose of this study was to examine rate of change during treatment in working memory, processing speed, executive function and attention among children diagnosed with ALL and receiving chemotherapy. We hypothesized there would be a decline from the initial measure relative to age-adjusted norm reference groups over the course of treatment in these particular cognitive processes. We also examined age at the time of diagnosis, risk group and gender. We were specifically interested in decline in working memory as a possible explanation for lower school achievement.

Methods

Design

The design of this study was a prospective, repeated measures design examining intra-individual change over time.

Participants

Seventy-one children were sequentially enrolled in the study over a period of 4 years. All were diagnosed with ALL and received treatment according to protocols from the Children's Oncology Group (COG). Participants received treatment according to COG protocols AALL0331 (n=34, all standard risk), AALL0031 (n=1, very high risk), AALL0622 (n=1, high risk), AALL0232 (n=15, 2 standard risk and 13 high risk), AALL0932 (n=11, 2 low risk, 8 standard risk, 1 high risk), AALL1131 (n=6, 5 high risk and 1 very high risk), and AALL0434 (n=3, 2 low risk and 1 standard risk). Children were assigned to treatment risk group twice: at diagnosis according to National Cancer Institute Rome Criteria (Smith et al., 1996) and post-induction according to the specific COG protocol followed. The second risk assignment which was used in this analysis includes considerations of genetic markers and response to induction therapy. Treatment varied in length from approximately 2 to 3.5 years. Specific medications were determined by the therapy protocol; that is, not all children received all medications. None of the children in this analysis were treated with cranial

irradiation. Children were between 2 and 15 years of age when diagnosed and between 3 and 17 years when participating in the cognitive testing. The measures in the cognitive battery are available in English and participants had to be sufficiently fluent in English to complete the measures without an interpreter (although non-English speaking parents could be consented in their dominant language). Exclusion criteria included diagnoses of neurological disorders or neurodevelopmental disabilities (e.g. seizures and Down syndrome).

Procedures

Participants were recruited from two pediatric oncology treatment centers, with approval from the University of Arizona Human Subjects Protection Program and Baylor University Committee for Protection of Human Subjects. Children assented to study involvement while parents provided formal informed consent as soon as possible following diagnosis. Children who agreed to participate were tested using a cognitive battery as soon as they could be scheduled following initiation of treatment and then annually as scheduling allowed.

Measures

A demographic form was used to gather information on the child's age and gender, maternal and paternal achieved education, race/ethnicity and treatment risk. Cognitive measures were used to assess working memory, processing speed, executive function and attention.

Working memory was assessed with the Wide Range Assessment of Memory and Learning 2nd edition (WRAML2)(Adams & Sheslow, 2003). Specifically, the subtests used were Finger Windows and Number Letter. Finger Windows is a visual-spatial memory task (the child must replicate a pattern where the administrator inserts the blunt end of a pencil into predetermined holes of a plastic template) whereas Number Letter is a verbal working memory task. The Number-Letter subtest requires the child listen to the administrator read a series of numbers and letters that are presented in no particular order. The child is required to repeat the numbers in numerical order and the letters in alphabetical order. As the items are completed correctly, the number of numbers and letters increases. Each subtest and the composite were converted to age-adjusted standard scores with a mean of 100 and a standard deviation of 15 using national norms. Testing with the WRAML2 begins at 5 years of age (Table 1).

Processing speed was assessed with the Woodcock-Johnson 3rd Edition (WJ III) Tests of Cognitive Abilities (Woodcock, McGrew, & Mather, 2001), specifically two subtests, Visual Matching and Decision Speed. Both are timed tests that require children to find matching items in rows. Visual Matching comes in two versions: a version with numbers for school-age children and a version with shapes for younger children. Decision Speed consists of rows of pictures with a pair of similar items in each row. The child is asked to select the two pictures that are similar. Standard scores were obtained for each measure and for the composite of processing speed based on a mean of 100 and a standard deviation of 15. The WJ III tests were completed by participants of all ages.

Executive function was measured using Animal Sorting, Auditory Attention and Response Set, Clocks, Design Fluency, Inhibition and Statue subtests on the NEPSY-II (Korkman, Kirk, & Kemp, 2007). The advantage of the NEPSY-II is the opportunity to obtain indicators

of executive function that are age appropriate. Animal Sorting tests the ability to make unique sets of cards by finding similarities and to shift to create new sets. Auditory Attention assesses attention vigilance and requires the child listens to a series of words and respond when a target word is heard. The Response Set subtest, part of auditory attention, requires that the child listen to a new set of words and respond in a different manner to target words. The Response Set tests the ability to shift to a new task and inhibit automatic responses. For the Clocks measure, children are directed to draw analog clocks to assess planning and organization. The Design Fluency subtest gives children one minute to create as many unique designs as possible on a grid with 5 dots. The Inhibition subtest is composed of 3 parts: naming, inhibition, and switching. Each section involves naming shapes, but the rules change for inhibition and switching. Children must inhibit automatic responses in order to score well on the subtest. The Statue subtest measures a young child's ability to ignore distractions and remain focused and still. A composite executive function score was calculated by averaging the subtest scores. The specific battery of subtests administered was based on the child's age. Children 3 to 4 years of age completed *only* the Statue subtest, children 5 to 6 years of age completed the Auditory Attention, Design Fluency, Inhibition and Statue tests, while children 7 to 12 years of age completed all of the subtests *except* for Statue and children 13 to 17 years of age completed all of the subtests except for the Statue and Design Fluency subtests. A composite executive function score was calculated by averaging standard scores on the subtests.

Attention was assessed with the Conner's Continuous Performance Test Second Edition (CPT II) (Conners, 2004) and Kiddie Continuous Performance Test (K-CPT) (Conners, 2006). For the CPT II, children are shown one letter at a time on a blank screen and instructed to press the space bar every time a letter is seen *except* for when an "x" appears. The K-CPT is the same except that simple pictures are used rather than letters and a soccer ball is used in place of the "x". An overall CPT score was calculated by averaging the T-scores for omissions, commissions, and perseverations. With more omissions you will have less opportunity for commissions; however, in the setting of more omissions and then commissions on the attempted items, the total errors are meaningful. The K-CPT is appropriate for children ages 4–5 and the CPT II is used for children ages 6 and older.

Achievement was assessed with the Woodcock-Johnson III Tests of Achievement (Woodcock et al., 2001) using the tests for Letter-Word identification and Calculation. Letter-Word identification measures word skills initially by requiring the participant to identify letters and then advancing to the identification of words. The Calculation test assesses ability to perform computations. Initially, the child must write single numbers. The remaining items require addition, subtraction, multiplication, division and combinations of these operations. Items for older children and those of high ability assess geometric, trigonometric, logarithmic and calculus operations. The tests of Letter-Word Identification and Calculation are appropriate for children ages 5 to 19 years.

Statistical Analyses

Descriptive statistics were computed for demographic characteristics. Performance on neurocognitive measures was reported as age-adjusted standard scores. Age-adjusted

standard scores account for the expected improvement in cognitive ability during development hence change in age-adjusted standard scores reflect change in ability. Analysis of the longitudinal data used growth curve modeling (also known as linear mixed effects models with random coefficients), the initial value and growth rate for each participant was composed of both fixed (population) and subject-specific random effects, enabling the estimate of the rate of change over time. Time Since Diagnosis (TSD) was a fixed effect allowing for variation in data collection intervals among participants. Data were collected over three time periods; as soon as possible after treatment began and one and two years following.

Academic abilities were assessed with the Woodcock Johnson III Letter-Word Identification and Calculation tests in a subset of children who were available for testing at the completion of ALL treatment. The intent was to examine correlations between the slopes for the cognitive tests that showed significant declines relative to the age-adjusted norm reference group and measures of achievement.

Main effects of age at the time of diagnosis, gender and leukemia risk level were obtained. There were only 4 children categorized as low risk, so for the purposes of comparing risk, this group was combined with the standard risk group (total = 49) and the very high risk group contained only 2 children who were combined with the high risk group (total = 22). When the main effects were significant, planned comparisons examined rate of change in each cognitive assessment between the youngest age group and the pooled three oldest age groups and between genders. The planned comparisons were based on the literature indicating that younger age at diagnosis and gender predict worse cognitive outcomes (von der Weid et al., 2003).

Missing data occurred because occasionally the child declined to complete the measure. We assume the “missingness” mechanism is missing at random (MAR) (Mazza, Enders, & Ruehlman, 2015; Muthen, 1991; Nesselroade, 1991). Latent growth curve modeling uses Full Information Maximum Likelihood (FIML) for inference, and is robust to MAR missing data.

Results

Seventy-one children diagnosed with ALL were enrolled and assented to participation while parents/legal guardians consented to participation in the “Childhood Leukemia: Oxidative Stress, Cognitive Changes & Academic Outcomes Study.” Thirty-nine were female and 32 were male with a mean age of 6.18 years ($SD \pm 3.07$) at the time of diagnosis. At the time of diagnosis, there were 32 children between 3 to < 5 years of age, 16 children 5 to < 7 years of age, 9 children aged 7 to < 9, and 14 children 9 years of age. Specific characteristics of the sample are provided in Table 2.

There were no significant differences in maternal education by age group at time of diagnosis ($F=1.330, p = .27$) or gender ($t=-1.08, p = .28$) and no significant differences in paternal education by age group ($F=0.285, p = .836$) or gender ($t=0.341, p = .734$). There were no main effects for risk group on any of the cognitive measures over time.

In the model that included age at diagnosis, gender and risk, there were no differences in rate of change for Finger Windows, Decision Speed, NEPSY-2 or CPT-II. There were main effects of age at diagnosis on Number Letter ($F=2.98, p < .05$) and in the composite WRAML2 ($F=3.52, p < .05$). Examination of contrasts revealed that Number Letter and WRAML2 growth rates for participants diagnosed younger than 5 years were significantly different than for participants who were at least 5 years of age at diagnosis (Table 3). Children who were less than age 5 at the time of diagnosis showed greater negative slopes in Number Letter over the three measurement occasions ($t = 2.91, p < .01$). Children who were less than 5 years of age at diagnosis also differed significantly on the WRAML2 ($t = -3.21, p < .01$) compared to those who were 5 years of age or greater at diagnosis. The Number Letter subtest of the WRAML2 shows a negative slope indicating decline over the measurement occasions; however, when Number-Letter is combined with Finger Windows the slope is positive (see Table 3). There was a main effect of gender on visual matching with females showing greater decline ($F = 4.14, p < .05$).

Correlations between the Woodcock Johnson III tests of Letter-Word Identification, Calculation, Visual Matching and the WRAML composite score and the individual components of Number Letter and Finger Windows (see Table 4) were obtained on a subgroup of 43 children for visual matching and 29 children for the WRAML2. The slope representing change over time in verbal working memory was significantly associated with both Letter Word Identification and Calculation tests ($r=.552, p<.01$ and $r=.434, p<.05$). The slope representing change over time in Finger Window, as a measure of visual spatial memory, was significantly correlated with Calculation ($r=.371, p<.05$).

Discussion

Findings indicate a main effect of age on verbal working memory (Number Letter) where children diagnosed with ALL and treated with chemotherapy show decline compared to age based norm references over the 3 data collections. Although children who were diagnosed when under 5 years of age were not assessed for working memory until 5 years old, when they were assessed they show greater decline in verbal working memory compared to children who were diagnosed 5 years and older. To our knowledge intraindividual change in cognitive processes during treatment has not previously been assessed. Although the negative slope was steepest for the youngest participants, children older than 5 years of age at diagnosis also had negative slopes in verbal working memory. Verbal working memory performance decreased across all age groups during treatment. These findings converge with prior cross sectional studies with survivors of childhood ALL indicating age at diagnosis is a risk factor for poorer outcomes even among children treated with chemotherapy only (Ashford et al., 2010; von der Weid et al., 2003) and provides new information regarding when decline can be observed and hence has implications for the timing of interventions to prevent or minimize decline.

The WRAML2 composite is considered a measure of working memory. It is comprised of Finger Windows, the visual spatial memory task and Number Letter, the verbal working memory task. The WRAML2 as the composite was also significant in planned contrasts using < 5 years and ≥ 5 years old. However, the slopes were positive. While not significant,

Finger Windows, the visual spatial memory measure, improved over the three measurement occasions. Visual spatial memory may have improved due to practice. In a study examining the effect of practice on Finger Windows, a significant Study Years by Age subgroups interaction was found indicating differential practice effects for different age subgroups (Slade et al., 2008). Children in this study were between the ages of 8 to 11 years and it was noted younger children benefitted more from practice. Improvements on retest can also be due to the child feeling better and performing higher on the measure. To counter this argument, improvements in verbal working memory as assessed with Number Letter were not seen, in fact decline was observed. Data collection for Finger Windows and Number Letter were obtained during the same testing session. Finding that children with ALL treated with chemotherapy performed better on the visual spatial memory measure compared to verbal working memory in the WRAML2 suggests these measures differ. That is, visual spatial memory as measured with Finger Windows is not a working memory measure although it is part of the working memory composite. Here we find potential for ambiguity in interpreting a composite measure. The WRAML2 composite measure of working memory is constructed from tasks that perform very differently from each other. Reliance on the composite WRAML2 would suggest that working memory is not adversely affected in children with ALL exposed to chemotherapy, when in fact the story is quite different when a more thoughtful approach deciphering components of the WRAML2 is taken. The Number Letter component of the WRAML2, wherein children must both hold in memory and manipulate the order of numbers and letters as the string of numbers and letters increases, is characteristic of working memory tasks and shows decline over time in this sample.

Implications of declines in verbal working memory may signal an increased risk for diminished school achievement and greater difficulty in everyday function. In this study, declines in verbal working memory during treatment were associated with lower achievement scores in both letter word identification and calculation one year later. Others have found working memory performance and phonological awareness were predictors of learning among young children initially tested in kindergarten and then 2 years later (Alloway, Alloway, & Wootan, 2014; Alloway, Gathercole, Kirkwood, & Elliott, 2009; Christopher et al., 2012). Working memory is also linked to reading achievement independent of phonological skills (Christopher et al., 2012; Nevo & Breznitz, 2011). Measures of working memory in the current study may also be capturing mental flexibility and inhibition, cognitive processes more often thought of as executive processes in adults, since among young children mental flexibility may be less differentiated from working memory and inhibition (St Clair-Thompson & Gathercole, 2006).

Achievement in calculation was significantly associated with the verbal working memory and visual spatial memory. Survivors of childhood cancer have reported increased difficulty with concentration, working speed and working memory (Wengenroth et al., 2015). Converging evidence for the associations found here is offered in a nonclinical population of 11 and 12 year olds when examining working memory and English and mathematics achievement (Bull & Lee, 2014; St Clair-Thompson & Gathercole, 2006). Measures of working memory, specifically listening recall, backward digit span, Odd-one-out and spatial span, were associated with achievement in English and Odd-one-out and spatial span were associated with achievement in math. In the same study, it is noted that children who have

poor working memory also have difficulty remembering and carrying out instructions, keeping track of school related tasks, writing while planning text and carrying out mental arithmetic. Hence, declining working memory during treatment may affect school achievement.

The expected trajectory of development of working memory in children appears to be adversely affected by chemotherapy. Importantly interventions to address negative sequelae are underway, but presently considered to be under developed (see for example a review of cognitive training programs Olson & Sands, 2015). Knowledge of the affected cognitive processes during treatment could inform interventions to prevent or manage changes and decrease the deleterious effects on school achievement and everyday function. Further, it is possible that earlier interventions occurring while the child is receiving treatment might alter the negative trajectory of decline in verbal working memory and consequent negative association with academic achievement.

Female gender was associated with more vulnerability compared to males. In particular, we noted a downward trajectory in one measure of processing speed. Other studies suggest differential effects in treatment for females compared to males (Jain et al., 2009; von der Weid, 2001), but have not always cited differences in processing speed. This could be due to differences in the tests used to measure processing speed. Different cognitive assessments are not necessarily pure measures of specific processes. For example, Jain and her colleagues identified poorer performance for girls specific to shifting and sustaining attention. Processing speed is sometimes found to be congruent with measures of sustained attention and may be captured in measures of problem-solving or fine/visual-motor processing. Processing speed and attention may involve overlapping dependent neurosystems since speed is related to attention. Hence, the evidence may be more consistent than at first glance. However, it is not clear why girls appear to be particularly vulnerable to the effects of leukemia treatment.

We did not find decline in executive function or attention in this study. One explanation is that other studies may have used different assessments for these specific processes. For example, working memory has been combined with measures of executive function (see for example Krull et al., 2013). Further, it is sometimes unclear how attention is measured. Clear indications of the specific subtests used to assess cognitive processes would improve understanding of the exact processes affected rather than using global terms (e.g. attention) only. Further, commission errors are considered signs of impulsivity and hence may reflect executive function rather than attention per se (Fahie & Symons, 2003). In the current study, we combined errors of omission, commission and perseveration as the measure of attention.

Contrary to expectation, risk group was not a predictor of differences in rate of change among the cognitive measures although there is concern that categorization of risk group was heterogeneous and overlapping with additional concern that the low number of children in the low and very high risk groups required pooling of these extremes into the standard and high risk groups respectively. A larger sample size may have afforded the ability to find cognitive differences. Characteristics of this sample may have influenced the lack of significant differences found between risk group and cognitive outcomes.

Implications For Nursing

Pediatric oncology nurses are frequently the main point of communication with the child's family and school. It is important to inform parents/caregivers of the potential impact of treatment on working memory and academic abilities so they will be better positioned to advocate for resources to support their child's academic success. Once the child is medically stable and able to return to school educators need to be aware of the potential impact of ALL treatment on cognitive and academic abilities in order to provide any necessary accommodations and possible referrals for neuropsychological testing. Finally it is essential that pediatric oncology nurses who practice in long-term followup/survivorship programs query parents about cognitive problems such as working memory during comprehensive assessments and make referrals for formal neurocognitive evaluations when indicated.

Implications For Research

Describing decline in particular cognitive processes among children being treated for ALL does not provide an explanation of the potential causal factors for this decline. Academic and social factors related to absenteeism in school and isolation from normal school related activities as well as the implications of stress given the diagnosis and consequent treatment could contribute to causal mechanisms of decline. Finally, the effect of chemotherapy on the developing brain needs further investigation to examine mechanisms for decline and point to targeted interventions.

Conclusions

In summary, changes in survival rates for children receiving treatment for leukemia are leading to greater focus on the specific cognitive processes affected. Such knowledge can inform interventions to prevent and/or manage the deleterious effects of leukemia and suggest early referral to engage school resources. This study presents findings that indicate working memory in younger children is particularly vulnerable and can be demonstrated during treatment. Female gender is also a risk factor for decline in processing speed. In this study, risk group was not predictive of decline in cognitive processes, but particular sample characteristics (few children considered low risk or very high risk) may have affected this outcome.

The current study uniquely examined change over time in several cognitive processes during treatment for ALL with chemotherapy. Using latent growth curve modeling with longitudinal data collected over the course of treatment, we were able to model intraindividual change and obtain a slope for each participant. Examining change over time rather than the usual approach of comparing children with ALL with other groups (e.g. siblings, healthy children, children with other tumor types or chronic conditions) showed decline from where they started. Decline does not suggest impairment rather a difference in where the child started at the beginning of treatment. This study adds to the literature on the potential effects of chemotherapy by examining intraindividual change over time during treatment. Hence, the findings provide implications for the timing of potential interventions that could improve the trajectory for school achievement among survivors.

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Knowledge Translation

- Children with leukemia may experience decline in working memory during the course of treatment particularly children who were diagnosed when less than 5 years of age compared to a norm reference.
- Decline in working memory during treatment was associated with lower school achievement.
- Decline in spatial memory during treatment was associated with lower calculation scores.
- Girls show decline in processing speed during treatment compared to boys.

Table 1

Cognitive abilities assessed

Variable	Description	Measures
Working memory – visual spatial	Temporary holding and manipulation of visual spatial information; involves both attention and capacity.	Finger Windows from WRAML2 ^a
Working memory – verbal	Temporary holding and manipulation of verbal and auditory information; involves both attention and capacity.	Number Letter from WRAML2 ^a
Processing speed	Automatically and fluently perform relatively easy tasks. These are timed tests.	Visual Matching and Decision Speed from WJ III ^b
Executive function	Executive functions are control processes that regulate thoughts and behavior through inhibition, updating and monitoring.	Animal Sorting, Auditory Attention and Response Set, Clocks, Design Fluency, Inhibition and Statue from NEPSY-II ^c
Attention	Assessment of sustained and focused attention.	Conners CPT II and Kiddie CPT ^d
Achievement	Grade level standard achievement in letter-word identification and calculation.	Letter-Word Identification and Calculation from WJ-III ^b

^aWide Range Assessment of Memory and Learning 2nd edition (Adams & Sheslow, 2003)

^bWoodcock-Johnson 3rd Edition (Woodcock, McGrew, & Mather, 2001)

^c(Korkman, Kirk, & Kemp, 2007)

^dContinuous Performance Test (Conners, 2004, 2006)

Table 2

Participant characteristics

	Sample							
	Overall	Working Memory	Processing Speed	Visual Matching	Decision Speed	Executive Function	Attention	
<i>N</i>	71	60	66	67	65	71	60	
Age at diagnosis (M, SD)	6.18	3.07	6.71	6.71	3.04	6.33	3.12	3.06
Maternal Education (M, SD) ^a	13.31	2.36	13.38	2.34	13.43	2.35	13.44	2.42
Paternal Education (M, SD) ^b	12.94	2.72	13.00	2.85	13.00	2.72	13.05	2.83
Gender (<i>n</i> , %)								
Male	32	45.1	27	45.0	29	43.9	30	44.8
Female	39	54.9	33	55.0	37	56.1	37	55.2
Race/ethnicity (<i>n</i> , %)								
Caucasian	28	39.4	23	38.3	26	39.4	26	38.8
Hispanic	36	50.7	32	53.3	34	51.5	35	52.2
African-American	3	4.2	2	3.3	3	4.5	3	4.5
Native American	2	2.8	1	1.7	1	1.5	1	1.5
Other	2	2.8	2	3.3	2	3.0	2	3.0
Treatment Risk (<i>n</i> , %)								
Low	4	5.6	3	5.0	3	4.5	4	6.0
Standard	45	63.4	39	65.0	42	63.6	42	62.7
High	20	28.2	17	28.3	19	28.8	19	28.4
Very High	2	2.8	1	1.7	2	3.0	2	3.0

Table 3

Contrast test results

Measure	Contrast	Estimate	<i>T</i>	<i>p</i>
Number Letter	Age	0.391	2.91	.007
WRAML	Age	−0.005	−3.21	.003

Table 4

Correlation coefficients for change over time and achievement

	Letter-Word Identification	Calculation	Visual Matching slope	WRAML slope	Finger Windows slope	Number Letter slope
Letter-Word Identification	—					
Calculation	.558**	—				
Visual Matching slope	.076	.218	—			
WRAML slope	.105	.359	.091	—		
Finger Windows slope	.240	.371*	.167	.600**	—	
Number Letter slope	.552**	.434*	.181	-.051	.026	—

Note.

* = $p < .05$,

** = $p < .01$