

# Effects of Perinatal Stroke on Executive Functioning and Mathematics Performance in Children

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## Abstract

The goal of this study was to examine executive functioning, math performance, and visuospatial processing skills of children with perinatal stroke, which have not been well explored in this population. Participants included 18 children with perinatal stroke (aged 6-16 years old) and their primary caregiver. Each child completed standardized tests of executive function and visuospatial processing skills, Intelligence Quotient (IQ), and math achievement. Performance on executive function, IQ, math, and visuospatial processing tests was significantly lower in children with perinatal stroke when compared to normative means. Poorer inhibitory control was associated with worse math performance. Increased age at testing was associated with better performance on visuospatial ability (using standardized scores), and females performed better than males on a test of inhibitory control. Children with perinatal stroke displayed a range of neuropsychological impairments, and difficulties with executive function (inhibition) may contribute to math difficulties in this population.

## Keywords

perinatal stroke, executive functioning, mathematics, visuospatial processing performance, neurobehavioral outcomes

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## Introduction

Perinatal stroke is a localized, cerebrovascular brain injury that takes place between 20 weeks of gestation and 28 days of life.<sup>1</sup> Perinatal stroke is estimated to occur in up to 1:1100 live births<sup>2</sup> and accounts for most cases of hemiparetic cerebral palsy<sup>3</sup> with many other neurologic morbidities.<sup>4-7</sup> Children with perinatal stroke may experience cognitive, linguistic, and/or spatial difficulties<sup>8</sup> that may vary in severity among different stroke subtypes, including arterial presumed perinatal ischemic stroke, neonatal arterial ischemic stroke, and periventricular venous infarction. Individuals with perinatal stroke often experience intellectual<sup>9</sup> and visual-spatial impairments.<sup>8</sup> Cortical lesions,<sup>9</sup> larger infarct volume,<sup>10</sup> and comorbid epilepsy<sup>8-12</sup> increase the risk of cognitive impairments.

There is considerably less research specifically examining executive functioning among children with perinatal stroke population. Executive functioning, which includes inhibitory control, attention, cognitive flexibility, and working memory, is critical for many functional life outcomes.<sup>13</sup> Furthermore, findings related to executive functioning in perinatal stroke have been inconclusive since the neuropsychological measures used and stroke types recruited differ across studies. For example, Kolk and colleagues<sup>14</sup> found that most executive

functioning abilities are relatively unaffected among children (aged 3-12 years) with neonatal (n = 21) and pediatric stroke (n = 10), with the exception of attention. In contrast, Hajek and colleagues<sup>15</sup> found that children with neonatal arterial ischemic stroke (aged 6-15 years; n = 36) performed worse than controls on inhibitory control. Bosenbark and colleagues<sup>16</sup> found that children with neonatal arterial ischemic stroke and arterial presumed perinatal ischemic stroke (age range 3-16 years; n = 41) were impaired on attention, verbal retrieval, cognitive flexibility/shifting, planning and organization, and processing speed, with inhibition being the most impaired and

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working memory being the least impaired. In comparing the different age groups, increased age was associated with worse performance on working memory, attention, and planning and organization subtests.<sup>16</sup> Thus, children with perinatal stroke may present with a range of executive functioning difficulties, particularly on measures inhibition and attention; however, further research is needed to substantiate these findings.

Executive functioning is important for mathematics development in young children<sup>17</sup> and children with neurodevelopmental disabilities<sup>18</sup>; however, math has *rarely been studied in children with perinatal stroke*. Children with pediatric stroke show significant math difficulties, which are highly correlated with parental ratings of executive functioning, particularly metacognition.<sup>19</sup> Glenn and colleagues<sup>20</sup> investigated math and number processing skills among preschool children (aged 3–4 years) with prenatal and perinatal lesions (recruited through childhood stroke groups,  $n = 31$ ). Children with prenatal and perinatal lesions performed lower than controls on tests of number knowledge and mathematics. However, the authors<sup>20</sup> also found that parental use of “number talk” (the frequency with which a parent uses number- or math-related language around their child<sup>21</sup>) with their children was positively associated with math performance, which suggests that math performance following early brain injury may be somewhat resilient and plastic.

Children with perinatal stroke also have difficulty on measures of visuospatial skills,<sup>22</sup> including difficulty with visual and tactile abilities, as well as and spatial neglect.<sup>23,24</sup> In particular, children with perinatal lesions show difficulty on tasks of drawing and block construction (see Stiles et al<sup>25</sup> for a review). Furthermore, motor problems may be associated with visuospatial deficits in both the childhood<sup>26</sup> and perinatal<sup>27</sup> stroke populations. Visual-spatial abilities are associated with math ability in typically developing children<sup>28</sup>; however, this association has not been well studied in children with perinatal stroke.

The aims of the current study were to examine the patterns of performance on measures of executive functioning, visuospatial processing, intellectual ability, and math among children with perinatal stroke. We hypothesized that children with perinatal stroke would perform below established norms on measures of executive functioning, visuospatial processing, intellectual ability, and math. Owing to math performance being highly dependent on underlying executive functioning skills, we also hypothesized that math skills would be associated with executive functioning performance, an association that has not been studied in perinatal stroke. We also examined the impact of age and sex on these outcomes. Identifying areas of impairment in children with perinatal stroke can assist primary caregivers, school employees, and health professionals with providing personalized interventions to improve neurobehavioral and academic outcomes.

## Materials and Methods

### Participants

We recruited 20 participants with a diagnosis of perinatal stroke aged 6–16 years. However, 2 children were not able to complete

any of the cognitive measures and thus could not be included in the analyses, resulting in a final sample of 18 children. Participants were recruited through the northern arm of the Alberta Perinatal Stroke Project (N-APSP). The Alberta Perinatal Stroke Project is a population-based provincial research cohort that identifies participants through both retrospective ascertainment and prospective stroke programs.<sup>29</sup> Inclusion criteria were as follows: (1) age 6–16 years at the time of assessment (due to get restrictions on some of the tests); (2) clinicoradiographic confirmation of perinatal stroke diagnosis; and (3) English as a first language. The diagnosis of perinatal stroke and subtypes of neonatal arterial ischemic stroke, arterial presumed perinatal ischemic stroke, and periventricular venous infarction was confirmed by a pediatric stroke neurologist (A.K.) according to established criteria<sup>30</sup> hemorrhagic stroke and cerebral venous thrombosis stroke types were excluded.

### Procedure

This study was a cross-sectional, observational study, which was part of a larger study examining neurobehavioral outcomes among children with perinatal stroke.

### Measures

The following measures were administered by 2 graduate research students, with the requisite training necessary for administering the cognitive test batteries and were supervised by a clinical psychologist. The 2 graduate research students were blinded to clinical information that may have given rise to bias, such as child medical history and caregiver factors, as clinical information was collected through a demographic questionnaire that was completed by the caregiver, simultaneous to their child’s cognitive testing, which was administered in a separate room.

**Demographic questionnaire.** Caregivers completed the demographic questionnaire for each participant on the day of testing which included information on: age, sex, family health history, caregiver factors (ie, marital status at the time of testing, highest level of education of both parents, household income bracket), and child medical history (ie, any history of epilepsy/seizures). Stroke type and any history of epilepsy/seizures were confirmed through the Alberta Perinatal Stroke Project.

**NEPSY—second edition (NEPSY-II).** The NEPSY-II is a standardized, neuropsychological measure designed to evaluate a variety of cognitive abilities in children aged 3–16 years.<sup>31</sup> NEPSY-II subtests assess a child’s ability to formulate concepts, selectively attend to stimuli, flexibly engage in mental shifts, inhibit automatic responses, initiate and monitor behavior, and engage in visuospatial processing.<sup>32</sup> Executive function constructs were measured using Animal Sorting (which measures concept formation and shifting), Auditory Attention and

Response Set (which measures selective and sustained attention as well as shifting), Design Fluency (which measures fluency in creating novel designs), and Inhibition (which measures inhibition and switching). Visuospatial processing was measured using Arrows. Each subtest is scaled to 1 to 19, with a normative mean of 10 (standard deviation [SD]=3). A higher scaled score indicates stronger executive functioning abilities. Sample sizes varied across subtests (see Figure 1) as some participants did not fall within the specified age range on some of the subtests, and some participants chose not to complete certain subtest.

**Wide Range Intelligence Test.** The Wide Range Intelligence Test is a standardized assessment of general intellectual functioning (ie, Intelligence Quotient [IQ]) for individuals of all ages.<sup>33</sup> The Wide Range Intelligence Test assesses both verbal IQ and nonverbal abilities (visual IQ), and when combined together forms the general intellectual functioning score (general IQ). A standard score is yielded for each subscale and composite. The normative mean is 100 (SD=15), with a higher standard score indicating better intellectual functioning.

**Woodcock-Johnson III Tests of Achievement (WJ-III ACH).** The WJ-III ACH is a standardized assessment of academic achievement for individuals of all ages.<sup>34</sup> The WJ-III ACH assesses reading, writing, and mathematical skills through 22 tests. A standard score is yielded for each subtest, which can be combined into a composite score for each academic area. For this study, we only focused on math scores. The math composite score is derived from performance on Calculation (assesses individual's skills in accessing and applying knowledge of numbers and calculation procedures); Math Fluency (assesses individual's ability to rapidly apply calculation skills to single-digit addition, subtraction, and multiplication facts); and Applied Problems (assesses individual's ability to analyze and solve math problems, using quantitative reasoning and math knowledge) subtests. The normative mean is 100 (SD=15), with a higher score indicating stronger math skill.

**Statistical analyses.** All analyses used scaled scores and were conducted on SPSS, version 23. Descriptive statistics were obtained for each of the NEPSY-II, Wide Range Intelligence Test, and WJ-III ACH math scales, and the data were verified such that there were no major violations of normality. For each of the NEPSY-II, Wide Range Intelligence Test, and WJ-III ACH Math scales, mean scores of the perinatal stroke sample were compared to the normative mean using a 1-sample *t* test, in order to capture significant difference in performance. Pearson correlations were run to examine associations between NEPSY-II and WJ-III ACH subscale scores and composite scores. As this was an exploratory study with a small clinical sample, the alpha was set to 0.05 for all analyses, and corrections were not used.

## Results

### Demographics

Demographic and clinical characteristics of the population are summarized in Table 1. At the time of examination, the mean age of the 18 participants (8 males) was 9.9 years (SD=3.1, range 6-16 years). Most were Caucasian and from middle- to high-income families. With respect to clinical characteristics, 10 children were diagnosed with arterial presumed perinatal ischemic stroke, 6 had neonatal arterial ischemic stroke, and 2 had periventricular venous infarction. A history of seizure was reported in 47% of the children.

### Global Intellectual Functioning Profile

At the group level, children with perinatal stroke scored in the below-average range on all measures of global intellectual functioning (ie, IQ). Compared to the normative mean (mean=100, SD=15), the perinatal stroke population had significantly lower composite scores on verbal IQ (mean=87.06; SD=11.74),  $t(15)=-4.41$ ,  $P=.001$ , visual IQ (mean=89.67; SD=14.11),  $t(14)=-2.84$ ,  $P=.01$ , and general IQ (mean=85.93; SD=13.05),  $t(14)=-4.17$ ,  $P=.01$ .

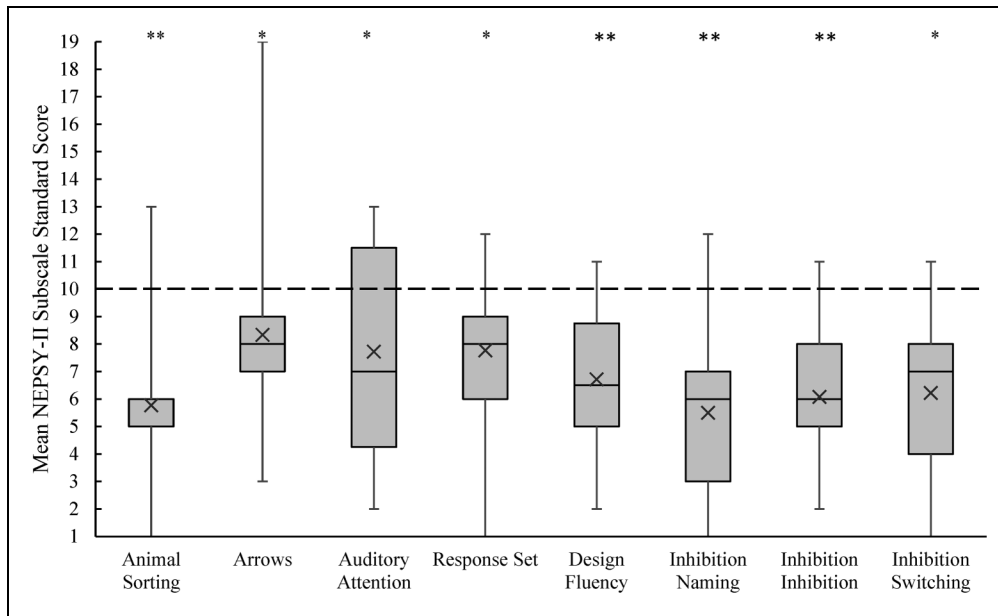
### Executive Functioning Profile and Visuospatial Processing Skills

Figure 1 shows the mean scaled scores obtained from the 8 NEPSY-II subtests. Children with perinatal stroke performed significantly worse than the normative mean of 10 on all NEPSY-II subtests, including Animal Sorting,  $t(12)=-5.08$ ,  $P<.001$ ; Arrows,  $t(17)=-2.19$ ,  $P=.04$ ; Auditory Attention,  $t(17)=-2.62$ ,  $P=.02$ ; Response Set,  $t(12)=-2.81$ ,  $P=.02$ ; Design Fluency,  $t(13)=-4.60$ ,  $P<.001$ ; Inhibition-Naming,  $t(15)=-6.07$ ,  $P<.001$ ; Inhibition-Inhibition,  $t(12)=-4.78$ ,  $P<.001$ ; and Inhibition-Switching,  $t(9)=-4.17$ ,  $P=.002$ .

For each NEPSY-II subtest, the following are the percentages of children with standard scores that fell below the 1-SD cutoff score in our sample: Animal Sorting (84%), Arrows (44%), Auditory Attention (56%), Response Set (38%), Design Fluency (64%), Inhibition-Naming (81%), Inhibition-Inhibition (69%), and Inhibition-Switching (67%).

### Math Achievement Profile

Figure 2 shows the mean scaled scores obtained from the 3 WJ-III ACH Math composite scores. At the group level, children with perinatal stroke scored in the low average range on all measures of math performance. Compared with the normative mean of 100, children with perinatal stroke had significantly worse (lower) scores on Calculation (mean=83.27, SD=13.68),  $t(14)=-4.74$ ,  $P<.001$ ; Math Fluency (mean=80.13, SD=12.67),  $t(14)=-6.07$ ,  $P<.001$ ; and



**Figure 1.** Box plot of group-level performance of children with perinatal stroke on NEPSY-II subscales measuring executive functioning. Animal Sorting (n = 13), Arrows (n = 18), Auditory Attention (n = 18), Response Set (n = 13), Design Fluency (n = 14), Inhibition-Naming (n = 16), Inhibition-Inhibition (n = 13), Inhibition-Switching (n = 9). X represents the mean; the dashed line represents the normative mean (t = 10). Significant difference from the normative mean: \*P < .05 and \*\*P < .01.

Applied Problems (mean = 85.59, SD = 11.14),  $t(16) = -5.34$ ,  $P < .001$ .

On each of the WJ-III ACH Math composites, the following are the percentages of children within our sample with standard scores below the 1-SD cutoff score in our sample: Calculation (60%), Math Fluency (67%), and Applied Problems (41%).

**Table 1.** Participant Demographic and Clinical Characteristics.<sup>a</sup>

Variable	n (%)	Mean (SD)
Gender		
Male	8 (44.4)	
Age		9.9 (3.1)
Ethnicity		
Caucasian	13 (72.2)	
Father's education		
University/college equivalent	10 (55.6)	
Mother's education		
University/college equivalent	11 (61.1)	
Total household gross income		
>\$70 000	14 (77.8)	
Stroke presentation		
APPIS	10 (55.6)	
NAIS	6 (33.3)	
PVI	2 (11.1)	
Seizure history	8 (47.1)	
Cerebral palsy	15 (88.2)	
Motor impairment	12 (70.5)	

Abbreviations: APPIS, arterial presumed perinatal ischemic stroke; NAIS, neonatal arterial ischemic stroke; PVI, periventricular venous infarction.

<sup>a</sup>Total n = 18 except for seizure history, cerebral palsy, and motor impairment, where n = 17 (data were missing for 1 participant).

### Correlations Between NEPSY-II and WJ-III ACH Math Scores

Pearson correlations of the NEPSY-II and the WJ-III ACH Math scores are reported in Table 2. Poorer performance on NEPSY-II Inhibition-Inhibition was associated with poorer performance on WJ-III ACH Applied Problems ( $r = 0.747$ ,  $P = .003$ ). Although the relationship between NEPSY-II Response Set and WJ-III ACH Calculation was not significant, it was moderate in strength ( $r = 0.570$ ,  $P = .053$ ).

### Demographic/Clinical Factors

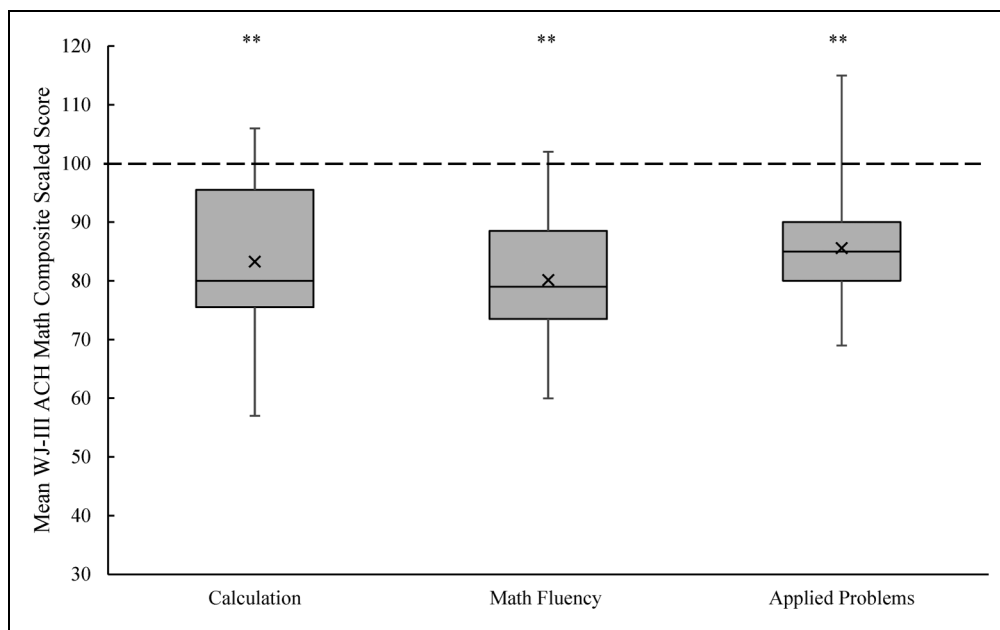
**Age.** Pearson correlational analyses revealed a significant correlation between age and performance on NEPSY-II Arrows ( $r = 0.56$ ,  $P = .02$ ,  $n = 18$ ). There was no significant relationship between age and WJ-III ACH Math scores.

**Sex.** Females performed significantly better than males on the Inhibition-Naming task:  $t(14) = -3.08$ ,  $P = .008$ ;  $d = 9.51$ . There were no significant differences between the sexes on WJ-III ACH Math scores.

### Discussion

The goal of this study was to examine the pattern of performance on executive functioning, visuospatial processing, cognitive functioning, and math in a sample of children with perinatal stroke.

Based on overall mean scores, children with perinatal stroke fell in the low average range on the Wide Range Intelligence



**Figure 2.** Box plot of group-level performance of children with perinatal stroke on NEPSY-II subscales measuring executive functioning. Calculation (n = 15), Math Fluency (n = 15), Applied Problems (n = 17). X represents the mean; the dashed line represents the normative mean (t = 10). Significant difference from the normative mean: \*\*P < .01.

Test measures of verbal, visual, and general IQ, with performance being significantly lower than the established norms. This finding is consistent with previous research demonstrating cognitive impairments among children with perinatal stroke,<sup>8,9,14,35,36</sup> although there have been inconsistent findings.<sup>37</sup>

On average, children with perinatal stroke scored significantly lower than the normative sample on all measures of executive functioning, consistent with our hypothesis and previous findings. Children in our study had the greatest difficulty with Animal Sorting and Inhibition-related subtests, indicating that

**Table 2.** Pearson Correlations Between NEPSY-II Subtests and WJ-III ACH Math Scores.<sup>a</sup>

Variable	WJ-III ACH Math score					
	Calculation		Math fluency		Applied problems	
	r	P	r	P	r	P
Animal sorting	0.04	.90	-0.14	.61	0.14	.62
Arrows	-0.07	.81	-0.04	.90	0.14	.62
Auditory attention	0.18	.50	0.25	.37	0.36	.19
Response set	<b>0.57*</b>	.02	0.05	.86	0.25	.37
Design fluency	0.17	.53	0.32	.25	0.46	.08
Inhibition-Naming	0.41	.11	0.33	.24	0.24	.39
Inhibition-Inhibition	0.44	.09	0.30	.27	<b>0.75**</b>	.001
Inhibition-Switching	-0.22	.41	0.33	.23	0.46	.08

Abbreviation: WJ-III ACH, Woodcock-Johnson III Tests of Achievement.

<sup>a</sup>n = 10-17.

\*P = .05

\*\*P < .01.

they struggled with tasks that require shifting and inhibitory control. Similar findings were reported by Bosenbark and colleagues<sup>16</sup> (ie, the most impaired executive functioning domains were shift and inhibition), even though they used different methods to ascertain executive functioning profiles among children with perinatal arterial ischemic stroke. The mean score of children with perinatal stroke on the visuospatial processing task (Arrows) was significantly lower than the population mean, indicating that our sample had difficulty determining line orientation.

As a group, children with perinatal stroke performed significantly worse than the normative mean on the math subtests of the WJ-III ACH. This is a novel finding among the perinatal stroke population, and it is consistent with previous research showing difficulties with number knowledge and math processing among preschool children with prenatal and perinatal lesions.<sup>20</sup> Our sample performed the weakest on the test of math fluency, suggesting that lower processing speed may further impact their math performance. Consistent with previous research showing that executive functioning is a strong predictor of math performance in other populations, our study demonstrated a strong positive correlation between performance on Inhibition-related tasks (ie, executive functioning) and performance on Applied Problems (ie, math) in children with perinatal stroke. This indicates that impaired inhibitory control mechanisms may contribute to greater difficulties with inhibiting irrelevant information when solving applied math problems. Furthermore, the positive correlation between Response Set (measures shifting set and inhibitory control) and Calculation approached significance, indicating that children with perinatal stroke may experience underlying

difficulties when shifting attention from one problem to another, and when inhibiting irrelevant information when solving calculation problems. Although visual-spatial abilities are highly correlated with math performance in typically developing children,<sup>28</sup> we did not find such a correlation in the current study with children with perinatal stroke. However, we only measured visual-spatial abilities using a single measure (Arrows); thus, further research using a variety of measures of visual-spatial processing is needed.

With respect to demographic and clinical factors, male children tended to perform worse than female counterparts on a test of inhibition. There is evidence to suggest that ratings of impulsiveness and prevalence of impulse control disorders are higher in males than in females in the typically developing population.<sup>38</sup> Westmacott and colleagues<sup>35</sup> have suggested that males are more susceptible to impairments following early brain injury. Finally, older age was associated with better performance on a test of visual spatial abilities (eg, arrows), indicating that younger children tended to show more difficulties (relative to the norm) on visual-spatial abilities than older children.

### Limitations

One limitation of our study was the absence of a matched control group, but we were able to use the age-standardized norms provided by the specific measures as an alternative. Our study was further limited by our small sample size (and missing data on some tests), limiting our ability to perform more sophisticated statistical analyses and separate groups by stroke type or seizure status. Larger, more lesion-specific studies (including laterality) will be important in future research. Larger samples would also allow for the examination of the unique contributions of executive functioning and visual-spatial abilities to math achievement in children with perinatal stroke, which is an important next step in this area. Lastly, our study may not be generalizable to all populations of children with perinatal stroke, as our sample was only recruited from a single tertiary clinic (and contained a disproportionately high percentage of children with epilepsy and arterial presumed perinatal ischemic stroke, both of which are associated with worse outcomes in this population.<sup>21</sup>

### Conclusions

The current study adds to the limited studies of executive functioning outcomes in children with perinatal stroke. We found a high prevalence of impairment across many elements of executive functioning in this population. We further demonstrated novel findings of significant math difficulties among children with perinatal stroke, which were highly correlated with executive functioning (inhibition). Additional long-term research is needed to advance our understanding of neurobehavioral trajectories in this population. Future studies should also look at the impact of clinical factors such as stroke type and history of seizure. It may be beneficial for parents and educational

supports to become aware of the group-level impairments, so that a combination of adapted supports can be provided for the child. Children with traumatic brain injury and their families have been shown to benefit from family support (ie, emotional and social), psychological services (ie, behavioral therapy and counseling), as well as physical activities.<sup>39</sup> Although there is no standardized plan of intervention and/or rehabilitation for children with perinatal stroke, providing families and patients with an interdisciplinary team may be the first step to assessing and then addressing the complex neuropsychological needs of children from this clinical population.

### Author Contributions

EL and LS recruited participants and collected data. MK, EL, and LS assisted with data entry. EL, LS, and CR contributed to the data analysis. EL drafted the manuscript. CR, JP, JY, JA, BB, and AK contributed to the overall study design. All authors read, edited, and approved the manuscript.

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### Declaration of Conflicting Interests

The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: BB and AK are coauthors of the Parental Outcome Measure, which is a public domain measure used in the larger N-APSP study (the present study is part of this larger study). BB receives royalties for the sales of the *Pediatric Forensic Neuropsychology* textbook (2012, Oxford University Press) and 3 pediatric neuropsychological tests (Child and Adolescent Memory Profile [Sherman and Brooks, 2015, PAR Inc], Memory Validity Profile [Sherman and Brooks, 2015, PAR Inc], and Multidimensional Everyday Memory Ratings for Youth [Sherman and Brooks, 2017, PAR Inc]). He has previously received in-kind support (free test credits) from the publisher of the computerized cognitive test CNS Vital Signs (Chapel Hill, NC). BB acknowledges salary funding from the Canadian Institutes for Health Research (CIHR) Embedded Clinician Researcher Salary Award. At the time of this study, CR was supported by a CIHR New Investigator Salary Award. Eliza Li acknowledges support from the CIHR Canada Graduate Scholarship–Master's Award, Women and Children's Health Research Institute Graduate Studentship, and the University of Alberta Thesis–Based Master's Recruitment Scholarship.

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## Ethical Approval

The Health Research Ethics Board-Health Panel at the University of Alberta and Alberta Health Services approved the study. Informed consent or assent was obtained from all participants and their caregivers.

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