SickKids



Attention in early school-aged children who are HIV-exposed uninfected

Julia M. Young^{1,2}, Vanessa Chen², Ari Bitnun^{3,4}, Stanley E. Read^{3,4}, Mary Lou Smith^{1,2,5}

¹ Department of Psychology, The Hospital for Sick Children; ² Neurosciences and Mental health Program, Research Institute, The Hospital for Sick Children; ³ Division of Infectious Diseases, The Hospital for Sick Children; ⁴ Department of Pediatrics, University of Toronto; ⁵ Department of Psychology, University of Toronto Mississauga

The authors have no conflicts of interest to disclose

Introduction & Methods

Introduction

- Children who are HIV-exposed uninfected (CHEU) experience multi-factorial risk factors for increased neurodevelopmental challenges such as perinatal HIV and anti-retroviral (ARV) medication exposure, increased likelihood of preterm birth, potential adverse maternal physical and mental health, and socioeconomic disadvantages.¹⁻³
- A limited number of studies have identified similar ADHD symptoms and performance on attention-based assessments in CHEU compared to children who are HIV-unexposed uninfected (CHUU).⁴⁻⁶ One study identified rates of ADHD in CHEU to be 10-12% in the United States, which is higher than international prevalence rates.⁷
- The objective of the present study is to understand risk factors and prevalence of attention difficulties in young CHEU based on parent-report, associations between attention and neurodevelopmental outcomes, and associations between attention, sociodemographic, and HIV-ARV-exposure related variables.

Methods

- 55 CHEU and 51 CHUU at 5.5 years of age were recruited from the Family Centered HIV Clinic at the Hospital for Sick Children and the community in Toronto, Ontario.
- Inclusion criteria included being born to a mother living with HIV (for CHEU), having a negative HIV status, and no known medical conditions affecting neurodevelopment.
- Parents completed the Attention Deficit Hyperactivity Disorder (ADHD) Rating Scale IV.⁸
- All children underwent neurodevelopmental assessments.⁹⁻¹²
- Demographic and maternal medical data were extracted through parent interviews and the child's medical records. (*See Table 1 and Table 2*).
- Demographic and neurodevelopmental variables were compared using t-tests, Fisher's exact test, and chi-square tests. Significance was held at p<0.01.

	CHEU	CHUU	P-value	
Child, Maternal, and Social Factors				
Total sample size	55	51	-	
Age (years)	5.56 (0.17)	5.55 (0.74)	0.905	
Sex (M/F)	21/34	22/29	0.748	
Gestational Age (weeks)	37.6 (2.8)	39.4 (1.48)	<0.001	
Birthweight (kg)	2.97 (0.67)	3.25 (0.49)	0.016	
In day care at 3 years	41 (83.7%)	42 (82.4%)	1.00	
Mother employed	19 (42.2%)	25 (51.0%)	0.518	
Both parents in house	32 (62.7%)	18 (35.3%)	0.010	
Maternal substance use	1 (1.8%)	2 (3.9%)	0.611	
Maternal education level				
High school or less	11 (31.4%)	12 (23.5%)	0 5 7 2	
High school plus	21 (60 60/)	30 (76 5%)	0.572	
	24 (00.0%)	39 (70.370)		
Language in home	24 (08.0%)	55 (70.570)		
Language in home Only English	27 (72.9%)	46 (90.2%)	0.045	
Language in home Only English English and other	27 (72.9%) 10 (27.0%)	46 (90.2%) 5 (9.8%)	0.045	
Language in home Only English English and other Region of maternal origin	27 (72.9%) 10 (27.0%)	46 (90.2%) 5 (9.8%)	0.045	
Language in home Only English English and other Region of maternal origin North America	27 (72.9%) 10 (27.0%) 9 (16.7%)	46 (90.2%) 5 (9.8%) 20 (39.2%)	0.045	
Language in home Only English English and other Region of maternal origin North America Other^	27 (72.9%) 10 (27.0%) 9 (16.7%) 45 (83.3%)	46 (90.2%) 5 (9.8%) 20 (39.2%) 31 (60.8%)	0.045	

Results

	5.5 Year (N = 55)	
Measure	N*	N (%)
Perinatal ARV medication		
Zidovudine	52	52 (100%)
Lamivudine	50	8 (16%)
Nevirapine	50	7 (14%)
Maternal CD4 count	30	
<u>></u> 500		23 (76.7%)
< 500		7 (23.3%)
Maternal Viral Load	45	
< 50		43 (95.6%)
<u>> 50</u>		2 (4.4%)
ARV medication regimen	52	
PI-based ARV		45 (86.5%)
NNRTI-based ARV		2 (5.8%)
Other		1 (3.8%)
None		2 (3.8%)
ARV initiation	44	
Prior to pregnancy		29 (65.9%)
1st trimester		11 (25.0%)
2nd trimester		3 (6.8%)
3rd trimester		1 (2.3%)
IV AZT during labor	54	52 (96.3%)
Other medical condition	53	36 (22.6%)
N*- total available data		

ADHD Questionnaire and Assessments **ADHD Rating Scale IV Raw Scores** CHEU CHUU p-value Subtest Ν Ν t 54 4.46 (2.88) 50 4.58 (2.84) -0.21 0.835 Inattention 5.10 (3.38) -0.59 0.553 Hyperactivity 52 4.71 (3.20) 48 53 9.26 (5.64) 48 9.54 (5.68) Combined -0.25 0.806 Wechsler Preschool and Primary Scale of Intelligence, Third Edition Standard Scores CHEU Subtest Ν Ν CHUU p-value t 55 100.44 (11.99) 114.26 (11.19) Full Scale IQ 50 -6.11 < 0.001 Verbal IQ 55 -5.06 99.82 (11.68) 51 111.25 (11.56) < 0.001 Performance IQ 55 100.07 (12.82) 113.59 (9.75) -6.14 51 < 0.001 Processing Speed 55 100.22 (13.27) 49 109.2 (12.95) -3.49 < 0.001 Wide Range Achievement Test, Fourth Edition Standard Scores Subtest CHEU CHUU p-value Ν Ν t 54 Word Reading 98.56 (17.46) 42 108.05 (17.98) -2.60 0.011 Spelling 102.17 (12.64) 107.33 (13.65) -1.89 53 42 0.062 53 Math Computation 101.94 (12.17) 42 110.38 (16.24) -2.80 0.007 **Beery-Buktenica Test of Visual Motor Integration Standard Scores** HEU HUU Subtest Ν Ν t p-value 53 -1.72 **Visual Motor Integration** 99.06 (8.92) 51 102.10 (9.06) 0.088 Vineland Adaptive Behaviour Scales, Second Edition Standard Scores HEU HUU p-value Subtest Ν Ν t Composite 52 98.13 (12.81) 51 106.14 (9.03) -3.67 < 0.001 52 101.92 (11.00) 109.16 (7.91) Communication 51 -3.84 < 0.001 Socialization 52 99.44 (13.65) 51 102.43 (9.49) -1.29 0.200 Daily Living Skills 52 99.54 (14.26) 108.14 (9.74) 51 -3.58 < 0.001 93.71 (13.84) 101.53 (11.66) Motor Skills 52 51 -3.10 0.003

Results



Results & Discussion

Hyperactivity/impulsivity and maternal employment Multiple regression models revealed significant associations between higher hyperactivity/impulsivity scores and maternal unemployment status across both groups.

Employed

Discussion

Unemployed

- CHEU were rated as exhibiting similar levels of inattention and hyperactive/impulsive behaviour as CHUU. Rates in both groups identified as meeting criteria for ADHD were low.
- CHEU obtained lower scores on adaptive behaviour and assessment measures of intelligence and early academics.
- Maternal unemployment was associated with higher scores of hyperactivity/impulsivity in both groups, suggesting a risk factor for poorer behaviour regulation.
- Monitoring of attention and developmental outcomes is important to elucidate risks of attention difficulties and their relation to cognition as CHEU develop through childhood and adolescence.

References

¹Anderson, K., Kalk, E., Madlala, H. P., et al. (2021). Increased infectious-cause hospitalization among infants who are HIV-exposed uninfected compared with HIV-unexposed. Aids, 35(14), 2327–2339. ²Evans, C., Jones, C. E., & Prendergast, A. J. (2016). HIV-exposed, uninfected infants : new global challenges in the era of paediatric HIV elimination. The Lancet, 16, e92–e107. ³Wedderburn, C. J., Yeung, S., Rehman, A. M., Stadler, J. A. M., Nhapi, R. T., Barnett, W., Myer, L., Gibb, D. M., Zar, H. J., et al. (2019). Neurodevelopment of HIV-exposed uninfected children in South Africa: outcomes from an observational birth cohort study. The Lancet Child and Adolescent Health, 3(11), 803–813. ⁴Mpango, R. S., Kinyanda, E., Rukundo, G. Z., et al. (2017). Prevalence and correlates for ADHD and relation with social and academic functioning among children and adolescents with HIV/AIDS in Uganda. BMC Psychiatry, 17(1), 1–8. ⁵Burkey, M. D., Murray, S. M., Bangirana, P., et al. (2015). Executive function and attention-deficit/hyperactivity disorder in Ugandan children with perinatal HIV exposure. Global Mental Health, 2. ⁶Jantarabenjakul, W., Chonchaiya, W., Puthanakit, T., et al. (2020). Behavioral problems in perinatally HIV-infected young children with early antiretroviral therapy and HIVexposed uninfected young children: prevalence and associated factors. AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV, 32(4), 429–437. ⁷Gadow, K. D., Chernoff, M., Williams, P. L., et al. (2010). Cooccuring psychiatric symptoms in children perinatally infected with HIV and peer comparison sample. Journal of Developmental and Behavioral Pediatrics, 31(2), 116–128. ⁸DuPaul, G., Power, T., Anastopoulos, A., & Reid, R. (1998). ADHD rating scale-IV. Checklists, norms, and clinical interpretation. Guilford Press. ⁹Wechsler, D. (2002). Wechsler Preschool and Primary Scales of Intelligence, Third Edition. The Psychological Corporation. ¹⁰Wilkinson, G., & Robertson, G. (2006). Wide Range Achievement Test (Fourth Edi). Psychological Assessment Resources. ¹¹Beery, K., Buktenica, N., & Beery, N. (2010). Beery-Buktenica Test of Visual Motor Integration. The Psychological Corporation. ¹²Sparrow, S. S., Chicchetti, D. V., & Balla, D. . (2005). Vineland adaptive behaviour scales, second edition. Pearson Assessment.

Acknowledgements

SickKids



Correspondence: julia.young@sickkids.ca Dr. Julia Young is supported by CIHR (HIV-176646).



