Is there consensus in defining childhood cerebral visual impairment? A systematic review of terminology and definitions

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ABSTRACT

Background: The childhood condition of visual difficulties caused by brain damage, commonly termed cortical or cerebral visual impairment (CVI), is well established but has no internationally accepted definition. Clarification of its core features is required to advance research and clinical practice. This systematic review aimed to identify the definitions of childhood CVI in the original scientific literature to describe and critically appraise a consensual definition of the condition.
Methods: MEDLINE, EMBASE, PsychINFO, CINAHL and AMED databases were searched in January 2017. Studies were included if they: 1) were published original research, 2) contained a childhood CVI sample, 3) contained a definition of CVI, and 4) described their CVI identification/diagnostic method. Thematic analysis identified concepts within definitions and narrative synthesis was conducted. **Results**: Of 1150 articles, 51 met inclusion criteria. Definitions were subdivided according to detail (descriptive definition, description not reaching definition status, diagnostic/operationalizing criteria). Three themes concerning visual deficits, eye health and brain integrity, were identified (each containing subthemes), and analysed individually across definitions. The most common themes were 'visual impairment' (n=20), 'retrochiasmatic pathway damage'(n=13) and 'normal/near normal eye health' (n=15). **Discussion**: The most consensual definition identified here may not be the best quality for advancing our understanding of CVI. We argue for the alternative definition: *CVI is a verifiable visual dysfunction which cannot be attributed to disorders of the anterior visual pathways or any potentially co-occurring ocular impairment.* We propose reporting guidelines to permit comparison across studies and increase the evidence base, for more reliable clinical assessment and diagnosis.

Key words: Child health (paediatrics), Visual (cerebral) Cortex, Visual pathway, Visual perception

INTRODUCTION

Brain injury is the most common cause of severe visual impairment in the UK[1], yet 'cerebral visual impairment' as an entity remains vague. Affected children often have other impairments such as intellectual disability, movement disorders and epilepsy, and are likely to be assessed and managed by a wide range of professionals (including ophthalmologists, paediatricians, neurologists, psychologists and other allied healthcare professionals)[2-10]. Therefore clarity and agreement over what cerebral visual impairment means will improve communication and management.

The term *cerebral* or *cortical visual impairment* (CVI) refers to visual impairment or dysfunction originating in neural insult[11, 12]. The pathology of childhood CVI is established, however subtly different terminologies and definitions are applied to this disorder, which influence the selection of clinical assessment methodologies[13, 14]. In children with the classic presentation of visual acuity reduction in the absence of anterior pathway damage and a clinical history or direct indication of neural damage, clinical diagnosis may be relatively straightforward. However, in addition to visual impairment (significantly reduced visual acuity and/or visual fields[15]), the inclusion of a broad range of other indicators such as wider visual and ocular dysfunctions in CVI is commonly debated[2, 3, 13, 14, 16-21]. For example, a child with severe intellectual and mobility impairments may show poor visual responses but it can be difficult to ascertain whether this is due to global impairment or a specific visual deficit. This may be further complicated by co-occuring ocular pathology such as optic atrophy. Alternatively a child with known brain injury confirmed by MRI may show relatively good visual acuity but severe difficulties in functional use of vision in everyday life (such as interpreting crowded visual scenes, visuomotor control or route-finding), with visual perceptual impairment confirmed by neuropsychological assessment. Equally, a child with the above symptoms may not have a medical history or MRI evidence of brain injury. Cases such as the examples above may warrant and benefit from a diagnosis of CVI and implementation of management strategies. In children with more complex presentations, it is difficult to know where to

set the boundaries of the condition and whether to ascribe difficulties to CVI or other developmental conditions[16]. This has led to the debated proposal that there must be sufficient discrepancy between cognitive and visual perceptual quotients to establish a visual processing deficit[22-26]. The suspicion of neural damage is also often difficult to confirm clinically[13, 27], leading a recent systematic review exploring the visual perceptual dysfunctions of childhood CVI to conclude that the definition should be based on functional vision rather than neuro-anatomical landmarks[13].

To advance the understanding of childhood CVI for diagnostic and nosological purposes, clarification of its core features is recommended[14, 28]. This is important for guiding clinicians in selecting age- and developmentally appropriate assessments, for more accurate diagnosis[13, 28, 29]. However as there is currently no international consensus on the definition of childhood CVI which covers the range of childhood developmental abilities and age, there is consequently no universally accepted diagnostic assessment framework[30]. The diagnostic process may be based on ophthalmological examination, basic vision examination, standardized neuropsychological assessment, neuroimaging or any combination of these. No guidelines exist on which professionals can or should be qualified to make a clinical diagnosis of the condition. Moreover there are only a few evidence-based interventions, of limited scope, for childhood CVI, as it is difficult to evaluate potential treatments in the absence of a stable reference standard[31].

Previous efforts to reach an international consensus on the definition of childhood CVI have been undertaken by round table discussion by expert clinicians and researchers[12, 32, 33]. An alternative approach is to systematically scrutinise those definitions used in empirical studies of CVI. This will permit a critical examination of definitions already in use. To the authors' knowledge, such a systematic investigation has not yet been conducted. There are known to be multiple assessment approaches for testing CVI[3, 34, 35], but consideration of their usefulness and how they correspond with the definitions identified is beyond the scope of this review.

The aim of this systematic review is to identify and critically evaluate the terminologies and definitions of childhood CVI in the published peer-reviewed scientific and medical literature, thereby identifying if there is a consensual definition of childhood CVI in current practical use and the nature of such a definition.

METHOD

Search Strategy

The literature search was run in the Ovid MEDLINE®, Embase Classic+Embase, PsycINFO, CINAHL, and AMED databases in January 2017 by one author (HS) after development of the search strategy by three authors (HS, ND and TP). All free text terms and subject headings relating to CVI and childhood were used. Searches were restricted to original peer-reviewed research articles and the grey literature was excluded. No publication time limits were applied as this is a relatively new field of research with no previous consensus or systematic evaluation, and any possible effects of time on definitions and terminologies used were not known. A manual search was performed on four textbooks of childhood CVI[32, 36-38]. Results were stored in EndNote X7, and duplicates were removed. The reference lists of included articles were inspected manually for previously unidentified references. Only English language articles were included as there was no capacity for translation. See supplementary materials for full search details (Table S1).

Inclusion/exclusion criteria and process

Titles and abstracts were independently reviewed by two researchers (HS and TP). When there was insufficient detail to determine eligibility, the full text was obtained. Full texts were reviewed independently by the researchers. Articles were included if they 1) were original research papers published in peer-reviewed scientific journals, 2) contained a childhood CVI sample (aged 0-19

years), 3) contained a definition of CVI and 4) contained descriptions of the methods used to identify children with CVI/allocate children into the CVI group. Disagreements at both stages were resolved by discussion between reviewers.

Data extraction

A data extraction tool was designed for this review, concerning 1) demographics and identification of the articles, 2) terminology and definitions of CVI, and 3) methodological information and sample characteristics (see supplementary materials: Table S2 for full definitions, Tables S3 and S4 for methodological details).

Data analysis

Qualitative analysis was conducted to identify the characteristics that were included in the descriptive definitions and diagnostic/operationalizing criteria of CVI. Quantitative analysis of these characteristics was run to find the prevalence of components and summarize findings in a narrative synthesis.

Thematic analysis

Thematic analysis was conducted to analyse the content of definitions. This is a six-step qualitative method used to identify, analyse and report patterns within data[39]. Similar approaches have previously been used to analyse definitions in healthcare research[40, 41]. Definitions and diagnostic/operationalising criteria were analysed separately. All definitions and diagnostic/operationalizing criteria were extracted as data codes for inductive identification of themes. Data codes were split and organized according to themes within definitions and

diagnostic/operationalizing criteria and reviewed to identify possible subthemes, and re-reviewed. Themes and subthemes were named and described. Themes and subthemes were re-reviewed at the final stage to check that codes were correctly categorized. A second researcher independently coded 20% of data for interrater reliability. Cohen's Kappa was .85, indicating an excellent level of agreement[42].

Quality assessment

Quality of the included studies was assessed by the level of detail in each definition. Definitions of CVI were subdivided into three groups on the basis of detail provided. The 'descriptive definition' was classified as a statement which explicitly or implicitly described the core characteristics of CVI. In most papers the definition of CVI was clearly identified with phrases such as "[CVI] is defined as…"[17, 20, 43-46] or "[CVI] is a clinical syndrome manifested by…"[47]. These were taken to be explicit definitions. However, in some cases there was no explicit definition of CVI in a single phrase[30, 48]. These were considered 'descriptions not reaching definition status' as it was unclear whether they were a more general description or a narrower definition of CVI to suit a specific study or sample. 'Diagnostic/operationalising criteria' were often similar to the descriptive definition but were classified as explicit statements of how the participants were diagnosed or allocated into the CVI group. Examples of how such criteria were identified are "CVI was diagnosed clinically…",[49-53] "…clinical characteristics consistent with CVI…",[30] and "…diagnosis of CVI was based on…"[43]. Most articles contained both a descriptive definition of CVI (either explicit definition or implicit description not reaching definition status) and diagnostic/operationalising criteria for CVI. Both datasets were extracted in these cases, as these often differed.

A quality assessment tool was designed for this review. Studies were assessed for whether the definition of CVI provided was explicit and whether the definition and diagnostic or operationalising

criteria matched if both were reported. Studies which had an explicit descriptive definition, diagnostic/operationalising criteria and where the elements of the definition and diagnostic/operationalising criteria matched were rated as good quality. Studies which only had an explicit descriptive definition but no diagnostic criteria were rated as medium quality. Studies in which the elements of the definition and diagnostic criteria did not match or which only had operationalising/diagnostic criteria or a description not reaching definition status were rated as poor quality.

RESULTS

Article characteristics

Figure 1 shows the PRISMA diagram of the review process. Fifty-one articles included a descriptive definition or diagnostic/operationalising criteria of CVI and were included (Table 1). Although several papers were published by the same research groups, definitions of CVI varied between the papers. Seven papers published data from children at the VI programme at the Children's Hospital Vancouver, Canada[4, 30, 45, 54-57], six from the Wilhelmina Children's Hospital Utrecht, the Netherlands[58-60] three from the University of Pisa, Italy[18, 61, 62], two from a Pediatric Ophthalmology Unit in San Francisco, USA[5, 9], and two from the Bartimeus Institute, the Netherlands[49, 53]. Other articles may have also published on overlapping samples but all studies did not report their recruitment sources in enough detail to recognize this. It was not possible to identify exactly articles that reported data on the same or overlapping samples where several publications by single research groups fulfilled the inclusion criteria. Thus, all eligible articles were included in the analysis.

Thirty-three articles (65%) included both a descriptive definition and diagnostic/ operationalizing criteria, eight (16%) included only a descriptive definition and ten (20%) included only diagnostic/operationalising criteria. Of the 41 papers containing descriptive definitions, 35 (85%) had explicit definitions and six (15%) had 'descriptions not reaching definition status'. According to quality assessment, four papers had good quality, eight had medium quality and 39 had poor quality definitions (Table 1).

The studies covered a range of populations including children at risk of CVI, specific subgroups with diagnosed CVI and general CVI samples (see supplementary materials, Table S3). In 34 articles, CVI had been diagnosed before the study and in 17 there was an explicit diagnosis or allocation of children to the CVI group. In 47 articles, CVI was diagnosed on the basis of reduced visual acuity and in four articles on the basis of wider visual dysfunction (Table S3). Forty-seven articles (92%) reported sample size, with CVI-only samples ranging between 2-423 participants (*mdn*=34). Median gender distribution, reported in 23 studies (45%), was 55% male (range 38-78% male). Twenty-nine studies (60%) reported participant age, ranging between 0-45 years. Four studies (9%) that included single participants over 19 years (aged 45, 35, 25 and 20 years) were included as they were part of large childhood samples. Participants in the included studies were reported to have a number of comorbidities including intellectual disability, movement disorder, seizure disorder, hydrocephalus, hearing impairment and other conditions (supplementary materials, Table S4). However, no articles explicitly considered how to diagnose CVI in the context of other conditions.

Studies used a variety of methods to assess for and diagnose CVI (supplementary materials, Table S4). In 25 studies, the assessor was not reported. 16 studies partially reported the assessors or had only one professional assessing the participants. Ten studies reported assessment by a multidisciplinary team, three of which did not detail the team members. There were different professionals involved in the assessments of different studies including ophthalmologists, paediatricians, neurologists, psychologists and other allied health professionals (Table S4). In their

methods, 19 studies explicitly reported fundus examination, 19 explicitly reported refraction and 20 explicitly reported an ocular motility assessment. A variety of vision assessments were reported including visual acuity (n=34), very low vision (n=16), visual fields (n=15), neuropsychological (n=4 assessed, n=7 attempted), contrast sensitivity (n=3), and stereopsis (n=2). 28 studies conducted visual electrophysiology assessment. 31 studies reported conducting a neuroimaging assessment, including MRI, CT, cranial ultrasound and PET. Due to incomplete reporting of exact tests used, it was not possible to identify specific clinical assessments that may be used more widely in the identification of childhood CVI and systematic evaluation of assessments is beyond the scope of this review. In 25 articles, the assessor conducting the examination was not reported.

Figure 1: PRISMA diagram of literature review process

Table 1: Defintions, diagnostic criteria and sample characteristics of included studies

article ID	Terminology	Descriptive definition			Diagnostic criteria			Quality Assessment		
		Vision**	Brain†	Eye$^{\$}$	Vision**	Brain†	Eye$^{\$}$	Explicit definition*	Did the elements of the definition and diagnostic criteria match?	Quality grading
Frank & Torres (1979)[44]	Cortical and cerebral blindness	1	1	0	1	0	1	Yes	no	Poor
Mohn *et al.* (1983)[63]	Cortical blindness	1	0	1	1	0	1	Yes	yes	Good
Robertson *et al.* (1986)[57]	Cortical visual impairment	2	0	2	2	5	2	Yes	no	Poor
Roland *et al.* (1986)[54]	Cortical visual impairment	2	0	1	2	0	2	Yes	no	Poor
Jan *et al.* (1987)[55]	Cortical visual impairment	NR	NR	NR	2	6	2	NR	N/A	Poor
Bencivenga *et al.* (1989)[56]	Cortical visual impairment	0	6	0	2	5	1	DNRDS	no	Poor
Flodmark *et al.* (1990)[4]	Cortical visual impairment	2	2	0	NR	NR	NR	Yes	N/A	Medium
Taylor & McCulloch (1991)[64]	Cortical blindness	1	0	1	NR	NR	NR	Yes	N/A	Medium
Wong (1991)[65]	Cortical visual impairment	2	0	1	2	0	1	Yes	yes	Good
Chen *et al.* (1992)[66]	Cortical visual impairment	2	4	1	2	0	1	Yes	no	Poor
Frank *et al.* (1992)[47]	Cerebral blindness	1	5	1	1	0	1	Yes	no	Poor
Schenk-Rootlieb *et al.* (1992)[67]	Cerebral Visual Disturbance	3	4	0	2	0	2	Yes	no	Poor
Granet *et al.* (1993)[68]	Central visual impairment	3	0	1	2	2	1	DNRDS	no	Poor
Jan *et al.* (1993)[45]	Cortical visual impairment	2	2	0	NR	NR	NR	Yes	N/A	Medium
Schenk-Rootlieb *et al.* (1993)[69]	Cerebral visual impairment	3	4	0	2	0	2	Yes	no	Poor
Schenk-Rootlieb *et al.* (1994)[70]	Cerebral visual impairment	3	4	0	2	0	2	Yes	no	Poor
Eken *et al.* (1995)[59]	Cerebral visual impairment	NR	NR	NR	2	0	2	NR	N/A	Poor
Cioni *et al.* (1996)[62]	Cerebral visual impairment	3	2	0	2	0	0	Yes	no	Poor
Eken *et al.* (1996)[60]	Cerebral visual impairment	NR	NR	NR	2	0	2	NR	N/A	Poor
Kwok *et al.* (1996)[71]	Cortical visual impairment	NR	NR	NR	2	0	1	NR	N/A	Poor
Uggetti *et al.* (1996)[72]	Cerebral visual impairment	2	0	2	NR	NR	NR	Yes	N/A	Medium
Cioni *et al.* (1997)[61]	Cerebral visual impairment	2	2	0	NR	NR	NR	Yes	N/A	Medium
Lanzi *et al.* (1998)[73]	Cerebral visual impairment	2	0	2	NR	NR	NR	Yes	N/A	Medium
Stiers *et al.* (1998)[74]	Cerebral visual impairment	3	4	0	3	0	2	Yes	no	Poor
Huo *et al.* (1999)[9]	Cortical visual impairment	NR	NR	NR	2	0	2	NR	N/A	Poor
Oud *et al.* (1999)[58]	Cerebral visual impairment	3	4	0	0	4	1	Yes	no	Poor
Choi *et al.* (2001)[75]	Cortical visual impairment	1	5	0	2	0	1	Yes	no	Poor
Good (2001)[50]	Cortical visual impairment	2	1	2	3	0	1	Yes	no	Poor
Weiss *et al.* (2001)[76]	Cortical visual impairment	3	2	1	1	0	1	Yes	no	Poor

Brodsky *et al.* (2002)[77]	Retrogeniculate visual loss	0	3	0	2	2	2	DNRDS	no	Poor
Sakai *et al.* (2002)[46]	Cerebral visual impairment	3	4	0	2	2	1	Yes	no	Poor
Hoyt (2003)[5]	Cortical visual impairment	NR	NR	NR	2	0	2	NR	N/A	Poor
Skozenski & Good (2004)[78]	Cortical visual impairment	2	2	0	2	0	1	Yes	no	Poor
Sie *et al.* (2005)[48]	Cerebral visual impairment	0	4	0	2	0	1	DNRDS	no	Poor
Good & Hou (2006)[51]	Cortical and cerebral visual impairment	2	3	1	2	0	1	Yes	no	Poor
Matsuba & Jan (2006)[30]	Cortical visual impairment	0	2	0	3	0	0	DNRDS	no	Poor
Fazzi *et al.* (2007)[18]	Cerebral visual impairment	3	5	1	NR	NR	NR	Yes	N/A	Medium
Khetpal & Donahue (2007)[43]	Cortical visual impairment	2	0	1	3	0	2	Yes	no	Poor
Ghasia *et al.* (2008)[20]	Cerebral visual impairment	2	0	2	NR	NR	NR	Yes	N/A	Medium
Ferziger *et al.* (2011)[79]	Cerebral visual impairment	2	2	0	3	0	2	Yes	no	Poor
Good *et al.* (2012)[52]	Cortical visual impairment	NR	NR	NR	2	0	1	NR	N/A	Poor
Weinstein *et al.* (2012)[80]	Cerebral visual impairment	2	6	0	2	6	2	DNRDS	no	Poor
Bosch *et al.* (2014a)[53]	Cerebral visual impairment	2	5	1	3	0	2	Yes	no	Poor
Bosch *et al. (*2014b)[49]	Cerebral visual impairment	3	4	1	3	0	2	Yes	no	Poor
Cavascan *et al.* (2014)[34]	Cerebral visual impairment	2	4	1	2	4	1	Yes	yes	Good
Chong & Dai (2014)[81]	Cerebral visual impairment	2	4	1	2	0	1	Yes	no	Poor
Geldof *et al.* (2015)[82]	Cerebral visual impairment	3	2	0	3	2	1	Yes	no	Poor
Mezer *et al.* (2015)[83]	Cortical visual impairment	NR	NR	NR	2	2	0	NR	N/A	Poor
Binder *et al.* (2016)[84]	Cortical visual impairment	2	0	2	2	0	2	Yes	yes	Good
Kemmanu *et al.* (2016)[85]	Cortical visual impairment	NR	NR	NR	2	0	1	NR	N/A	Poor
Özturk *et al.* (2016)[86]	Cortical visual impairment	NR	NR	NR	2	5	1	NR	N/A	Poor

***Explicit definition**
Yes – explicit definition
DNRDS – description not reaching definition status

****Vision subthemes**
0. not present
1. complete blindness
2. visual impairment
3. visual dysfunction

†Brain subthemes
0. not present
1. brain damage
2. posterior visual pathway damage
3. optic radiation damage
4. retrochiasmatic pathway damage
5. retrogeniculate pathway damage
6. visual pathway damage including higher visual association areas

$Eye subthemes
0. not present
1. normal/near normal eye health
2. extent of vision problems not explained by any eye problems

NR – not reported

Terminology

Table 2 describes the geographical distribution of research groups and CVI terminologies used. Articles were published between 1979 and 2016 (Table 1). The most prevalent terminology was *cortical visual impairment* (43% of all papers), used most commonly in North America (67% of North American papers). The terminology most used by European research groups was *cerebral visual impairment* (41% total, 83% of European papers). Other terminologies identified were *cortical blindness, cerebral blindness, central visual impairment, cerebral visual disturbance* and *retrogeniculate visual loss*. These were used by eight papers (16%), the majority published before 2000.

Table 2: Geographical locations of research groups and CVI terminologies used

Geographical location of research group			Terminology		
Continent (n)	**Country (n)**	**City/State (n)**	**Cerebral visual impairment (n=21)**	**Cortical visual impairment (n=22)**	**Other (n=8)**
North America (24)	Canada (8)	Vancouver (7) Toronto (1)	2	16	6
	USA (16)	New York (2, 1*) San Francisco (5, 1*) Los Angeles (1) Philadelphia (2) Missouri (1) Minnesota (1) Arkansas (1) Nashville (1)			
Europe (18)	Belgium (1)	Leuven (1)	15	1	2
	Italy (5)	Pavia (3) Pisa (2⁺)			
	The Netherlands (11)	Amsterdam (2) Nijmegen (2) Utrecht (5, 1*) Rotterdam (1)			
	Turkey (1)	Izmir (1)			
Asia (5)	Hong Kong (2)	Hong Kong (2)	1	4	-
	India (1)	Bangalore (1)			
	Japan (1)	Sendai (1*)			
	South Korea (1)	Seoul (1)			
Middle East (2)	Israel (2)	Ramat Gan (1**)	1	1	-
		Haifa (1**)			
Oceania (1)	New Zealand (1)	Auckland (1)	1	-	-
South America (1)	Brazil (1)	Sao Paolo (1)	1	-	-

* Children recruited from this area and corresponding author based in this area, collaborating authors based in other regions nationally

** Children recruited from other regions nationally and corresponding author based in this area, collaborating authors based in other regions nationally

⁺ Children recruited from this area and corresponding author based in this area, collaborating authors based in other regions internationally

Definitions of CVI

Thematic analysis revealed three consistently occurring themes within the definitions of CVI (Table 3). Eleven papers (27% of all definitions) had definitions containing all three themes and were all rated as having explicit definitions. Theme combinations within definitions were very heterogeneous, thus themes were considered separately. The most common theme was *Vision Deficits* (in 90% of definitions) and contained three subthemes, of which *visual impairment* (according to WHO classification[15]), was the most prevalent (54% of subthemes). The theme of

Eye Health (in 51% of definitions) contained three subthemes of which *eye health normal/near normal* (e.g. “normal or minimal ocular findings”[57]) was most prevalent (71% subthemes). The theme of *Brain Integrity* theme (present in 76% of definitions) contained six subthemes of which *retrochiasmatic pathway damage* was most prevalent (42% subthemes).

Table 3: Process and results of thematic analysis

Process of Thematic Analysis				Results of Thematic Analysis			
→				**Descriptive definitions, n=41** Explicit definition n=35 (DNRDS*, n=6)		**Diagnostic/operationalizing criteria, n=43**	
Initial identification of themes	**Review of themes**	**Re-review and naming/defining themes**	**Identification of subthemes**	**Themes**	**Subthemes**	**Themes**	**Subthemes**
1. Vision	1. Vision	**1. Vision Deficits** Any references to difficulties with the conscious perception of vision	1. Complete blindness	35 (2*)	5	42	4
			2. Visual acuity reduction/visual impairment		19 (1*)		30
			3. Visual dysfunction		11 (1*)		8
2. Eye health normal	2. Eye health (including inconsistent vision-eye health)	**2. Eye Health** Any reference to the health of the ocular structures or the anterior visual pathways	1. Eye health normal/near normal	20 (1*)	14 (1*)	40	22
3. Inconsistent vision-eye health			2. Eye problems do not account for the extent of vision problems		6		18
4. Brain	3. Brain	**3. Brain Integrity** Any mention of brain or neural involvement	1. Brain damage	25 (5*)	2	12	0
			2. Posterior visual pathway damage		8 (1*)		5
			3. Optic radiation damage		1 (1*)		0
			4. Retrochiasmatic pathway damage		11 (1*)		2
			5. Retrogeniculate pathway damage		3		4
			6. Posterior pathway damage including higher processing/association areas		0 (2*)		1
5. Paediatric							
6. miscellaneous (including, aetiologies, assessment methods)							

**DNRDS - Description not reaching definition status*

Diagnostic criteria of CVI

In the 43 studies detailing diagnostic/operationalising criteria (84% of all papers), ten (23% criteria) mentioned all three content themes of CVI in different combinations (Table 3). The most commonly occurring theme was *Vision Deficits* (95% criteria), with its most common subtheme being *visual impairment* (70% subthemes). The most common subtheme of *Eye Health* (93% criteria) was *eye health normal/near normal* (51% subthemes). *Brain Integrity* was only present in 28% of diagnostic/operationalizing criteria, with the most common subtheme being *posterior visual pathway damage* (42% criteria).

DISCUSSION

This systematic review found commonality and diversity in the terminologies and definitions of childhood CVI, indicating some but not total consensus. Terminologies varied according to geographical location similarly to previous reports[11, 12, 20]. *Cerebral* and *cortical visual impairment* were most commonly used, the former in Europe and the latter in North America. Other terms showed no particular geographical patterns. Older terms such as *Cortical Blindness* are no longer used widely. They are not considered to represent CVI accurately as they imply total loss of vision whereas most children with CVI show some preserved visual function[2, 54, 65]. The overall consensus points towards use of the term *Cerebral visual impairment* or *Cortical visual impairment*. We argue that the term *cerebral* is more suitable than *cortical* to describe CVI as subcortical damage to the posterior visual pathways is a common and accepted cause of the condition [27, 73, 87]. The older term *cortical* continues to be used in North America, however, researchers may be moving towards using *cerebral* for a more precise description[11, 12, 29, 52, 84, 88]. Even researchers using the alternative term acknowledge that the term *cerebral* may most accurately describe the breadth of neural insults causing this condition[6, 11].

Diversity was found in the content of CVI descriptive definitions, in accordance with previous literature[13, 82, 88]. Although three core characteristics of CVI were identified, relating to visual deficits, eye health and brain integrity, the majority of definitions did not include all three characteristics. Based on this analysis, the most consensual definition of all three characteristics was *a visual impairment caused by damage to the retrochiasmatic pathways with normal/near normal eye health*. Diagnostic/operationalising criteria showed similar characteristics with one significant omission. The two most prevalent diagnostic/operationalising criteria were *visual impairment,* in the *context of normal/near normal eye health;* few papers mentioned *Brain Integrity*.

This analysis has highlighted issues which may need to be addressed for a clinically useful definition of childhood CVI. Firstly, although the term *visual impairment* is well accepted, there has been a question of whether it is sufficiently wide to describe the range of visual difficulties described in the population. Many children with CVI appear to have greater difficulty in everyday visual behaviours than is explained by visual acuity[16, 19, 55, 89]. Some have argued that the descriptor of a 'broad spectrum of visual dysfunctions' may better align with the recommendations of the WHO, the International Council of Ophthalmology and recent research suggesting that assessing vision difficulties should be based on wider visual function rather than visual acuity/field assessment alone impairment alone[13, 90, 91]. A related debate is the issue of what is included in the term 'visual impairment'. The International Classification of Diseases-10[15] refers to significant visual acuity and/or visual field reduction but there have been calls to expand the term to include wider visual deficits[3, 13, 16, 19]. Many children at risk of CVI with normal visual acuities show significant visual perceptual difficulties which affect daily living[17, 19, 89]. The question remains: should they be diagnosed with CVI? If childhood CVI does encompass wider visual dysfunctions, further sub-classification of the condition may be very important to ensure a meaningful diagnosis and appropriate support for the individual child. Of relevance, ICD-11 beta versions (http://apps.who.int/classifications/icd11/browse/f/en) do now include more functional descriptors

such as “Visual spatial neglect”, “Prosopagnosia” and “Dysfunction of reading ability” under the headings of “Specific visual dysfunctions” and “Complex Vision-related dysfunctions”.

Secondly, the description of *no/minimal eye involvement* may not be accurate as some ocular pathology is commonly reported in CVI[18, 79, 84, 87, 92]. For example, an ophthalmologist (author RB of this review) recently declined to operate on a child with dense cataracts because there was evidence of blindness from brain damage predating this, the cause of which was deemed CVI although eye health was not normal. A more appropriate description may be that ‘any degree of ocular/anterior pathway damage present cannot explain the degree of visual dysfunction’. This ensures that CVI is not overlooked in children with ocular/anterior pathway damage and conversely that the ocular needs of children with CVI are not neglected.

Finally, this review showed that the descriptions of *Brain Integrity* were the most limited in definitions and diagnostic criteria. The more accepted description of *retrochiasmatic pathway damage* gives minimal detail of the possible areas of brain damage. Current clinical neuroimaging methods may or may not show abnormalities in the presence of definite behavioural symptoms and clinical information supporting diagnosis[13, 27]. New experimental methods may reveal subtle morphological brain differences but these require powerful imaging and intensive data analysis, which is not feasible in current clinical practice[93-96]. This raises the question of how brain damage is clinically defined. For example, children born preterm may have elevated levels of visual perceptual difficulties even with MRI scans reported as normal[27]; is a known risk factor sufficient? Currently, the component of *Brain Integrity* is only inferential and assumes that clinical visual symptoms originate at brain level. The appropriate diagnosis of children with significant visual perceptual deficits but no apparent neurological insult remains a challenge.

In light of this review, we propose the following definition of childhood CVI, argued above: *Childhood cerebral visual impairment is a verifiable visual dysfunction which cannot be attributed to disorders of the anterior visual pathways or any potentially co-occurring ocular impairment.* We

suggest that the components of this definition are measurable and may be quantified using currently available clinical tools. A multidisciplinary approach to clinical assessment of childhood CVI may be valuable in cases where the ophthalmologist working on their own is unable to reach a diagnosis. Multidisciplinary input might involve full vision assessment, structured paediatric history including vision and general development, full ophthalmological examination and clinical neuroimaging (although it might be appropriate to defer this for a baby who would require a general anaesthetic for MRI and for whom the MRI findings are unlikely to change medical management). Neuropsychological assessment of cognition and higher visual processes could also be informative if visual perceptual impairment is suspected. However, multidisciplinary assessment may not be feasible in all clinical services. Assessment should always be conducted with the principal aim of improving the understanding of the child's visual needs and limitations, and helping to establish appropriate management strategies in a timely manner.

The limitations of this review must be considered when interpreting results. The inclusion of potentially overlapping samples across studies and several publications by the same research groups may have biased findings towards the views of more prolific researchers. However, definitions and diagnostic criteria of groups were not constant across studies, thus selection bias from these groups is unlikely. Although many articles were medical case note reviews, this analysis was based only on empirical research and may not reflect the full range of clinical practice or expert opinion. It will be important to ensure that a future consensual definition is clinically useful and applicable. Other developmental considerations of CVI not identified here may be important to address, such as the impact of age of onset (childhood or adulthood), which may lead to differing symptom presentations and outcomes[2, 5, 54, 97-99]. Another possibly relevant feature is aetiology, such as the difference between congenital and later acquired CVI from infection, trauma or brain tumour, which may affect the brain damage, visual difficulties and co-morbidities seen[5, 53, 77, 99]. A related consideration is how to best describe the heterogeneous symptomatology of CVI. In the future consensus may move towards a classification system with subgroups within the umbrella term of CVI[3], depending on

further empirical research. However divisions into subgroupings may not yet be feasible due to our limited understanding of the condition[13].

As our empirical understanding of childhood CVI increases, the content of the definition will be guided by new findings[88] which may lead to more reliable clinical assessment and diagnostic procedures. There is an emerging tendency towards multidisciplinary assessment including clinical history-taking[3, 89], neuropsychology[17, 18, 27] and visual electrophysiology[34, 51, 78] in the clinical identification of visual, neuropsychological and neurological symptoms which may be part of the CVI presentation. However, within the context of limited consensual definition and diagnostic procedures shown in this systematic review, clinicians and researchers will continue to draw on individual means of assessing and diagnosing the condition. As 77% of articles included in this analysis contained poor quality definitions, detailed reporting of methodologies is a necessity for future research. At minimum, research publications should always report the sample characteristics, descriptive definition and diagnostic or operationalising criteria of CVI as well as their exact assessment methods of CVI, to permit comparison across studies and increase the evidence base of the condition.

In summary, the consensual definition found in this review suggests that childhood CVI is *a visual impairment caused by damage to the retrochiasmatic pathways with normal/near normal eye health*. However, we argue for an alternative definition based on research findings, expert opinion and clinical applicability, that childhood CVI *is a verifiable visual dysfunction which cannot be attributed to disorders of the anterior visual pathways or any potentially co-occurring ocular impairment.* Diagnostic/operationalising criteria have been stronger in relation to characterizing visual deficits and eye health than in relation to brain integrity. It has been argued that future definitions and diagnostic criteria may need to expand further to encompass the wide spectrum of children presenting in clinical ophthalmology services with suspected CVI, including those with higher visual processing dysfunctions but relatively intact visual acuity. Accurate identification of CVI

in children with complex developmental presentations remains a major challenge for clinical diagnosis and treatment. Due to the lack of a unified definition and diagnostic process, children may receive very different clinical care and interventions depending on the clinical service they attend, both internationally and at a national level. This review proposes that further work is required for an internationally accepted consensus in definition for CVI to reflect advances in thinking about childhood CVI and to underpin future clinical and research developments. As previous expert round table discussion[12, 32, 33] and now systematic scrutinizing of terminologies, definitions and diagnostic criteria have been completed, the next stage of furthering such a consensus requires advances in empirical investigations to consider whether a more refined definition and classification system of CVI is required.

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None of the authors have potential conflicts of interest to be disclosed.

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CONTRIBUTORSHIP STATEMENT

Hanna Sakki: Conception or design of the work, data collection, data analysis and interpretation, drafting the article, final approval of the version to be published.

Naomi Dale: Conception or design of the work, data analysis and interpretation, critical revision of the article, final approval of the version to be published.

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