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Cognitive outcomes among Latino survivors of childhood acute lymphoblastic leukemia and lymphoma: A cross-sectional cohort study using culturally competent, performance-based assessment

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Abstract

Background—This study sought to characterize cognitive outcomes among Latino survivors of childhood acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LL).

Procedure—In this cross-sectional cohort study, Latino survivors of ALL (n = 57) and LL (n = 5) aged 6–16 years were pooled and evaluated using validated measures of cognitive, academic, and behavioral function and English language proficiency. Performance was compared with norms using single-sample *t*-tests.

Results—In this cohort ($n = 62$, 50% male), mean ages at diagnosis and testing were 4.5 and 10.8 years, respectively; mean time off treatment was 44.7 months. All participants spoke English and over half (57%) identified Spanish as the primary language in the home. Forty-two families (68%) placed in the two lowest Hollingshead socioeconomic status categories. Participants were below average for working memory ($P < 0.001$). Overall, participants were in the average range, but significantly lower than published norms on domain-specific measures of verbal comprehension ($P < 0.001$); perceptual reasoning ($P = 0.033$); processing speed ($P = 0.003$); visual memory ($P < 0.001$); visuomotor attention, scanning, and sequencing ($P = 0.005$); and reading comprehension ($P = 0.001$). Parents reported concerns with working memory ($P < 0.001$) and metacognition ($P = 0.014$).

Conclusions—Similar to other childhood ALL/LL survivors, overall cognitive function in this Latino sample was relatively preserved but selected deficits were observed. Routine cognitive screening is indicated in this population.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

Keywords

acute lymphoblastic leukemia; cancer; cognitive; late effects; Latino; sociodemographics

1 | INTRODUCTION

Long-term survival for children with acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LL) treated using contemporary regimens now approaches 85–90%.[1–3] Unfortunately, long-term survivors commonly develop clinically significant cognitive deficits resulting from treatment-related factors including intrathecal chemotherapy, systemic high-dose methotrexate, and cranial irradiation, as well as host-related factors, such as younger age at diagnosis and female sex.[4–7] Two recent meta-analyses suggest that even in the context of modern regimens where routine use of cranial irradiation is sharply reduced, ALL survivors treated only with chemotherapy still show cognitive impairment, particularly in attention and executive functioning.[8,9] Due to similarities in their biology, clinical behavior, effective treatment regimens, and long-term sequelae, distinction between ALL and LL is made on the basis of bone marrow involvement and is considered arbitrary.[2] Consequently, survivors of ALL and LL are typically analyzed as a single group in research concerning neurocognitive outcomes.[7]

Clinically apparent cognitive dysfunction among long-term survivors of childhood ALL typically has a subtle, protracted onset and often manifests years after treatment.[10] Deficits in working memory, attention, executive functioning, and processing speed are commonly detected.[4,5,11–13] These deficits impede learning and have been associated with declines in general cognitive ability and academic achievement. Long-term consequences of such deficits are significant, including educational and economic disparities among young adult survivors.[13–15]

Survivors of childhood ALL from racial/ethnic minorities and those with lower socioeconomic status (SES) have reason to be at even higher risk. In typically developing children, strong relationships have been documented between SES, cognitive abilities, and academic achievement.[16–18] This is particularly important in Latino samples, as research has consistently found lower performance by Latinos when assessed with the Wechsler Intelligence Scale for Children–Fourth Edition (WISC-IV) relative to standardization samples.[19] This pattern may reflect the multiple areas of difficulties assessing Latinos and other minorities, such as test construction, standardization samples, and language, particularly effects of language proficiency on test performance.[19] Domains most affected by SES disparities include language abilities (i.e., vocabulary, phonological awareness, syntax, and reading comprehension skills), executive functioning (i.e., planning, cognitive flexibility, working memory), attention, and memory.[16–18] Although these risk factors are well established in the general population, there is limited information about how they might modify outcomes of childhood ALL survivors. For example, in two recent meta-analyses that summarized sociodemographic characteristics, only one-third of the studies reported the racial/ethnic composition of their samples, and nearly 80% of the participants identified as White/Caucasian; SES was unable to be included as an analytic variable due to insufficient

data reporting.[6,9] Using parent-reported measures, a single recent cohort study of Latino childhood ALL survivors identified difficulties with attention, school-based learning, and peer relationships.[20]

To help address these knowledge gaps, we conducted a multidimensional study of cognitive outcomes using a combination of performance-based, parent report, and teacher report measures in a sample of Latino childhood ALL and LL survivors treated with contemporary regimens. The primary aim was to characterize their cognitive performance relative to published norms. Given the combined risk of treatment-related sequelae and lower SES within this cohort, we hypothesized that this sample would perform lower than normative populations.

2 | METHODS

2.1 | Participants

This was a cross-sectional cohort study nested in our Institutional Review Board approved childhood cancer survivorship research database that is registered on ClinicalTrials.gov (NCT01518400). As described in detail elsewhere,[21] we developed a parent-directed clinical service as part of the standard of care that offers culturally and linguistically competent cognitive assessment and parental training in school advocacy and support for children and adolescents undergoing their initial survivorship evaluation following treatment for ALL and LL. At our institution, the standard for posttreatment care includes referral to our specialized cancer survivorship clinic, making eligible participants representative of our institution's survivorship population as a whole. Survivors of both ALL and LL are provided this service and were included in this analysis because of their similarities in treatment exposures, cognitive risk, and long-term neurocognitive outcomes.[4,5] Authorization for analysis and reporting of clinical data was obtained by written informed consent/assent.

Participants consisted of Latino survivors of pediatric ALL or LL aged 6–16 years, due to age specifications of the assessment measures. Having been born and educated in the United States, all participants spoke English as their primary language, whereas caregivers primarily spoke either Spanish or English. Nonparticipants were those who attended survivorship clinic and consented to the survivorship database research, but chose not to complete the assessments. Patients were excluded from the analysis if they had a preexisting neurodevelopmental or psychological disorder likely to impact their performance on the study measures, including established intellectual disability and/or developmental delay, autism, or severe mental health concerns. Additional criteria for exclusion from the analysis were history of relapse or cranial irradiation, or being non-Latino.

2.2 | Measures

2.2.1 | Medical and sociodemographic information—Through a combination of medical chart abstraction and caregiver history, information was collected on treatment variables (cumulative doses of intrathecal methotrexate and cytarabine, high-dose systemic methotrexate, receipt of cranial irradiation), language predominantly spoken in the home, insurance type (public or private), household size, and zip code to estimate income.[22]

Hollingshead SES classifications were scored based on parental marital status, education, and employment, with categories ranging from I (high SES) to V (low SES).[23]

2.3 | Testing battery

The battery was based on recommendations from the Children's Oncology Group (COG) Long-term Follow-up Guidelines for Survivors of Childhood, Adolescent and Young Adult Cancer,[24] and the standardized testing battery specified in the COG study ALTE07C1 (NCT00772200),[25] which evaluates critical functional domains empirically shown to be most affected by pediatric cancer and its treatment. Relative to ALTE07C1, our study battery was expanded to address the demographic profile of our patient population by adding more comprehensive evaluations across domains, standardized parental measures in Spanish, and a standardized measure of English language proficiency. Teacher measures were also included to provide a more complete understanding of functioning in school. Children in this sample were English dominant and tend to be categorized in school as English Language Learners.[26] Therefore, all tests were administered using the English version following standardized procedures by a fully bilingual English/Spanish pediatric psychologist (native speaker Spanish). Published measures in Spanish (Behavior Assessment System for Children, Second Edition [BASC-2], Behavior Rating Inventory of Executive Function [BRIEF]) were utilized for parents when needed per their language preference. Table 1 summarizes a comparison of both batteries. Normative data for each measure were collected by the test developers, generally from large samples of typically developing and healthy children reflecting demographics of the United States census. Following are the measures included in our battery; reliability is expressed as Cronbach alpha values unless otherwise indicated.

2.3.1 | Cognitive functioning—The WISC-IV is a test of intellectual function in individuals 6–16 years of age.[27] The Verbal Comprehension, Perceptual Reasoning, Working Memory, and Processing Speed Indices were derived from prorated scores based on eight subtests. Reliability is 0.79–0.97; construct validity is well established.

2.3.2 | Academic functioning—The Reading Comprehension and Numerical Operations subtests from the Wechsler Individual Achievement Test–Third Edition (WIAT-III) are used for children ages 4 and older.[28] Reliability for these subtests is >0.80.

2.3.3 | Language proficiency—The Woodcock-Muñoz Language Survey–Revised (WMLS-R) was administered to English language learners and provides norm-referenced measures of reading, writing, listening, comprehension, and cognitive-academic language proficiency (CALP) from Level 1 (negligible) to Level 6 (very advanced).[29] Reliability is 0.76–0.91.

2.3.4 | Attention—The Conner's Continuous Performance Test (CPT-3) is a computerized test for individuals ages 8 and older and measures sustained visual attention, response inhibition, and task vigilance.[30] Split-half and test–retest reliability are 0.92 and 0.67, respectively.

2.3.5 | Executive functioning—The Delis–Kaplan Executive Function System (D-KEFS) assesses higher order cognitive problem solving and executive functioning in individuals ages 8–89 years.[31] In our study, the two subtests of cognitive flexibility given were (1) Trail Making Test, which measures visuomotor attention, scanning, and sequencing, and (2) Color-Word Interference Test, which measures rapid naming and inhibition of overlearned responses. Internal consistency and test–retest reliability for these subtests are 0.70–0.79.[32]

2.3.6 | Verbal learning and memory—The California Verbal Learning Test–Children's Version (CVLT-C) is a verbal list learning task involving memorization of a list of words over multiple learning trials, delayed recall, and recognition recall for ages 5:0–16:11.[33] Test–retest reliability of this measure is 0.80–0.84.

2.3.7 | Nonverbal memory—The Memory for Designs and Memory for Designs Delayed from the NEPSY-II is normed for children ages 5–16 and is designed to assess spatial memory for novel and abstract visual information.[34] Internal consistencies are 0.44–0.92 depending on the age.

2.3.8 | Parent and teacher measures—The BRIEF is designed to assess executive functioning in school-aged children within the home and school environments.[35] The BRIEF provides standardized observational reports of behavioral and emotional regulation, working memory, organization and planning, and attention in everyday life. Internal consistency is between 0.80–0.98; test–retest reliability is between 0.76 and 0.85. The BASC-2 provides a multidimensional measure of psychosocial and behavioral functioning.[36] The Attention Problems scale measures problems a child or adolescent might have with different levels of attention. The scales and composites have high internal consistency of approximately 0.80–0.90, and test–retest reliability of approximately 0.70–0.80.

2.4 | Statistical analysis

Comparability of study participants and nonparticipants was assessed using analysis of variance tests. To evaluate cognitive outcomes as compared to normative means, one-sample *t*-tests were used and score distributions were calculated. Survivors of ALL and LL were pooled for all analyses. Analyses were completed using SPSS Version 17.0 (Chicago, IL).

3 | RESULTS

There were 149 patients screened for eligibility between January 2013 and December 2015. As shown in Figure 1, the analytical sample comprised 62 Latino children and their caregivers, as well as 36 teachers, after excluding from the analysis those who consented but did not schedule or otherwise return for assessments ($n = 40$), had one of several conditions known to increase cognitive risk above that of typical survivors in first remission ($n = 20$), were non-Latino ($n = 16$), did not provide consent ($n = 6$), had cranial irradiation ($n = 3$), or had relapsed ($n = 2$). See Table 2 for demographic and clinical characteristics. Participants had a mean age (±SD) of 10.8 ± 2.9 years at the time of assessment, 50.0% were male, and 56.5% of families identified that primarily Spanish was spoken in the home. Seventy-one percent of parents/caregivers reported Mexico as their specific Latino background, followed

by Guatemala (11%), El Salvador (10%), and Colombia (3%), with 5% who did not specify country of origin. The majority of the sample (67.7%) were placed in the two lowest Hollingshead SES categories; 85.5% had public insurance. The mean posttreatment interval was 44.7 ± 30.4 months.

The study sample did not differ significantly from all ($n = 40$) or the Latino subgroup ($n = 20$) of nonparticipants for clinical treatment or sociodemographic characteristics of interest. Potential differences in SES could not be assessed because only participants could provide data required for Hollingshead classification; however, there were no differences in estimated income or type of insurance. There were no demographic differences between those participants whose teachers did complete study measures ($n = 36$) and those that did not.

Test results for the cohort compared to normative data are shown in Table 3. Overall, participants performed similarly to published norms on most measures. However, the WISC-IV Working Memory Index ($t=-9.58$, $P<0.001$) was significantly lower in the below average range and was the only variable found to have a large effect size (Cohen's d = 1.22). Significant differences were noted on additional measures, though remained within the average range and had small to moderate effect sizes. Specifically, participant mean scores were significantly lower on the WISC-IV Indices of Verbal Comprehension ($t = -6.49$, $P < 0.001$), Perceptual Reasoning ($t = -2.19$, $P = 0.033$), and Processing Speed ($t = -3.34$, $P = 0.001$). The WIAT-III Reading Comprehension ($t = -3.49$, $P = 0.001$) and immediate visual recall on the NEPSY-II Memory for Designs ($t = -4.23$, $P < 0.001$) were also lower than the mean group. Cohort means were similarly lower for visuomotor attention, scanning, and sequencing on the D-KEFS Trails Letter-Number Switching ($t = -3.14$, $P = 0.003$).

Participants had more difficulties per parent report on the BRIEF Working Memory ($t = 4.35$, $P < 0.001$) and Metacognition Indices ($t = 2.53$, $P = 0.014$) when compared to normative data. Teacher report of more concerns on the BRIEF Working Memory approached significance ($t=2.02$, $P=0.051$). There were no differences in parental report on the BRIEF or BASC-2 for those children whose teachers did ($n = 36$) and did not complete a report.

Areas of relative strength in the average range were also identified, as participants had a relatively lower number of commission errors (impulsive responding to nontarget stimuli) while sustaining basic visual attention on the CPT-3 ($t = -2.50$, $P = 0.019$). They approached significance for a relatively higher free long delay recall ($t = 1.97$, $P = 0.054$) on the list learning tasks on the CVLT-C.

In addition to mean differences, Table 3 shows the distribution of the sample's scores. As the measures' normed scores are interpreted based on the normal curve, which places 68% of a distribution within one standard deviation above and below the mean, it is notable that a substantial proportion was in the below-average range of the 16th percentile on several measures. For example, while the WISC-IV Verbal Comprehension Index mean was in the average range, 32.3% of participants were below average, which is double the expected 16%. This pattern was seen in both those scores with significantly lower means in the

average range and for several results that were not significantly lower, such as 34.5% below average for the CVLT-C Trial 5. The scores on the WMLS-R CALP[29] in this sample of "very limited" (5.3%) and "limited" (19.3%) proficiency correspond with California schools' general population, where a quarter of students are classified as English Language Learners.[37]

4 | DISCUSSION

The aims of this study were to describe, using performance-based measures and parent/teacher reports, the cognitive profile of a Latino sample of childhood ALL and LL survivors and compare their outcomes to published norms. Our findings indicate that, although overall function was in the average range, multiple relative weaknesses in verbal comprehension, perceptual reasoning, working memory, processing speed, reading comprehension, nonverbal memory, and cognitive flexibility were present. While our results are broadly consistent with previously published studies of primarily on white/non-Hispanic subjects,[5,10–12] our results represent an important contribution by including comprehensive evaluation of a Latino population, which has historically been underrepresented in this area of research.

Our study confirms research utilizing mostly white/European-American samples of ALL survivors exhibiting overall average cognitive functioning, with specific areas of mild deficits in the lower average range.[5,10–12] These patterns were seen even though our sample at testing was relatively young (mean age 10.9 years) and early posttreatment (mean interval 43 months). Consistent with previous studies, our sample had significant differences in some measures of memory. The WISC-IV Working Memory Index, which has a strong component of auditory attention, was below average and parents reported clinical concerns in this area, as well. Visually based reasoning, executive functioning, and memory measures were also significantly lower, suggesting both auditory and visual abilities were impacted in this sample.

Although overall functioning was within the average range, a diverse group of cognitive functions were lower than norms, supporting the broad mild weaknesses of late effects for this group. Our results yield two practical implications for clinical practice and research. First, systematic cognitive evaluation of childhood ALL and LL survivors is indicated for detection of mild, but clinically important weaknesses that may not be readily apparent in the classroom and at home.[38–40] This report adds important information about the growing population of Latino survivors of childhood ALL and LL, as, to our knowledge, only one other published study has focused on this group.[20] Second, clinical care and research should routinely include race/ethnicity and sociodemographic variables, such as income, household size, parental education, and employment.[20,38,41] It is important that SES not be conflated with ethnicity and race. As highlighted by Patel and colleagues, it is inappropriate to attribute poor outcomes due to ethnicity alone, as lower SES has a negative impact across ethnic groups.[20] For example, a study of predominantly white survivors of childhood ALL found that household income below $80,000 per year was associated with poor physical, social, and emotional functioning.[42] Additionally, English language development needs to be accounted for as language plays a central part in cognitive and academic evaluations.

[19,43,44] Studies able to adjust for these covariates may be able to delineate their effects from those of treatment but require larger samples to gain precision.

Our findings support providing expert, culturally competent cognitive evaluation for childhood ALL and LL survivors because cognitive deficits and academic difficulties may be subtle.[38–40] As overall scores of our sample were within the average range, these weaknesses alone may not trigger intervention by conventional criteria. However, lower performance on a combination of functions likely negatively impacts academic achievement and may contribute to delayed identification and intervention. As many survivors do not have obvious behavioral and emotional difficulties, their struggles might be undetected or attributed to lack of effort. Parent and teacher reporting measures are frequently used to screen for cognitive and academic difficulties. Although there are concerns about the reliability and sensitivity of these reports, they are readily completed and inexpensive. The availability of teacher reports was modest (36/62, 58%) with common reasons for nonavailability being parent forgetting to ask, teachers not mailing it back, and children being tested during vacation. Nonetheless, we found that parent and teacher reports were mostly congruent with direct measurements of their children's function. By parent report, small but statistically significant differences were identified in working memory and executive functioning. These suggest that subtle deficits can impact daily life for survivors, which may be particularly relevant in a population where higher stress levels,[45] low education levels, and low English fluency hinder parents' ability to assist with school work. Thus, a truly comprehensive approach for providing academic support to these survivors in the home, community, and school must take account of sociodemographic disparities.[41]

An important strength of this study was the use of detailed, direct cognitive performance measures in addition to parent and teacher reports, despite limitations of a low rate of teacher return. Utilizing multiple information sources provides a more complete perspective, but is seldom included in the literature concerning childhood ALL/LL survivors. Limitations of this study include the lack of matched controls to delineate more precisely the relative contributions of treatment and sociodemographic risk factors. On the other hand, our use of normative comparisons reflects common clinical and research practice. Another limitation is that while our participants are representative of the Latino population we serve, our sample was fairly homogeneous with respect to SES. Compounding this is the possibility of selection bias. As this study was nested within our clinical survivorship service, it was sometimes challenging to engage families where cognitive assessment was perceived as threatening, unnecessary, or addressable through existing academic supports. Given size and characteristics of our sample, we were not able to complete additional analyses to identify potential risk and protective factors in cognitive outcomes. Finally, another limitation is our cross-sectional study design, which cannot assess change over time.

Thus, opportunities for future research include the inclusion of comparison groups, larger samples, a wider representation of sociodemographic diversity, measures of acculturation for parents and survivors,[46] and longitudinal designs that can evaluate long-term functioning and the impact of interventions. Although bilingualism is postulated to be a protective cognitive factor,[47] underdeveloped English language skills as commonly found in many Latino children and households can have negative implications for academic achievement.

[48,49] Consequently, a better understanding of how language-related variables impact childhood ALL/LL survivors is also needed.

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Abbreviations

ALL	acute lymphoblastic leukemia
CALP	cognitive-academic language proficiency
COG	Children's Oncology Group
LL	lymphoblastic lymphoma
SES	socioeconomic status

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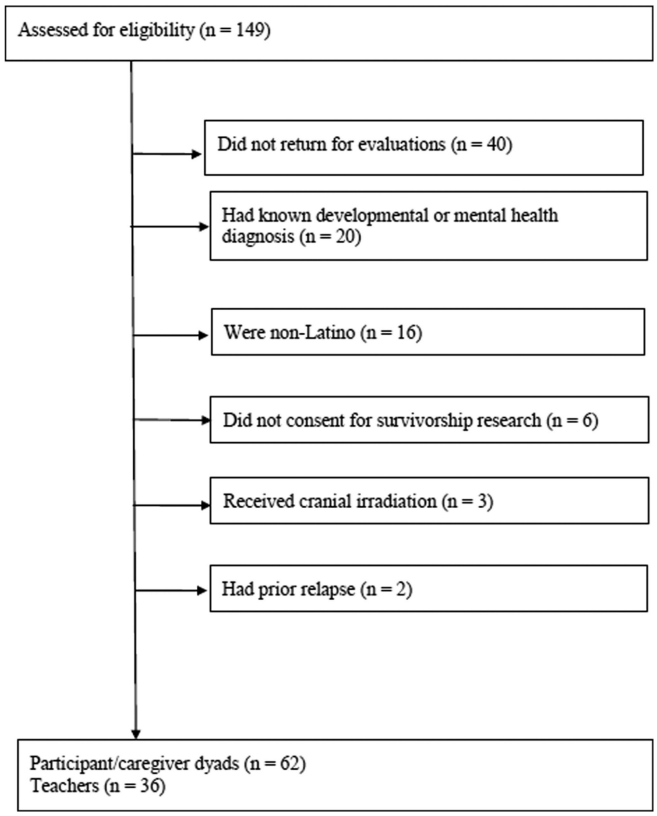

FIGURE 1.
Study profile

TABLE 1

Cognitive and behavioral battery (ages 6:0–16:11)

Domain/test	ALTE07C1[a]	This study
Children		
Intelligence		
WISC-IV	Vocabulary, Block Design	Vocabulary, similarities, block design, matrix reasoning
English language proficiency		
WMLS-R		Included
Processing speed/attention		
WISC-IV	Coding, Symbol Search	Coding, symbol search
CPT-3		Included
Memory		
CMS	Story Memory, Faces, Dot Location	
NEPSY-II		Memory for designs, memory for design delayed
CVLT-C	Included	Included
WISC-IV	Digit Span	Digit span, letter-number sequence
Executive functioning		
D-KEFS		Trails, color-word interference
Academic achievement		
WIAT-III		Reading comprehension, numerical operations
Parents		
	COG Language Preference Questionnaire	Sociodemographic survey
Attention and behavioral/social/emotional function		
BASC-2	Included	Included
Executive function		
BRIEF	Included	Included
Adaptive function		
ABAS-II	Included	
Quality of life		
PedsQL4.0	Included	
Teachers		
Attention and behavioral/social/emotional function		
BASC-2		Included
Executive function		
BRIEF		Included

[a] ALTE07C1 test battery.[24]

TABLE 2

Participant characteristics (n = 62)

	N (%)	M± SD
Demographic characteristics		
Age at time of testing (years)		10.8 ± 2.9
Sex		
Male	31 (50)	
Female	31 (50)	
Race/ethnicity		
Latino	62 (100)	
Treatment characteristics		
Acute lymphoblastic leukemia	57(91.9)	
Lymphoblastic non-Hodgkin lymphoma	5(8.1)	
Age at diagnosis (years)		4.5 ± 2.7
Time posttreatment (months)		44.7 ± 30.4
Cumulative dose of intrathecal methotrexate (mg)		231.5 ± 48.2
Cumulative dose of intrathecal cytarabine (mg)		65.0 ± 26.43
Received high-dose IV methotrexate (>1 g)	9 (14.5)	
Social characteristics		
Primary home language		
English	27 (43.5)	
Spanish	35 (56.5)	
Hollingshead SES category		
Category I	1(1.6)	
Category II	14 (22.6)	
Category III	5(8.1)	
Category IV	14 (22.6)	
Category V	28 (45.2)	
Household size		5.3 ± 1.5
Estimated household income (US dollars)		$46,519 ± $14,653
Insurance type		
Public	53 (85.5)	
Private	9 (14.5)	

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TABLE 3

Participant outcomes in comparison to normative means

Measure	Mean ± SD	Range	≤16th percentile *n* (%)	17–84th percentile	≥85th percentile	*t*[b]	*P*	Effect size[b]
Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV)[c] *n* = 62								
Verbal Comprehension Index	90.60 ± 11.41	65–124	20 (32.3)	40 (64.5)	2 (3.2)	−6.49*	<0.001	0.82
Perceptual Reasoning Index	96.35 ± 13.12	69–123	13(21.0)	44 (70.9)	5 (8.1)	−2.19*	0.033	0.28
Working Memory Index	87.53 ± 10.25	68–116	23(37.1)	38 (61.3)	1 (1.6)	−9.58*	<0.001	1.22
Processing Speed Index	94.55 ± 12.73	62–126	18 (29.0)	41 (66.1)	3 (4.8)	−3.34*	0.001	0.43
Wechsler Individual Achievement Test-Third Edition (WIAT-III)[c] *n* = 59								
Reading Comprehension	95.02 ± 10.78	69–118	10(17.5)	45 (78.9)	2 (3.5)	−3.49*	0.001	0.46
Numerical Operations	98.54 ± 13.49	67–129	10(16.9)	43 (72.9)	6(10.2)	−0.08	0.410	0.11
Woodcock-Munoz Language Survey-Revised (WMLS-R)[d] *n* = 57								
Broad English CALP	3.64 ± 0.65	2–5	3(5.2)	47 (82.5)	7 (12.3)	1.61	0.113	0.21
Conner's Continuous Performance Test (CPT-3)[e] *n* = 27								
Omissions	51.85 ± 9.58	42–79	0	21 (77.8)	6(22.2)	1.01	0.324	0.19
Commissions	46.78 ± 6.70	35–57	7(25.9)	20 (74.1)	0	−2.50*	0.019	0.48
Hit Reaction Time	51.89 ± 9.17	37–79	3 (11.1)	19 (70.4)	5 (18.5)	1.07	0.294	0.21
Variability	50.85 ± 12.28	38–87	3(11.1)	20 (74.1)	4(14.8)	0.36	0.722	0.07
Preservations	49.30 ± 6.50	44–70	0	25 (92.6)	2 (7.4)	−0.56	0.578	0.11
Hit Reaction Time Block Change	54.63 ± 12.85	20–87	1 (3.7)	18 (66.7)	8 (29.6)	1.87	0.072	0.36
Delis-Kaplan Executive Function System (D-KEFS)[f] *n* = 50–52								
Color Word Inhibition	10.08 ± 2.20	5–15	6(11.5)	40 (77.0)	6(11.5)	0.25	0.802	0.03
Color Word Inhibition-Switching	9.90 ± 2.63	1–13	8 (15.7)	34 (66.7)	9 (17.6)	−0.27	0.791	0.04
Trails Letter-Number Switching	8.54 ± 3.29	1–13	15 (30.0)	31 (62.0)	4 (8.0)	−3.14*	0.003	0.44
The California Verbal Learning Test-Children's Version (CVLT-C)[g] *n* = 58								
Trial 1	0.04 ± 1.05	−2.0 to 3.0	11 (19.0)	32 (55.2)	15 (25.8)	0.31	0.755	0.04
Trial 5	−0.26 ± 1.09	−3.5 to 2.0	20 (34.5)	26 (44.8)	12 (20.7)	−1.81	0.076	0.24

Measure	Mean ± SD	Range	≤16th percentile	17–84th percentile	≥85th percentile	t[b]	P	Effect size[b]
Short Delay Free Recall	0.02 ± 0.84	−2.0 to 2.0	8(13.8)	38 (65.5)	12 (20.7)	0.16	0.876	0.02
Short Delay Cued Recall	0 ± 0.82	−2.0 to 1.5	9(15.5)	35 (60.3)	14(24.1)	0	1.000	0
Long Delay Free Recall	0.21 ± 0.80	−2.5 to 1.5	5 (8.6)	38 (65.5)	15 (25.8)	1.97	0.054	0.26
Long Delay Cued Recall	0.09 ± 0.80	−2.0 to 2.0	6(10.3)	39 (67.2)	13(22.4)	0.90	0.372	0.12
Discriminability	0.03 ± 0.77	−3.0 to 1.5	7(12.1)	45 (77.6)	6(10.3)	0.26	0.799	0.03
NEPSY-Second Edition (NEPSY-II)[f] *n* = 57–59								
Memory for Designs	8.44 ± 2.78	3–15	22 (38.6)	31 (54.4)	4(7.0)	−4.23*		0.56
Memory for Designs Delayed	9.44 ± 3.00	3–18	14 (24.6)	34 (59.6)	9 (15.8)	−1.42	0.162	0.19
Behavior Rating Inventory of Executive Function (BRIEF) Parent Report[e] *n* = 61–62								
Behavioral Regulation Index	48.81 ± 9.15	36–80	10(16.1)	43 (69.4)	9 (14.5)	−1.03	0.308	0.13
Working Memory Scale	56.55 ± 11.86	38–85	4(6.5)	36(58.1)	22 (35.5)	4.35*	<0.001	0.55
Metacognition Index	53.51 ± 10.85	35–85	7 (11.5)	38 (62.3)	16(26.2)	2.53*	0.014	0.32
Behavior Rating Inventory of Executive Function (BRIEF) Teacher Report[e] *n* = 35								
Behavioral Regulation Index	47.74 ± 8.04	41–83	3 (8.6)	21 (60.0)	11 (31.4)	−1.66	0.106	0.28
Working Memory Scale	54.86 ± 14.22	38–96	2 (5.7)	24 (68.6)	9(25.7)	2.02	0.051	0.34
Metacognition Index	53.26 ± 11.76	37–80	2 (5.7)	24 (68.6)	9 (25.7)	1.64	0.110	0.28
Behavior Assessment System for Children, Second Edition (BASC-2) Parent Report[e] *n* = 61								
Attention Problems	51.08 ± 10.23	35–75	12 (19.7)	33(54.1)	16(26.2)	0.83	0.412	0.11
Behavior Assessment System for Children, Second Edition (BASC-2) Teacher Report[e] *n* = 36								
Attention Problems	48.06 ± 9.46	37–69	11 (30.6)	19(52.8)	6 (16.7)	−1.23	0.226	0.21

[a] One-sample *t*-test comparing survivors to normative means.

[b] Cohen's d.

[c] Mean = 100, SD = 15.

[d] Mean = 3.5, SD = 0.5.

[e] Mean = 50, SD = 10.

[f] Mean = 10, SD = 3.

[g] Mean = 0, SD = 1.

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* $P < 0.05$.