Poster # 820

TRAJECTORY ANALYSIS OF COGNITIVE OUTCOMES IN CHILDREN WITH PERINATAL HIV

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INHCC International NeuroHIV Cure Consortium

CROI 2019
March 4-7
Seattle, WA

Yale University School of Medicine

Background

- Cognitive impairment is common in children with perinatally-acquired HIV (pHIV).
- Traditional analytic models are not well suited to disentangle complex clinical phenotypes of cognitive development.
- Definitions of cognitive impairment vary between studies and are dependent on the availability of local normative data, limiting the applicability of these methods to cohorts residing in resource-limited settings.
- Group based trajectory analysis can classify subgroups of children with distinct cognitive profiles across time using a semi-parametric approach and maximum likelihood estimation.

Objectives

1. Identify subgroups of children with similar longitudinal cognitive trajectories using group based trajectory modeling
2. Identify baseline predictors of belonging to the lowest scoring trajectory group

Methods

Study Participants

- ART-naïve children with perinatally-acquired HIV without history of AIDS defining (CDC category C) illnesses, ages 1 to 12 years, enrolled in the PREDICT study at 7 sites across Thailand and 2 sites in Cambodia (Detailed demographics in Table 1).

Data Collected

- Sex, age, ethnicity, caregiver status and household income was obtained at baseline using standardized study questionnaires.
- Laboratory evaluations were completed annually and included CD4 count, CD4 percentage and plasma viral load.
- Neuropsychological testing was completed semiannually by Thai and Cambodia psychologists and trained nurses. Testing included Wechsler Preschool & Primary Scale of Intelligence, 3rd ed., Wechsler Intelligence Scale for Children, 3rd ed., Children's Color Trials Test (CTT) 1 & 2, and Beery-Buktenica Developmental Test of Visual-Motor Integration (Beery VMI).

Statistical Analyses

- Each neuropsychological test was analyzed independently. Raw scores were transformed to scaled scores using US based norms. Best fit of trajectory group number and shape was determined using Bayesian Information Criterion (BIC). Group homogeneity was assessed using minimum fit criteria: average posterior probability of individual assignment > 0.7 and odds of correct classification > 4.5.
- Change in standardized cognitive test scores across age was assessed using linear regression with the score at the earliest time point as a reference group. Change in scores was considered significant if linear coefficients for change from baseline test score across consecutive age groups met the threshold of $p < 0.05$. Trajectories not meeting this criterion were considered to reflect stable scores across age.
- Multiple logistic regression was used to identify baseline variables associated with belonging to the lowest scoring trajectory group (Table 2).

Results

TABLE 1. Demographic and Treatment Variables

	Intelligence Quotient test*	Color Trails test†	Beery VMI
n	165	264	286
Age at baseline ND test [Median (IQR)]	8.2 (6.3-10.3)	8.7 (8.3-10.0)	7.0 (4.6-9.1)
Sex [n (percentage)]			
Male	62 (37.58)	110 (41.67)	121 (42.31)
Female	103 (62.42)	154 (58.33)	165 (57.69)
Ethnicity [n (percentage)]			
Thai	165 (100.0)	161 (60.98)	170 (59.44)
Cambodia	0 (0.00)	103 (39.02)	116 (40.56)
On ART at start ND test [n (percentage)]			
No	68 (41.21)	88 (33.33)	139 (48.60)
Yes	97 (58.79)	176 (66.67)	147 (51.40)
On ART at last ND test [n (percentage)]			
No	25 (15.15)	35 (13.26)	37 (12.94)
Yes	140 (84.85)	229 (86.74)	249 (87.06)
Week on ART at first ND test [Median (IQR)]	45.0 (17.9-72.0)	102.0 (57.1-242.0)	36.0(11.9-60.0)
Week of follow-up (first ND to last ND) [Median (IQR)]	279.9 (217.7-314.7)	200.4 (79.4-283.6)	297.1(278.1-316.1)
Primary caregiver [n (percentage)]			
Biological Parent	63 (38.18)	166 (62.88)	183 (63.99)
Other relative	65 (39.39)	63 (23.86)	65 (22.73)
Orphanage	37 (22.42)	35 (13.26)	38 (13.29)
Household Income [n (percentage)]			
Low income	67 (40.61)	147 (55.68)	162 (56.64)
Average or above average	57 (34.55)	78 (29.55)	82 (28.67)
Unknown	41 (24.85)	39 (14.77)	42 (14.69)

* Only Thai children completed Intelligence Quotient testing due to language constraints for the WISC-III and WPPSI tests

† Fewer children completed Color Trails Test (CTT) compared to Beery-Buktenica Developmental Test of Visual-Motor Integration (Beery VMI) due to differences in age restrictions for each test

TABLE 2. Predictors of Belonging to Lowest Scoring Group

TEST/PREDICTOR	UNIVARIATE			MULTIVARIATE		
Performance IQ	**OR**	**95%CI**	**P**	**OR**	**95%CI**	**P**
Age at study entry (years)						
<8	Ref					
≥8	**2.72**	**(1.31-5.65)**	**0.01***			
Color Trails Test 1	**OR**	**95%CI**	**P**	**OR**	**95%CI**	**P**
Household Income						
Below average	Ref					
Average or above average	**0.33**	**(0.17-0.65)**	**0.001***			
Unknown	0.87	(0.32-2.35)	0.79			
Berry VMI	**OR**	**95%CI**	**P**	**OR**	**95%CI**	**P**
Household Income						
Below average	Ref			Ref		
Average or above average	**0.40**	**(0.22-0.72)**	**0.002^**	**0.41**	**(0.22-0.74)**	**0.003***
Unknown	1.35	(0.55-3.3)	0.51^	2.56	(0.95-6.94)	0.06
Primary caregiver						
Parent	Ref			Ref		
Other	**0.58**	**(0.34-0.99)**	**0.05^**	**0.42**	**(0.22-0.82)**	**0.01***

^Denotes variables included in multivariate analysis using the cutoff of p<0.15 as inclusion criteria

Denotes variables significantly associated with belonging to the low scoring trajectory group

Results

FIGURE 1: Performance and Verbal IQ Trajectory Groups

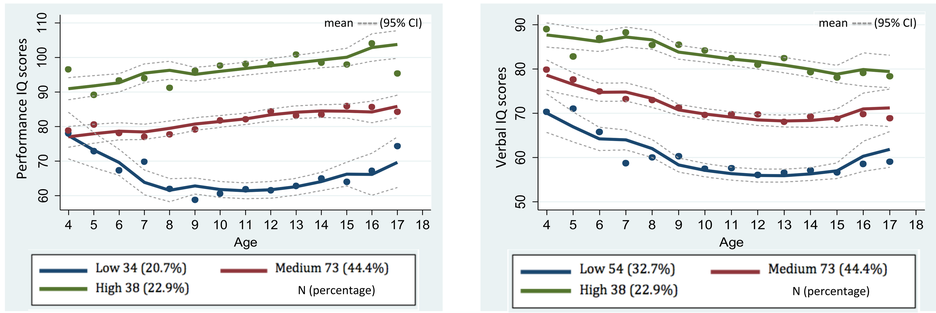


FIGURE 2: Color Trails Test Trajectory Groups

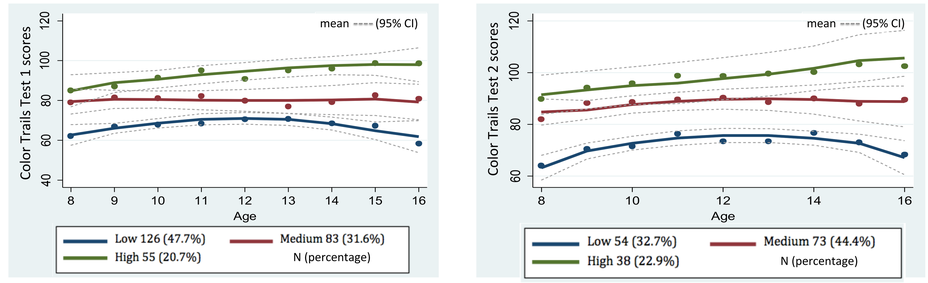
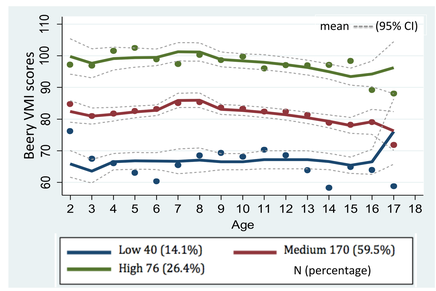


FIGURE 3: Beery Visuomotor Integration Trajectory Groups



- Trajectory modeling revealed a 3-cluster classification for each cognitive test.
- Trajectory groups were labeled as high, medium and low scoring groups.
- Most subgroup scores remained constant across age.
- Exceptions include the three trajectory verbal IQ groups, which declined across age (Fig 1), and high scoring trajectory groups for Color Trails Tests 1 & 2, which increased by ~10 points across older childhood and adolescence (Fig 2).

Conclusions

- Group based trajectory analyses visually displayed the continuum of cognitive outcomes among our cohort and most trajectory scores remained stable across age.
- Verbal function may decline as children with pHIV age or verbal IQ scales may be an insensitive measure of verbal function in older children residing non-native English speaking settings.
- The high scoring trajectory groups in the Children's Color Trails Tests 1 & 2 with increasing scores across adolescence may represent subgroups of children with better cognitive reserve.
- Poverty and longer duration of untreated HIV may predispose children to suboptimal cognitive development.
- Clinical significance of these trajectories cannot be determined without Thai and Cambodian uninfected, unexposed controls.

Acknowledgements We are grateful for the PREDICT and Resilience study participants and support through the International NeuroHIV Cure Consortium (INHCC.net) This work was supported by NIH grants: U19 AI53741 & R01MH102151, as well as the US Military HIV Research Program. **Disclaimer** The views expressed are those of the authors and should not be construed to represent the positions of the U.S. Army or the Department of Defense.

UMSL MIMH Missouri Institute of Mental Health · MHRP U.S. Military HIV Research Program · สภากาชาดไทย The Thai Red Cross Society ศูนย์วิจัยโรคเอดส์ · Yale University School of Medicine · NIH