Focused Cognitive Function Testing in Young People with Perinatal HIV in England

Alejandro Arenas-Pinto[1], Hannah Castro[1], Diane Melvin[2], Marthe Le Prevost[1], Caroline Foster[2], Kate Sturgeon[1], Alan Winston[3], Lindsay Thompson[1], Di Gibb[1], Ali Judd[1] and the Adolescent and Adults Living with Perinatal HIV (AALPHI) Steering Committee

[1] MRC Clinical Trials Unit at University College London, London, UK; [2] Imperial College Healthcare NHS Trust, London, UK; [3] Imperial College London, London, UK

Presentation: 821

Background

- AALPHI – Adolescents and Adults Living with Perinatal HIV
  - Prospective cohort study comparing young people with perinatal HIV (PHIV) and HIV negative (HIV-) young people (mainly siblings of PHIV) in England
- Our previous research (Judd et al. *Clin Infect Dis* 2016; 63:1380-1387) reported:
  - Cognitive performance was lower than normative data in both groups at baseline interview
  - Performance in young people with PHIV without a CDC C diagnosis (PHIV/no C) was similar to HIV-
  - Performance was worst for PHIV with CDC C diagnosis (PHIV/C)
- Our aim was to assess cognitive performance in the same cohort a median [IQR] of 1.9 [1.3, 2.5] years later, at second interview, with focused testing of learning and memory

Methods

- A total of 234 PHIV and 68 HIV- young people aged 14-26 years from the AALPHI cohort completed a neurocognitive assessment consisting of 9 tests representing six neurocognitive domains at their second interview (Table 1).

Table 1 – Neurocognitive domains, tools and tests

Domain	Tool	Test
Executive function	NIH Toolbox	Flanker inhibitory control and attention
	NIH Toolbox	Dimensional change card sort
Speed of info. processing	NIH Toolbox	Pattern comparison
Verbal learning	HVLT-R	Hopkins verbal learning (sum of 3 trials)
Verbal delayed recall	HVLT-R	Hopkins verbal delayed recall
Memory	NIH Toolbox	List sorting
	NIH Toolbox	Picture sequence
Verbal language measures	WIAT-II	Word reading
	BPVS	British picture vocabulary scale (BPVS)

- For each test, z-scores were calculated using normative data:
  - NIH Toolbox and Hopkins Verbal Learning Test-Revised (HVLT-R) normative data were adjusted for age, gender, ethnicity and years of education.
  - Weschler Individual Achievement Test (WIAT-II) and BPVS normative data were adjusted for age.
- For domains with more than 1 test, z-scores were averaged to give a mean z-score.
- For each domain, mean z-scores were compared across HIV-, PHIV/no C, PHIV/C, using ANOVA tests. Cohort characteristics were compared using the Chi squared test for proportions and Wilcoxon rank sum/ Kruskal-Wallis test for medians.

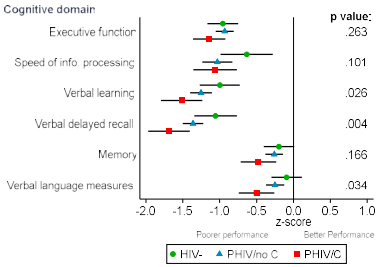
Cohort characteristics

	HIV-	PHIV	
	HIV- (n=68)	No CDC C (n=179)	CDC C (n=55)
	n (%) or median [IQR]		
Male	20 (29)	68 (38)	27 (49)
Age (years)	18 [16,21]	19 [17,21]	18 [17, 21]
Ethnicity (black)	52 (76)	154 (86)	48 (87)
Born outside UK/Ireland	30 (44)	122 (63)	24 (44)
Death of one/both parents	16 (26)	73 (44)	19 (36)
In education	51 (75)	132 (74)	43 (78)
Ever fostered/adopted	1 (2)	14 (13)	4 (12)
Age (years) at first presentation		6.0 [2.1,9.4]	2.2 [0.3,7.1]
Year of first presentation (years)			
Up to 1996		28 (16)	9 (17)
1997-2000		32 (18)	20 (37)
2001 onwards		119 (66)	25 (46)
Age (years) at initiation of ART (years)		9.2 [4.8,12.8]	3.6 [0.5,8.5]
Year initiated ART			
Up to 1996		11 (7)	4 (7)
1997-2000		25 (15)	25 (46)
2001 onwards		131 (78)	26 (47)
Viral load <50 c/ml at interview 2		100 (72)	31 (62)
CD4 nadir (cells/mm^3)		234 [168,380]	166 [17,330]
CD4 at interview 2 (cells/mm^3)		555 [402,784]	641 [485,776]

- 55 (24%) of PHIV had a CDC diagnosis.
- The median age was 18.5 years and similar across groups. Most were black ethnicity and were in education.
- More PHIV had lost a parent (p=0.021) and had been fostered/adopted (p=0.048) than HIV-.
- For PHIV, 38% had presented to services prior to 2001, 89% were currently on ART, 70% had suppressed viral load <50/copies/ml within +/- 6 months of the interview and median CD4 was 581 cells/mm^3.
- PHIV/C presented to services and started ART at a younger age (p=0.005, p<0.001 respectively) and earlier year (p=0.008, p<0.001), and with a lower nadir CD4 (p=0.003), than PHIV/ no C.

Neurocognitive performance by domain, HIV status and CDC class

Figure – Neurocognitive performance



- Mean z-scores were below population norms in all groups and domains, suggesting some impairment.
- NIH Toolbox executive function, speed of information processing and memory tests z-scores were similar for all 3 groups.
- For HVLT-R learning and delayed recall, PHIV/C had the lowest performance, although mean z-scores were ≤-1 SD below the reference mean for all groups.
- However, nearly all young people (97%) improved their score over the 3 learning trials, and this was seen in all groups (p=0.65).
- PHIV/C also had lower performance in verbal language measures, however mean z-scores were within 1 SD below the reference mean for all groups, indicating mild impairment.

Conclusions

- Cognitive function was similar between PHIV and HIV- young people in most domains/tests. However:
  - Performance was still lower than population norms in all groups
  - Performance was lowest in verbal learning and delayed recall domains
- Lowest performance was still seen in PHIV with CDC C diagnosis
  - History of AIDS and early HIV disease may be associated with increased risk of neurocognitive impairment
  - Supports wider findings that earlier ART initiation may protect aspects of cognitive development
- Further analyses are planned looking at predictors of performance and changes over time

Acknowledgements: We thank all PHIV and HIV- young people, parents and staff from all the clinics and voluntary services in AALPHI. Project team: S. Brice, A. Judd, M. Le Prevost, A. Mudd, F. Parrott, K. Rowson, K. Sturgeon. Investigators: M. Conway, K. Doerholt, D. Dunn, C. Foster, D.M. Gibb, A. Judd (PI), S. Kinloch, N. Klein, H. Lyall, D. Melvin, K. Prime, C. Sabin, M. Sharland, C. Thorne, P. Tookey. MRC CTU Data Services: C. Diaz Montana, K. Fairbrother, M. Rauchenberger, N. Tappenden, S. Townsend. Steering Committee chairs: D. Gibb, D. Mercey (2012-2015), C. Foster (2016-). Patient and public involvement: Children's HIV Association Youth Committee. Neurocognitive subgroup: A. Arenas-Pinto, C. Foster, A. Judd, D. Melvin, A. Winston. NHS clinics (named alphabetically): LONDON: Chelsea and Westminster NHS Foundation Trust, F. Boag, P. Seery; Great Ormond Street Hospital NHS Foundation Trust, M. Clapson, V. Novelli; Guys and St Thomas' NHS Foundation Trust, A. Callaghan, E. Menson; Imperial College Healthcare NHS Trust, C. Foster, A. Walley; King's College Hospital NHS Foundation Trust, E. Chesterton, E. Hamlyn; Mortimer Market Centre, Central and North West London NHS Foundation Trust, R. Gilson, T. Peake; Newham University Hospital, S. Liebeschuetz; North Middlesex University Hospital NHS Trust, J. Daniels; Royal Free London NHS Foundation Trust, T. Fernandez, S. Kinloch de Loes; St George's University Hospitals NHS Foundation Trust, S. Storey, K. Prime. REST OF ENGLAND: Alder Hey Children's NHS Foundation Trust, S. Paulus, A. Riordan; Birmingham Heartlands, Heart of England NHS Foundation Trust J. Daglish, C. Robertson; Bristol Royal Infirmary, University Hospitals Bristol NHS Foundation Trust, J. Bernatoniene, L. Hutchinson, University Hospitals Bristol NHS Foundation Trust, M. Gompel, L. Jennings; Leeds Teaching Hospitals NHS Trust, M. Dowie, S. O'Riordan; University Hospitals of Leicester NHS Trust, W. Ausalut, S. Bandi; North Manchester General Hospital, Pennine Acute Hospitals NHS Trust, P. McMaster, C. Murphy; Royal Liverpool and Broadgreen University Hospitals NHS Trust, M. Chaponda, S Paulus. Voluntary services (named alphabetically): Blue Sky Trust, C. Dufton, B. Oliver; Body and Soul, J. Marsh; Faith in People, I. Clowes; Positively UK, M. Kiwanuka; Positive Parenting & Children, B. Chipalo. Funding: Monument Trust and PENTA Foundation.
Lead contact for the AALPHI Steering Committee: Prof Ali Judd, A.Judd@ucl.ac.uk