Data-derived subtypes for Cerebral Visual Impairment in school and clinic samples of children.

Rebecca Rewbury[1], Cathy Williams[1,2], Sajeevika Amarakoon[1], Penny Warnes[1] and the CVI Prevalence Study Group.

[1]University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, UK; [2]Bristol Medical School, Bristol, UK.

Introduction

- Cerebral Visual Impairment (CVI) comprises a number of impairments of the central, retrochiasmal visual system[1].
- Two main visual processing streams have been described: the **Dorsal** or "where" pathway and the **Ventral** or "what" pathway[2].
- Subtypes of CVI relate to these streams, with children displaying either Dorsal or mixed Dorsal and Ventral ('Dorsal plus') visual impairments[3,4].
- We aimed to:

a) determine whether vision test results that we had already collected might group in a similar way to previous reports, using a data-driven cluster analysis approach, as recently described[4]

b) investigate whether CVI subgroups generated using this framework are associated with clinical diagnoses or behaviour.

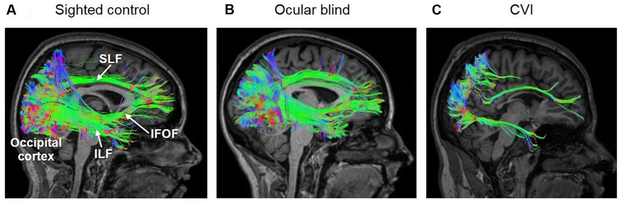


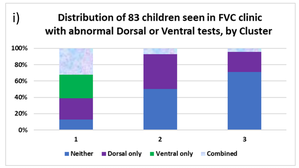
Figure 1: White matter reconstructions of the main visual pathways: superior longitudinal fasciculus (SLF; the dorsal stream), inferior longitudinal fasciculus (ILF; the ventral stream) and inferior fronto-occipital fasciculus (IFOF; mediating visual attention and orienting). From Martin et al. [5]

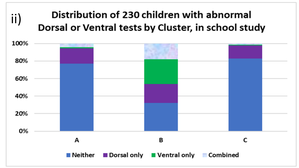
Results (1)

- Functional vision clinic data: 83 children, median (IQR) age 8 years (7-11y).
- Primary school data: 230 children, median (IQR) age 8 years (6-9y).

For research question (a):

- There was reasonable separation between the 3 clusters in terms of children with clinical impairments in the Dorsal or Ventral tests (Figure 2).
  - The mean scores for the **Ventral** tests were statistically different ($p<0.05$) between the clusters for 2 of the 4 tests in the FVC data and 3 of the 4 tests in the school data. The other Ventral test results had similar but less marked differences between the clusters.
  - The mean scores for the **Dorsal** tests were statistically different ($p<0.05$) between the clusters for 2 of the 4 tests in the FVC data. 1 test showed a similar trend and 1 no difference. However, in the school data only 1 Dorsal test was statistically different between clusters. 2 other Dorsal tests showed a similar trend.
- There were some children with **only Ventral** problems and almost all were in the group with the **highest frequency of abnormal test results in each dataset**: *cluster 1* in the FVC dataset and *cluster B* in the school dataset.
- The overall distribution of children with clinically abnormal test results (Dorsal, Ventral or Combined) was similar in the FVC and school data (Figure 3).





Clinic results

Cluster (1) 83% Dorsal/Ventral/Combined, 17% Normal
Cluster (2) 50% Dorsal/Combined, 50% Normal
Cluster (3) 29% Dorsal/Combined, 71% Normal

Primary school results

Cluster (B) 68% Dorsal/Ventral /Combined; 32% Normal
Cluster (A) 23% Dorsal/Combined; 77% Normal
Cluster (C) 17%, Dorsal/Combined, 83 % Normal

Figure 2: Distribution of children with abnormal Dorsal or Ventral test results, by Cluster, in the FVC (i) and School (ii) datasets.

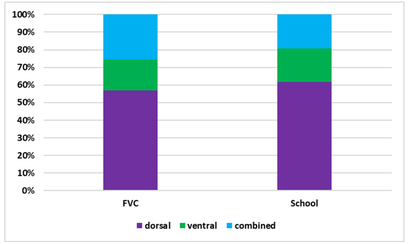


Figure 3: Overall distribution of clinically abnormal vision test results.

Methods

- We carried out secondary data analysis on two datasets. The first dataset comprised children seen consecutively in our Functional Vision Clinic (FVC) at the Bristol Eye Hospital between 2016 and early 2020. The second dataset was collected from primary school children during 2017-18 in a study already reported[6]. We included all children who had results for CVI-related tests.
- From each dataset, we extracted vision test results that related primarily to either the Dorsal or Ventral streams:

  Dorsal: eye movements (pursuits and saccades), crowding, attentional field loss and the post box task

  Ventral: focal field loss, rectangle matching task, contour detection threshold and the Motor-free Visual Perception Test (MVPT)
- We used hierarchical cluster analysis (STATA) and set the analysis to produce 3 clusters for each dataset. We hypothesised that these clusters would comprise one with Dorsal problems, one with Dorsal *and* Ventral problems, and one with *no* Dorsal or Ventral problems (test results within normal).

Results (2)

For research question (b): Table 1 compares the characteristics and clinical diagnoses in each cluster of the clinic and school data.

- **In the FVC**: children with cerebral palsy, epilepsy, learning difficulties or abnormal MRI findings were more likely to be in cluster 1.
- **In the school study:** children with specific learning difficulties were more likely to be in cluster A. Children with neurodevelopmental disorders or receiving extra help at school were more likely to be in clusters A or B . The "random 5%" of children, who were not thought to be at extra risk of CVI, were more likely to be in cluster C.

Variable	% in Cluster 1 (n=31)	% in Cluster 2 (n=28)	% in Cluster 3 (n=24)	P value Cluster 1 vs 2 vs 3
Functional Vision Clinic data				
Extra help at school (n=40)	17 (43%)	15 (38%)	8 (19%)	0.063
Abnormal MRI (n=19)	13 (68%)	4 (21%)	2 (21%)	0.015
Chromosomal /genetic (n=11)	7 (64%)	3 (27%)	1 (9%)	0.149
Cerebral palsy or infarct (n=14)	10 (71%)	4 (29%)	0	0.004
Epilepsy (n=9)	8 (89%)	1 (11%)	0	0.003
Autistic spectrum disorder (n=10)	6 (60%)	2 (20%)	2 (20%)	0.368
Learning difficulties or developmental delay (n=17)	12 (71%)	1 (6%)	4 (23%)	0.003
Specific learning difficulty (n=8)	0	5 (63%)	3 (37%)	0.032
ADHD suspicion or diagnosis (n=7)	2 (29%)	1 (14%)	4 (57%)	0.280

Variable	% in Cluster A (n=69)	% in Cluster B (n=28)	% in Cluster C (n=133)	P value Cluster A vs B vs C (*A+B vs C)
Primary School data				
Random 5% (n=39)	6 (15%)	3 (8%)	30 (77%)	0.006*
Extra help at school (n=129)	45 (34.8%)	18 (14.0%)	66 (51.2%)	0.021*
Any neurodevelopmental disorder (n=37)	17 (46.0%)	4 (11%)	16 (44%)	0.050*
Chromosomal /genetic (none)	-	-	-	-
Cerebral palsy or infarct (n=3)	1 (33%)	0	2 (67%)	1.00
Epilepsy (n=2)	0	0	2 (100%)	0.652
Autistic spectrum disorder (n=12)	6 (50%)	1 (8%)	5 (42%)	0.317
Learning difficulties or developmental delay (n=8)	2 (25%)	2 (25%)	4 (50%)	0.502
Specific learning difficulty (n=8)	6% (75%)	0	2 (25%)	0.025
ADHD suspicion or diagnosis (n=12)	7 (58%)	1 (8%)	4 (34%)	0.078*

Table 1: Frequency of clinical diagnoses in each cluster, in the clinic and school populations.

Summary and Conclusions

- The cluster analyses shown here produced results with similarities to those reported by Sakki et al[4]. In each dataset there was a cluster of children with fewer, mainly Dorsal problems, and a cluster with combined Dorsal and Ventral problems, possibly resembling the 'Dorsal' and 'Dorsal plus' subtypes of CVI[3].
- In our data, the separation between clusters was more marked for the Ventral than the Dorsal tests results, and we observed more children with Ventral problems than anticipated.
- In the FVC, children with brain-related pathologies were more likely to be in cluster 1, as were children with the highest frequency of Dorsal or Ventral problems.
- These data suggest that the set of vision tests we used, despite being different to those used in previous reports, can usefully identify children as having different subtypes of CVI, and therefore help with clinical management and service planning.

References

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