Title: The relation between visual orienting functions, daily visual behaviour and visuoperceptual performance in children with (suspected) cerebral visual impairment

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Abstract

Background: Children with cerebral visual impairment (CVI) present heterogeneous visual orienting functions (VOF) and higher-order perception. Multiple assessment methods evaluate CVI, but the relations between them remain unclear.

Aim: To investigate the relations between VOF and (1) daily life behaviour and (2) visuoperceptual tests in children with (suspected) CVI.

Methods and Procedures: VOF were tested with a validated eye tracking-based paradigm. Visual perception was assessed using the children's visual impairment test for 3- to 6-year olds (CVIT 3-6) and (retrospective) visuoperceptual dimension results. Caregivers completed the Flemish cerebral visual impairment questionnaire (FCVIQ) and an expert panel scored relations between VOF and the other methods. We compared experts' survey responses with data-based results (linear mixed models and correlations).

Outcomes and Results: Fourty-four children (23 boys, 21 girls; median age=7y11mo, SD=2y7mo) participated. Twenty-one experts completed the survey. Slower VOF was significantly associated with (1) object and face processing impairments, (2) visual (dis)interest, (3) worse visual spatial perception (to local motion and form stimuli), and (4) worse CVIT 3-6 object and scene recognition (to cartoon stimuli).

Conclusions and Implications: Integration of VOF with existing visual assessments provides a better clinical picture of CVI and can prevent misdiagnosing children as inattentive, incapable, or unmotivated.

Highlights

- Better object and face processing was related to faster orienting responses.
- Higher visual interest was related to faster orienting responses to visual stimuli.
- Better visual spatial perception was related to faster orienting to visual stimuli.
- Better object and scene recognition was related to faster orienting responses.

- Integrating visual orienting into a child's perceptual profile adds clinical value.

What this paper adds?

Cerebral visual impairment (CVI), often caused by diffuse brain lesions, can occur early in the developmental trajectory of a child and results in a complex and heterogeneous clinical picture. Multiple assessment methods are routinely implemented to evaluate CVI, but the relations between them remain unclear. This study highlights the potential of applying assessment tools for visual orienting functions (VOF) as well as higher-level visual perception in children with (suspected) CVI, which are both commonly impaired in CVI. The extent to which information is processed at higher levels of vision depends on VOF and attention. This study explores the relations between VOF and different assessment methods for CVI, including questionnaires as a proxy to daily life functioning and clinical visuoperceptual tests. The results indicate that children with object and face processing impairments or visual (dis)interest in daily life showed slower orienting to visual stimuli. Moreover, children with better visual spatial perception or better object and scene recognition showed faster orienting responses. There is potential of integrating a VOF paradigm into the diagnostic procedure as additional information for assessment. The presence of delayed orienting can explain the limited visual attention span and shortened gaze behaviour often seen in CVI, and can prevent misdiagnosing children as inattentive, incapable, or unmotivated. The results are of relevance not only for children with CVI, but may be beneficial for other disabilities characterized by heterogeneity in visual and perceptual functions such as autism spectrum disorder and cerebral palsy.

Keywords

Cerebral visual impairment; Visual orienting functions; Remote eye tracking; Visual perception

1. Introduction

Visual perception affects numerous aspects of development, including neuromotor (Braddick & Atkinson, 2013), cognitive (Dale et al., 2017), and emotional development (Huurre & Aro, 1998). Moreover, when visual perception is impaired, reduced psychosocial and physical quality of life are reported (Sakki et al., 2020). Impaired visual perception is characteristic for CVI (Philip & Dutton, 2014), but also occurs in conditions such as cerebral palsy (Ego et al., 2015) and autism spectrum disorder (Dakin & Frith, 2005; Evers et al., 2018). Visual perceptual functions include visual discrimination and matching (i.e., detecting features for processing the differences and similarities among visual stimuli), object recognition (e.g., even when shown under an incomplete representation), visual spatial perception (i.e., determining spatial relations within and between objects, perceiving depth, topographic orientation and wayfinding), figure-ground perception (i.e., differentiating relevant object information from distracting background information), motion perception (which is also essential for navigating and understanding a constantly changing visual environment), and visual memory (i.e., integrating visual information with previous experience) (Schneck, 2010; van der Zee et al., 2019).

CVI is defined as 'a verifiable visual dysfunction which cannot be attributed to disorders of the anterior visual pathways or any potentially co-occurring ocular impairment' (Sakki et al., 2018, p. 430). The causative brain lesion of CVI is highly heterogeneous resulting in a broad clinical profile of visual impairments (Bennett et al., 2020). Although CVI is not attributable to ocular impairments, both eye and oculomotor conditions as well as higher-order visual perception dysfunction can be seen in CVI. Examples of eye conditions include refractive error and impaired accommodation (Dutton & Bax, 2010), and oculomotor conditions include strabismus and nystagmus, or abnormalities with smooth pursuit, saccades, and fixation (Salati et al., 2002). Impairments in visual orienting functions (VOF) are also common (Dutton & Jacobson, 2001), affecting the way information enters the system for further processing, in accordance with Rybak et al.'s (1998) model of attention-guided visual perception and recognition. Specifically, if VOF are impaired, dysfunction in higher visual processing, possibly occurring concurrently with dysfunction in the ocular motor system, may be apparent (Boot et al., 2013; Kooiker et al., 2019). Higher-order visual perception dysfunction can be linked to the ventral and dorsal stream framework (Goodale, 2013). This model poses that the ventral stream, connecting the occipital to the temporal lobe, is responsible for visual memories facilitating object recognition, face recognition, and route finding (Dutton, 2013). The dorsal stream, which links the occipital lobe to the parietal regions, is responsible for visual guidance of movement, navigation, and difficulty in handling complex visual scenes (Dutton, 2003). Feedforward connections from the primary visual cortex (V1) ascend through the two visual streams, and reciprocal feedback connections carry information back about the behavioural context, highlighting the interconnectedness and complexity of these systems (Gilbert & Li, 2013).

According to the guidelines in the European perspective on CVI (Ortibus et al., 2019), a CVI diagnosis is achieved through a multidisciplinary team, covering all previously mentioned aspects of the disorder. The CVI intake procedure generally involves structured history-taking, questionnaires (e.g., the Flemish cerebral visual impairment questionnaire) (Ortibus et al., 2011), observations, and a clinical examination involving standardized neuropsychological assessment of visuoperceptual (VP) abilities. Recently, tools such as the children's visual impairment test for 3- to 6-year olds (CVIT 3-6) have also been implemented in clinical testing (Vancleef et al., 2019). The main focus of the tests administered in clinics in Belgium is on assessment of visual perception to profile a child's strengths and weaknesses (Ben Itzhak et al., 2021). In previous research, six visuoperceptual dimensions namely 'Visual discrimination and matching', 'Object or print recognition', 'Visual spatial perception', 'Figure-ground perception', 'Motion perception', and 'Visual short-term memory' were developed to quantify a child's profile (Ben Itzhak et al., 2021).

VOF can be operationalized by measuring visually-guided eye movements (Boot et al., 2013), for example using an eye tracking paradigm developed by Pel et al. (2010). This paradigm employs a preferential looking approach in which a child's reflexive eye movements to specific visual stimuli are analysed to understand their detection level and their processing efficiency. Previous research has shown promising results with regard to the possible use of VOF as a screening tool for CVI. As a group, children with CVI showed abnormal VOF reflected as delayed orienting response times (especially to highly salient cartoon stimuli) and less accurate fixations (Kooiker et al., 2015). Furthermore, attending to visual targets was highly dependent on the visual salience of the target, whereby highly salient stimuli triggered faster and less variable responses compared to low-salient visual stimuli (Kooiker, van der Steen, et al., 2016).

In spite of the potential of VOF to screen for one of the important aspects known to be affected in CVI, no readily available measurement of VOF has been implemented in the clinical intake procedure. While it is apparent that multiple assessment methods are crucial to evaluate complex conditions such as CVI, it remains unclear what relations exist between VOF and daily life functioning nor between VOF and VP dimensions.

Also, given the heterogeneous origin and clinical presentation of CVI, the validity of the method and its relation with higher-order perception in the individual child with CVI is still unknown. To better understand the high heterogeneity of CVI, both reflexive orienting responses as well as VP skills need to be quantified to obtain a complete clinical picture of a child. To reach this goal, two research groups from Belgium and the Netherlands (with expertise in visual perception, neuropsychology, and child neurology) joined forces to investigate from different angles this complex topic with multilayer connections. The aims of the present study were to evaluate whether there is a relation between (1) VOF and daily life behaviour, and (2) VOF and VP tests used in the clinic in children with (suspected) CVI.

2. Participants/Materials & Methods

2.1. Participants and clinical characteristics

The current study was conducted at the Centre for Developmental Disabilities (COS) at the University Hospitals of Leuven, Belgium. Children were recruited via the CVI clinic in COS or through the Cerebral Palsy Reference Centrum, Belgium. Recruited children either already had a confirmed CVI diagnosis, were actively undergoing CVI testing due to suspicion of CVI (VP impairments), had a suspicion of CVI but did not yet begin the CVI testing trajectory, or had a suspicion of CVI but had not received a CVI diagnosis. A CVI diagnosis was established in accordance with recommendations in Ortibus et al. (2019) To ensure reliable estimates, children were excluded when they had a visual acuity < 0.2 (decimal scale), oculomotor apraxia (a deficiency in the ability to move eyes in a voluntary, horizontal, lateral, and fast manner, compensated for by head movements), severe physical disabilities, or severe epilepsy (for which children actively take the antiepileptic medication vigabatrin as it has been found to reduce contrast sensitivity and result in abnormal colour perception) (Hilton et al., 2004). Parents provided written informed consent. Data collection took place between July 2019 and January 2021 (due to COVID-19, the participant recruitment and testing spanned over a longer period). A total of 44 children were included in this study. Information on (1) gestational age, (2) birth weight, (3) comorbidities, (4) performance age, (5) ophthalmological data, and (6) VP test results were obtained from clinical records when present. Performance age was calculated as in Ben Itzhak et al. (2021). The presence of strabismus, nystagmus and use of glasses was recorded. Far-distance visual acuity data (using age-appropriate visual acuity tests) was extracted from the clinical records and was reported in decimal and in LogMAR equivalents. The following VP tests were extracted from the database: (1) the visual-perceptual battery L94 (L94), (2) the test of visual perceptual skills (TVPS-3), (3) the Beery-Buktenica developmental test of visual-motor integration (Beery-VMI-6), (4) motion perception tasks, (5) preschool judgment of line orientation (PJLO), (6) subtests of the developmental neuropsychological assessment (NEPSY-II-NL-arrows and NEPSY-II-NL-geometric puzzles), and (7) subtests of the revisie Amsterdamse kinderintelligentie test (RAKIT-2 hidden figures and RAKIT-2 figure recognition) when present. Children's VP test data were used to calculate a profile with an average z-score for each of the six VP dimensions, where possible, in accordance with Ben Itzhak et al. (2021). The six VP dimensions were (1) visual discrimination and matching, (2) object or picture recognition, (3) visual spatial perception, (4) figure-ground perception, (5) motion perception, and (6) visual short-term memory. The presence of cerebral palsy, classified according to the Surveillance of cerebral palsy in Europe (2000), autism spectrum disorder, developmental coordination disorder, attention deficit hyperactivity disorder, and epilepsy were recorded. The study was approved by the ethical committee of UZ/KU Leuven (no. S61226).

2.2. General procedure: Eye tracking-based paradigm measuring VOF

The eye tracking-based preferential looking paradigm measures reflexive visual orienting behaviour operationalized by six visual stimuli (see Figure 1) appearing in one of four quadrants. Using these six visual stimuli, three dynamic 1) cartoons, 2) global motion, and 3) local motion, and three static 4) form, 5) contrast, and 6) colour, different parameters reflecting VOF and the first steps of processing these visual 'functions' can be calculated. More specifically, based on the gaze responses, eye tracking parameters were calculated for each child separately for every stimulus type: (1) number of calculated RTs, (2) number of stimuli seen, and (3) average reaction time to fixation (RTF; in ms), while for cartoon stimuli only, an additional two parameters were calculated (4) spontaneous fixation duration (FD; in ms), and (5) gaze fixation area (GFA; in °) (Kooiker, Pel, et al., 2016; Kooiker, van der Steen, et al., 2016). RTF reflects the average time taken to detect visual information and execute an eye movement toward an area of interest and measures the timing of reflexive visual orienting. FD is the average time that the eyes remain on the area of interest and is a measure of spontaneously sustained visual attention. GFA is the average diameter of the fixated area and is a measure of the accuracy of fixating visual attention on a target. Children's RTF results for all stimuli, and GFA and FD for cartoon stimuli were compared with norm data provided by Kooiker et al. (2016).

VOF was measured with an eye tracking system sampling at 120Hz (Tobii Pro X3-120, Tobii Corporation, Danderyd, Sweden) attached to a presentation monitor (DELL S2716DG, 27 inch, screen resolution of 1920 x 1080 and 60 Hz screen frame rate). Children sat at 60cm distance from the screen, either on a comfortable chair, in their wheelchair, or on their parent's lap. If the child sat on their parent's lap, their parent wore sunglasses to prevent the eye-tracker from tracking the parent's eyes. Side panels were used around the setup to avoid the child getting distracted. The experiment room was quiet and ambient light conditions were maintained. First, children were presented with a 5-point calibration procedure. If this calibration failed then the eyes were post-calibrated before data analysis according to Pel et al. (2010). After the calibration, children were presented with an experiment consisting of images and short movies of the six stimuli lasting a total of ~ 6 minutes. Children saw the cartoons 12 times (three times in each quadrant) while the other stimuli were shown four times each (once in every quadrant).

The child's caregiver was asked to fill out the Flemish cerebral visual impairment questionnaire (FCVIQ) after their child completed the eye tracking experiment and the CVIT 3-6.

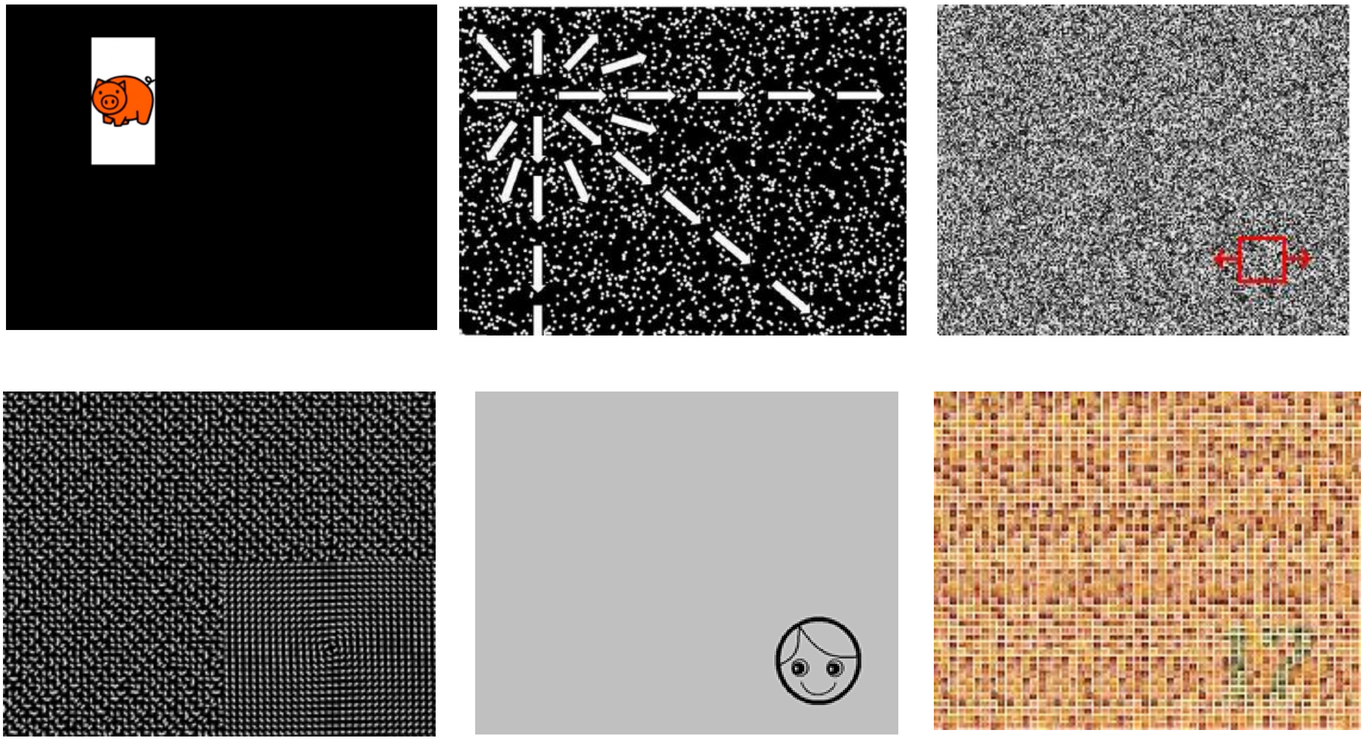

Figure 1. Visual stimuli presented in the study. Top left = cartoon stimuli, top centre = global motion stimuli, top right = local motion stimuli, bottom left = form stimuli, bottom centre = contrast stimuli, bottom right = colour stimuli. Adapted from and with permission of Kooiker et al. (2016).

2.2.1. Children's visual impairment test for 3- to 6-year-olds (CVIT 3-6) (Vancleef et al., 2019)

Each child who met inclusion criteria (a performance age between 3-6 years) and collaborated with the assessment, underwent CVIT 3-6 testing. This test consists of 14 subtests categorized into four subscales namely 'object and scene perception', 'degraded object recognition', 'motion perception', and 'global–local processing'. Each child received a percentile score on each of the 14 subtests, as well as an average percentile score on the four subscales. This percentile score was calculated by comparing the child's score with a sample of typically developing children in an age bracket of 6 months from the child's performance age. For more details on the subtests of this tool, please refer to Vancleef et al. (2019). This test has shown good test-retest reliability (*r* = 0.82), high correlations with other similar visual perceptual tests (e.g., L94, an $r = 0.74$), and low correlations with non-related tests (e.g., Beery-VMI, an $r = 0.25$, $p = 0.09$) (Vancleef et al., 2020).

2.2.2. Flemish cerebral visual impairment questionnaire (FCVIQ) (Ortibus et al., 2011)

The Flemish cerebral visual impairment questionnaire (FCVIQ) is a 46-item binary response format tool, which aims to screen children who need to be referred for CVI testing. In addition to individual item responses, a score on five factors can be obtained to provide a quantified profile for a child. The five factors are (1) object and face processing impairments, (2) visual (dis)interest, (3) clutter and distance viewing behaviours, (4) moving in space impairments, and (5) anxiety-related behaviours. A score on each of the five factors ranges between 0 and 1, and the calculation steps can be found in Ben Itzhak et al. (2020). The FCVIQ has shown a sensitivity of 80% and a specificity of 60% (Ortibus et al., 2011).

2.2.3. Expert panel on inter-assessment relations

A survey was designed to provide a hypothesis-driven means to determine which eye tracking stimuli and resulting VOF parameters relate to the FCVIQ items, VP dimensions, and the CVIT 3-6 subtests. Experts were defined as professionals with experience in researching visual perception, developing tests and therapy for vision disorders, and/or working in a clinical setting diagnosing and treating visual (perceptual) impairment and/or other developmental conditions. Twenty-one experts filled out the survey including 12 researchers, seven clinicians (orthoptist, intellectual disability physician, three (child) neuropsychologists, child neurologist, and a medical physicist), and two experts who were both neuropsychologists and researchers). The survey, designed as a Google Form, was distributed to experts via email. The survey was split into three main sections, in which experts were asked whether and how the eye tracking paradigm outcomes related to 1) the FCVIQ (46 items), 2) VP dimensions (6 items), and 3) the CVIT 3-6 subtests (14 items). If experts answered yes on this first (general) level of questions, they were asked to specify to which of the (six) eye tracking stimuli the statement relates in the second (specific) level of questions. An example item for the FCVIQ included: ‘Does the FCVIQ item 'Absent eye contact' relate to the eye tracking paradigm?’, if the expert answered yes, a second item was presented asking ‘To *which* eye tracking stimulus/stimuli does the FCVIQ item 'Absent eye contact' relate?’. The same structure of questions was followed for the items of the VP dimensions as well as the CVIT 3-6 subtests.

3. Data analysis and statistics

3.1. Participants and clinical characteristics

Descriptive statistics on the children's demographic and clinical characteristics were gathered and analysed using Statistical Package for Social Science (SPSS) for Windows version 27 (IBM Corp, 2017).

3.2. Eye tracking-based paradigm measuring VOF

Eye movement responses to the presented stimuli were analysed using the same method as outlined in Kooiker et al. (2019). For each stimulus presentation, we recorded whether a child detected the stimulus target area (parameters 'seen') and if yes, calculations regarding how fast the eyes reached the target were calculated into an average RTF for that stimulus type. Number of stimuli seen and number of RTs were analysed in all 44 children. Averages of eye tracking parameters for RTF, GFA, and FD were only included for further statistical analysis when RTs could be calculated for at least 25% of each stimulus type (i.e., at least three RTs out of 12 for cartoons, and at least one RT out of four for all other stimuli) to ensure reliable estimates (Kooiker, van der Steen, et al., 2016). For additional/more detailed criteria of when the stimuli was classified as 'seen' and how VOF parameters were calculated, please see Kooiker et al. (2019). In previous work, the effective saliency of the eye tracking stimuli was split into three levels of salience with cartoons and contrast stimuli classified as high salient, local motion and form stimuli as intermediate salient, and global motion and colour as low saliency (Kooiker, van der Steen, et al., 2016). In the present study, in addition to raw eye tracking data, z-scores on all stimuli and eye tracking parameters (where norm data was present) were calculated per child using normative reference samples previously collected by Kooiker et al. (2016). Twelve age bins were created each of 1 year from the age of under 1 year until 12 years, and the 12th age bin included children aged 11 and above. Mann-Whitney U tests (MWU) were conducted to compare eye tracking parameters between (1) children with and without CVI, (2) children with and without strabismus, and (3) children with and without nystagmus. The effect size of the MWU tests for non-normally distributed data were calculated using the following formula (Fritz et al., 2016): $r = \frac{z}{\sqrt{N}}$ where *r* denotes the effect size, *z* the *z*-value, and *n* the sample size. A large effect = 0.5, a medium effect = 0.3, and a small effect = 0.1 (Cohen, 1988). Eye movement data were analysed using MATLAB. All analyses were conducted using SPSS (IBM Corp, 2017).

3.3. Global inter-assessment relations

To obtain a more global/higher level perspective in understanding the relation between the eye tracking RTF z-scores and (1) the FCVIQ factor scores, (2) VP dimensions, and (3) the CVIT 3-6 subscales, we applied linear mixed models for repeated measures separately for each relation. Linear predictor variables (fixed factors) were FCVIQ factor scores, VP dimensions, and the CVIT 3-6 subscales. A random intercept for participant was incorporated to take the repeated measurements into account. The dependent variable was eye tracking RTF z-score. First, the models were fitted with an interaction effect between the predictor and stimulus, if an interaction was found, it would mean that the effect is different for different eye tracking stimuli types. Moreover, if this interaction was not significant, only the model without the interaction term is presented. A main effects model means that the association between the scale scores and the eye tracking z-scores are similar for all eye tracking stimuli types. All analyses were conducted using SPSS (IBM Corp, 2017).

3.4. Expert panel on inter-assessment relations

To obtain a more fine-grained/item-level and theory driven perspective, experts' responses on the eye tracking survey were integrated. An overall Fleiss Kappa was calculated as a measurement of the general agreement between all of the 21 experts, between only the researchers, and only the clinicians (on the FCVIQ, the VP dimensions, and the CVIT 3-6). The interpretation of the Kappa was performed in accordance with Landis and Koch (1977) where a Kappa of < 0 = poor, 0 – 0.2 = slight, 0.21-0.4 = fair, 0.41 – 0.6 = moderate, 0.61 – 0.80 = substantial, and 0.81 – 1.0 = almost perfect. The data was split in three main sections, the FCVIQ, the VP dimensions, and the CVIT 3-6. For the FCVIQ items, MWU tests were conducted to see whether there were differences between children who had an FCVIQ item present compared to children who did not have an FCVIQ item present (and effect sizes were calculated as explained in the formula, see Section 3.2.) on all of the eye tracking results on all parameters (number of stimuli seen, number of RTs, RTF, FD, and GFA) was also calculated on the stimuli and the items with a high percentage of experts finding an FCVIQ item associated with the eye tracking paradigm. Moreover, for the VP dimensions and the CVIT 3-6 subtests, Spearman correlations were calculated between the child's eye tracking results and the items with a high percentage of experts finding the item associated with the eye tracking paradigm. When ≥52% of the experts classified an item as associated with the eye tracking paradigm it was considered as highly related and hence was tested statistically. Analyses were performed using SPSS (IBM Corp, 2017).

4. Results

4.1. Participants and clinical characteristics

Table 1 shows the demographic and clinical characteristics of the 44 children. The median calendar age was 7 years and 11 months and the median performance age was 6 years and 2 months. Thirty-three children had a confirmed CVI diagnosis. Autism spectrum disorder was present in 19 children, developmental coordination disorder in nine children, attention deficit hyperactivity disorder in three children, epilepsy in six children, and cerebral palsy was present in 13 children. Moreover, nystagmus was present in 14 children and strabismus in 29 children.

Table 1. Children's demographic and clinical characteristics

Clinical characteristics		
Calendar age (months)	Range (median; SD)	39-181 (95; 31)
Performance age (months)	Range (median; SD)	33-150 (74; 29)
Gender	Male: Female	23:21
Gestational age (weeks)	Mean (SD; Range)	35 (4.7; 26-42)
Birth weight (grams)	Mean (SD; Range)	2412 (943; 815-4165)
Visual acuity LogMAR	Mean (SD; Range)	0.135 (0.278; -1 to 0.8)
Visual acuity Decimal	Mean (SD; Range)	0.70 (0.22; 0.16 to 1.2)
		Number of children
Nystagmus		14
Strabismus		29
Glasses		24
Cerebral visual impairment		33
Autism spectrum disorder		19
Developmental coordination disorder		9
Attention deficit (hyperactivity) disorder		3
Epilepsy		6
Cerebral palsy		4 spastic unilateral; 9 spastic bilateral

Notes. SD: Standard deviation. N: Number of children who present the clinical characteristic.

4.2. Eye tracking-based paradigm measuring VOF

Table 2 shows the total percentage of visual stimuli seen, and the RTF results (both in z-score and in raw milliseconds) for all stimuli, and FD and GFA results for the cartoon stimuli. The total percentage of stimuli seen was the highest for highly salient stimuli (contrast and cartoon) followed by stimuli with intermediate saliency (form and local motion), and was lowest for stimuli with low saliency (global motion and colour). RTF results were also related to stimulus salience whereby children reacted on average the fastest to cartoon stimuli followed by contrast, form, local motion, global motion, and colour. Children with confirmed or suspected CVI showed the largest deviant z-scores (i.e., higher/more delayed RTF) compared to the typically developing norm group on cartoon stimuli, followed by local motion, then contrast, and then form. RTF to colour and global motion were within normal performance as the z-scores were between 0 and -1. Moreover, compared to the norm group, FD for the cartoon stimuli was close to normal, while GFA for the cartoon stimuli was largely abnormal.

Table 2. Total percentage of stimuli seen, median reaction time to fixation, median fixation duration, and median gaze fixation area results on the eye tracking stimuli.

Stimulus [N]	Salience level	Total % seen[a]	Median RTF (IQR, raw ms)	Median RTF (IQR, z-score compared to norm)	Median FD (IQR, raw ms)	Median FD (IQR, z-score compared to norm)	Median GFA (IQR, raw ms)	Median GFA (IQR, z-score compared to norm)
Cartoon [43]	High	83	243 (219 – 291)	-3.05 (-6.7 to -2.14)	1186 (1128 to 2646)	-0.76 (-2.12 to 0.86)	3 (2.80 to 3.60)	-4.28 (-5.69 to -2.98)
Contrast [40][b]	High	81	323 (283 – 388)	-2.19 (-5.27 to -1.50)				
Form [35]	Intermediate	69	489 (386 – 723)	-1.77 (-5.60 to -0.47)				
Local motion [36]	Intermediate	62	526 (401 – 775)	-3.00 (-6.42 to -1.14)				
Global motion [33]	Low	61	629 (479 – 908)	-0.05 (-1.81 to 0.50)				
Colour [17]	Low	29	823 (706 – 1010)	-0.66 (-2.32 to 0.23)				

Notes. [a]Total percentage stimuli seen includes all 44 children, while all other presented z-score and raw score results are calculated only for children who had reliable data. [b]One extreme outlier participant was excluded for contrast stimuli as their RT was ~300ms slower than the other participants. RTs: Individual reaction times. RTF: Average reaction time to fixation. FD: Fixation duration. GFA: Gaze fixation area. IQR: Interquartile range. ms: Milliseconds.

Children with a confirmed CVI diagnosis had a significantly slower form RTF and slower local motion RTF compared to children without CVI (see Appendix A). Moreover, children with strabismus had a significantly larger GFA for cartoon stimuli, saw and reacted to significantly less local motion stimuli, and had a significantly slower RTF to both local motion and global motion stimuli compared to children without strabismus (see Appendix B). Finally, children with nystagmus had a significantly larger GFA for cartoon stimuli and had a significantly slower RTF to local motion stimuli compared to children without nystagmus (see Appendix C).

4.3. Global inter-assessment relations

Table 3 shows linear mixed model results which revealed that FCVIQ factor 1 (object and face processing impairments) and FCVIQ factor 2 (visual (dis)interest) were negatively associated with eye tracking RTF z-score. Specifically, the greater the child's object and face processing impairments, and visual disinterest, the slower their orienting responses to the eye tracking paradigm globally. There was no interaction effect, hence there was no evidence for different associations for different eye tracking stimuli types. Moreover, an interaction effect between the CVIT 3-6 subscale 'object and scene recognition' and the eye tracking stimulus type was found ($p = 0.023$). Specifically, the better the child's percentile score on the CVIT 3-6 subscale 'object and scene recognition', the faster their orienting response to the cartoon stimuli (see Table 3), but no associations were found for the other eye tracking stimuli types.

Table 3. Linear mixed model results.

		Estimate (95% C.I.)	Significance
Flemish cerebral visual impairment questionnaire factors	Factor 1: Object and face processing impairments	-4.84 (-8.67 to -1.01)	0.014*
	Factor 2: Visual (dis)interest	-4.48 (-8.08 to -0.88)	0.016*
	Factor 3: Clutter and distance viewing impairments	-2.14 (-4.51 to 0.23)	0.076
	Factor 4: Moving in space impairments	-1.11 (-3.24 to 1.02)	0.300
	Factor 5: Anxiety-related behaviours	-1.00 (-3.93 to 1.92)	0.491

Visuoperceptual dimensions	Visual discrimination and matching	0.81 (-0.005 to 1.63)	0.052
	Object/picture recognition	0.64 (-0.02 to 1.31)	0.059
	Visual spatial perception	0.47 (-0.39 to 1.35)	0.274
	Figure-ground perception	0.52 (-0.31 to 1.36)	0.215
	Visual short-term memory	0.25 (-0.74 to 1.26)	0.602
Children's visual impairment test for 3- to 6-year-olds subscales	Object and Scene Recognition	Cartoon: 0.10 (0.03 to 0.18	Cartoon: 0.005**
		Contrast: 0.01 (-0.06 to 0.08)	Contrast: 0.781
		Form: -0.05 (-0.14 to 0.04)	Form: 0.270
		Local motion: 0.08 (-0.009 to 0.18)	Local motion: 0.075
		Global motion: 0.004 (-0.12 to 0.13)	Global motion: 0.949
		Colour: -0.06 (-0.27 to 0.14)	Colour: 0.530
	Degraded object perception	0.001 (-0.08 to 0.08)	0.971
	Motion perception	0.01 (-0.03 to 0.06)	0.484
	Global-local processing	0.01 (-0.03 to 0.06)	0.478

Notes. C.I.: Confidence interval. Significant *p*-values are marked as *< 0.05, **< 0.01, ***< 0.001.

4.4. Expert panel on inter-assessment relations

The overall agreement between the experts (including both researchers and clinicians) on the relation of the eye tracking-based paradigm with FCVIQ was fair, for the VP dimensions moderate, and for the CVIT 3-6 fair. When splitting the experts into two groups i.e., into researchers and clinicians (note that two experts belonged to both groups), the Fleiss Kappa values were higher in the researchers group compared to the clinicians group (see Table 4).

Table 4. Agreement between expert panel on inter-assessment relations.

Assessments	Clinicians and researchers Fleiss Kappa (95% C.I.)	Researchers Fleiss Kappa (95% C.I.)	Clinicians Fleiss Kappa (95% C.I.)
FCVIQ	0.243 (0.223 – 0.304)	0.325 (0.295 – 0.356)	0.163 (0.115 – 0.211)
VP dimensions	0.443 (0.388 – 0.498)	0.534 (0.450 – 0.618)	0.330 (0.196 – 0.463)
CVIT 3-6	0.340 (0.304 – 0.376)	0.449 (0.394 – 0.504)	0.190 (0.103 – 0.277)

Notes. The interpretation of the Fleiss Kappa was performed in accordance with Landis and Koch (1977): < 0 = poor, 0 – 0.2 = slight, 0.21-0.4 = fair, 0.41 – 0.6 = moderate, 0.61 – 0.80 = substantial, and 0.81 – 1.0 = almost perfect. FCVIQ: Flemish cerebral visual impairment questionnaire. VP: Visuoperceptual. CVIT 3-6: Children's visual impairment test for 3- to 6-year olds. C.I.: Confidence interval.

Appendix D represents items that had ≥52% of the experts classifying the item as associated with the eye tracking paradigm and to which eye tracking stimulus. In the survey, experts indicated that 15 out of 46 FCVIQ items were related to the eye tracking paradigm. Three items out of 15 belonged to factor 1 (object and face processing impairment), four to factor 2 (visual (dis)interest), one to factor 3 (clutter and distance viewing impairments), factor 4 (moving in space impairments), and factor 5 (this item also fell under factor 2), and finally six items did not fall into any factor in the original factor analysis and hence were termed as not applicable (NA). Out of the six VP dimensions, three were mentioned to be related to the eye tracking paradigm, namely motion perception, figure-ground perception and visual spatial perception. Finally, out of 14 CVIT 3-6 subtests, three were indicated to be related to the eye tracking paradigm namely global-motion detection, kinematic object segmentation, and object recognition.

Table 5 shows the correlations between the items that a high percentage of experts judged to be associated with the eye tracking paradigm and the significant relations found with the eye tracking-based stimulus-specific parameter results. MWU analyses revealed that six FCVIQ items judged to be associated by the experts indeed significantly related to the eye tracking paradigm: when parents indicated the presence of that item in their child, this child's orienting functions were impaired. Children whose parents' indicated that 'Does not see level differences e.g., stairs' and 'I often wonder: Does he not want to look at things or is he not able to?' as applicable to their child showed a lower accuracy of fixation to cartoon stimuli. Moreover, when the item 'I often wonder: Does he not want to look at things or is he not able to?' was indicated as being present, these children showed a slower RTF to cartoon stimuli. When the item 'Has no interest for simple pictures' was indicated, children saw and reacted to fewer contrast stimuli. The average RTF to form stimuli, and number of form stimuli seen, were slower and less, respectively, in children whose parents' indicated that their child 'Does not find his/her toy when he/she drops it'. Also, the average RTF to form stimuli was slower in children whose parents' indicated that 'More toys perturb visual attention'. Children whose parents' indicated that 'I often wonder: Does he not want to look at things or is he not able to?' as being present in their child, saw and reacted to less form stimuli. Finally, children whose parents indicated that their child 'Does not look spontaneously at an object, does not explore the room spontaneously' and that 'More toys perturb visual attention' showed a slower RTF to colour stimuli.

Spearman correlation analyses revealed that the visual spatial perception dimension significantly related to local motion and form stimuli, where a higher visual spatial perception z-score related to more form reacted to and more local motion stimuli seen and reacted to.

Additionally, a faster RTF on form stimuli related to a higher visual spatial perception z-score. Finally, no significant correlations were found between the CVIT 3-6 subtests and the eye tracking paradigm. In Table 5, it can be seen that the effect size over the different survey sub-parts was large for colour stimuli, while for form, cartoon, contrast, local motion, and global motion stimuli the effect size was medium.

Table 5. Survey items significantly related to the eye tracking paradigm.

Survey subpart	Item (item number)	Percentage of experts who find an item associated[c]	Specific eye tracking stimuli and parameters	P-value; effect size	Median (SD)[d]
FCVIQ[a]	Does not find his/her toy when he/she drops it (#6)	100%	Form #stimuli seen Form RTF	P = 0.048*; r = 0.30 P = 0.004**; r = 0.49	No = 3 (1.1); Yes = 2.5 (1.27) No = -0.84 (5.36); Yes = -5.0 (4.25)
	Does not look spontaneously at an object, does not explore the room spontaneously (#13)	86%	Colour RTF	P = 0.015*; r = 0.59	No = -0.16 (2.58); Yes = -2.32 (1.17)
	More toys perturb visual attention (#15)	73% (form), 64% (colour)	Form RTF Colour RTF	P = 0.019*; r = 0.40 P = 0.007**; r = 0.65	No = -0.70 (3.55); Yes = -4.26 (5.70) No = 0.23 (1.09); Yes = -2.15 (2.69)
	Does not see level differences e.g., stairs (#27)	91%	Cartoon GFA	P = 0.025*; r = 0.3	No = -3.77 (2.42); Yes = -5.28 (3.02)
		75%	Contrast #stimuli seen	P = 0.014*; r = 0.37	No = 4 (0.75); Yes = 3 (1.14)

	Has no interest for simple pictures (#30)		Contrast #RTs	$P = 0.035^{*}$; $r = 0.32$	No = 3 (0.93); Yes = 2.5 (0.99)
	I often wonder: Does he not want to look at things or is he not able to? (#46)	88% (cartoon), 88% (form)	Cartoon RTF	$P = 0.035^{*}$; $r = 0.33$	No = -2.66 (2.66); Yes = -5.16 (5.33)
			Cartoon GFA	$P = 0.004^{**}$; $r = 0.44$	No = -3.51 (2.45); Yes = -5.26 (2.8)
			Form #stimuli seen	$P = 0.034^{*}$; $r = 0.32$	No = 3 (1.15); Yes = 2 (1.2)
			Form #RTs	$P = 0.016^{*}$; $r = 0.36$	No = 3 (1.40); Yes = 1 (1.46)
VP dimension[b]	Visual spatial perception	77% (local motion), 77% (form)	Local motion #stimuli seen	$P = 0.013^{*}$; Spearman corr = 0.38	
			Local motion #RTs	$P = 0.009^{**}$; Spearman corr = 0.40	
			Form RTF	$P = 0.004^{**}$; Spearman corr = 0.49	
			Form #RTs	$P = 0.048^{*}$; Spearman corr = 0.31	

Notes. #stimuli seen and #RTs include all 44 children, while all other presented z-score results are calculated only for children who had reliable data. One extreme outlier participant was excluded for contrast stimuli as their RT was ~ 300ms slower than the other participants. Effect size was calculated using $r = \frac{Z}{\sqrt{N}}$ (Fritz et al., 2016). Statistical significance assessed by [a]Mann-Whitney U test or [b]Spearman correlation. [c]The percentage of experts who find an item associated refer to the number of experts who said 'yes' in level I and not the total 21 experts who filled out the survey. [d]For number of stimuli seen and number of reaction times to fixation the count is presented, for all other eye tracking parameters average z-score is reported. RTs: Individual reaction times. RTF: Average reaction time to fixation. FD: Fixation duration.. GFA: Gaze fixation area. FCVIQ: Flemish cerebral visual impairment questionnaire. VP: Visuoperceptual. CVIT 3-6: Children's visual impairment test for 3- to 6-year olds. Significant *p*-values are marked as $^{*}< 0.05$, $^{**}< 0.01$, $^{***}< 0.001$.

5. Discussion

This study evaluated whether there is a relation between VOF as measured with eye tracking and 1) daily life behaviour and 2) VP tests used in the clinic in children with (suspected) CVI. While VOF and daily life behaviour as well as VP testing are known to measure different functions, our results show that VOF are related to certain perceptual functions, and that low-level attention is important for perception, which is in line with Rybak et al.'s (1998) model of attention-guided visual perception and recognition. A relation was found between VOF and daily life behaviour, wherein children with object and face processing impairments or visual (dis)interest displayed slower orienting to visual stimuli. Specifically, children with a general reduction in attention for and interest in exploring their environment (on FCVIQ questionnaire items targeting more dorsal stream functions such as visual (spatial) attention and processing) showed slower orienting reactions to several visual stimuli. Moreover, VOF were also related to VP tests, specifically children with a better visual spatial perception score oriented faster, and children with a better object and scene recognition score (CVIT 3-6) oriented faster to the cartoon stimuli.

Clinical characteristics

Overall, children's visual orienting performance to the different stimuli was in accordance with the stimuli's saliency, specifically, the higher the saliency of the stimuli, the higher the percentage of stimuli seen, the faster the average reaction time, and the lower the variability in responses. These results are in accordance with a study using the same method in 220 typically developing children aged 1 to 12 years (Kooiker, van der Steen, et al., 2016), in whom highly salient stimuli resulted in faster and less variable orienting compared to low-salient visual stimuli. Additionally, the difference in RTs between children with (suspected) CVI and a typically developing norm group was largest for cartoon stimuli, followed by local motion, then contrast, and then form. On the other hand, reactions to the least salient stimuli, colour and global motion, were least impaired. This might not be surprising as even in a sample of typically developing children, RTs to those stimuli were the slowest and most variable (2016), which could suggest that no single aspect underlies the performance on these stimuli, and that the variability could be a result of the multidimensionality of the stimuli targeting different processes.

Within our study sample of children with (suspected) CVI, these previous results were partly confirmed as children with a confirmed CVI diagnosis had significantly slower orienting responses to form and local motion stimuli compared to children with a suspicion of CVI but who did not receive a CVI diagnosis. In previous research, children with CVI showed worse performance on a motion-defined form task compared to typically developing children (van der Zee et al., 2019). Additionally, Weinstein et al. (2012) found that global motion processing (activating higher cortical visual association areas e.g., V3, V5) was more severely impaired compared to local motion processing (activating mainly primary visual cortex V1) in children aged 5-16 years with CVI (11 out of 19 had periventricular white matter lesions due to prematurity). Furthermore, global motion perception has been found to be more variable, slower developing, and more susceptible to disruption (Braddick & Atkinson, 2011). While in the present study, average RTs to global motion stimuli were not significantly different from typically developing children, the raw milliseconds demonstrated that children with CVI took on average 100ms longer to react to global motion compared to local motion stimuli, which could indicate impaired global motion processing too.

Results seem to indicate that for specific risk groups, different eye tracking stimuli and orienting responses to them may aid in differential diagnosis. For instance, for CVI, speed of orienting responses to form and local motion stimuli were impaired, whereas for strabismus, lower fixational accuracy (GFA) to cartoon stimuli was coupled with slower responses to both local motion and global motion, while for nystagmus this coupling occurred only with slower responses to local motion. The discriminative ability of the different eye tracking stimuli for the detection of CVI, by means of, e.g., ROC analyses should be studied further.

Visual orienting and daily life behaviour

We found a clear relation between VOF and daily life impairments as indicated by caregivers. Children with impairments in object and face processing or increased visual (dis)interest in general oriented slower to all visual stimuli, to a similar degree. These results are in line with the experts' survey responses as they mentioned three items of the FCVIQ that were a part of factor 1 (object and face processing impairment) and four items that were a part of factor 2 (visual (dis)interest). While the eye tracking paradigm does not require recognition per se, it provides general measures of the ability to attend to visual stimuli. Likewise, the factor object and face processing in children is thought to relate to impaired global selective attention and the difficulty of overseeing a visual 'whole' such as a face or a crowded environment. Moreover, as reported in a study by Schraauwers et al. (2020), children with CVI showed difficulties in handling complex situations which may lead to a sensory overload resulting in withdrawal, which could explain the relation between visual (dis)interest and impaired orienting behaviour. Children who showed a general reduction in attention and interest in exploring their environment (on FCVIQ questionnaire items targeting more dorsal stream functions such as visual (spatial) attention and processing) showed slower orienting reactions to several visual stimuli, i.e., cartoon, form, contrast, and colour. In particular, abnormal reactions to form and colour stimuli were found in children whose parents indicated that they showed impairment in cluttered environments or when requiring simultaneous perception (e.g., 'Does not find his/her toy when he/she drops it' (belongs to factor 3 clutter and distance viewing impairments); 'More toys perturb visual attention'). Both form and colour stimuli require the child to separate the object (a square and the number 17, respectively) from its surrounding crowded background to identify it, possibly in a similar manner as requiring a child to process a crowded or cluttered scene with numerous toys. Specifically, in Bennett et al.'s (2018; 2019) Virtual Toy Box and Virtual Hallway paradigms, children with CVI demonstrated increased variability in search patterns as was shown by a more scattered/diffuse distribution of the heat map of eye movements, and showed slower reaction times when required to locate a target toy in a toy box with a high number of distractors, or a principle in a hallway with an increasing crowd density. These results demonstrated that with increasing visual complexity, a decrease in visual performance is apparent in CVI. In our study, children showed slower orienting to more cluttered images and this finding related to the expression of their behaviour in daily life in which cluttered environments were at play, confirming the usefulness of studying orienting patterns in CVI. The fact that we did not find similar relations with other patterned backgrounds or noisy visual stimuli such as local motion and global motion, could be due to the dynamic nature of these stimuli, making it easier to grab the child's attention. Specifically, previous research has shown that for children with CVI, movement was able to attract and hold attention, in line with observations of physicians, therapists, and parents indicating that children with CVI have a strong visual preference to moving objects (Cohen-Maitre & Haerich, 2005). Children with CVI also have strong preference for colours (Cohen-Maitre & Haerich, 2005), but it is likely that due to the low saliency of the colour stimulus in the present study, this stimulus was too weak in attracting attention, making it difficult to notice altogether, resulting in the delayed orienting response. To conclude, children who had FCVIQ items and factors that related to slower VOF ticked by parents, expressed a more global limited attention in daily life tasks (e.g., 'Does he not want to look at things or is he not able to?'; 'Has no interest for simple pictures'). When children presented themselves with limited attention in daily life this could be due to their delayed visual orienting and shortened gaze behaviour rather than a general inattention, being incapable, or unmotivated in tasks requiring vision (Ortibus et al., 2019).

Visual orienting and VP tests

With regard to the VP dimensions, according to the expert panel VOF were related to the visual spatial perception dimension. This was confirmed by the data where we found that children with a better visual spatial perception score oriented faster to the eye tracking paradigm (local motion and form stimuli). The visual spatial perception dimension is calculated based on 17 subtests of which certain subtests require the child to segregate a form from the background, detect, and recognize it (e.g., visual figure-ground or visual form constancy from the TVPS) (Ben Itzhak et al., 2021), which could be similar to the task of segregating and detecting the local motion and form stimuli. Previous research by Bauer et al. (2014) showed that two young adults with CVI demonstrated difficulties in visually guided attention and visual spatial processing, and found a reduction in frontal-occipital fasciculus and the superior and inferior longitudinal fasciculi, which play a crucial role in visual guided attention and eye movement control. Bennett et al.'s (2019) Virtual Hallway paradigm showed that a child with CVI had lower occipital activation in the intraparietal sulcus (IPS) compared to a control participant. The IPS has been implicated in perceptual-motor coordination (e.g., directing eye movements), visual attention, and visual spatial processing (Andersen, 1989; Colby & Goldberg, 1999; Culham & Kanwisher, 2001). This could support our findings that children with CVI can show simultaneously impaired visual spatial perception and visual orienting behaviour. Furthermore, experts indicated that the figure-ground perception VP dimension was related to the eye tracking paradigm but surprisingly this was not found. Due to the retrospective nature of the VP data, children in our sample had incomplete VP profile data which may have influenced the results. The VP subtests targeting figure-ground perception are more complex and target numerous dimensions (e.g., abstract versus figural stimuli) requiring an interplay between recognition and active discrimination (e.g., figures with overlapping noise, overlapping line drawings, hidden figures), whereas the eye tracking paradigm does not. Finally, experts also indicated that the motion perception dimension was highly related to the eye tracking paradigm (to global motion and local motion), as both stimuli are dynamic and similar to the motion perception tasks that comprise the motion perception dimension. Unfortunately, this strongly expected relation, could not be statistically tested as only four children had scores on that dimension.

In relation to the CVIT 3-6, children who scored better on the object and scene recognition subscale oriented faster to cartoon stimuli. For object recognition this finding is in line with the expert panel's expectations. The cartoon stimuli shown in the eye tracking paradigm are images of Dick Bruna depicting faces of animals and cartoon-like ‘people’, and in the CVIT 3-6 object recognition subtest children are required to recognize less cartoon-like everyday objects. This could offer support that orienting to an object is important for recognizing it, but nevertheless these two tasks are different, as for the eye tracking paradigm children only need to orient, while for the CVIT 3-6 children have to orient and recognize (name the object). Although we expected to find a positive relation between the CVIT 3-6 global motion detection subtest and global motion stimuli, this was not found. Common fate, or the grouping of elements that move in the same way, is necessary for detecting coherent motion in the moving dots (Wagemans et al., 2012) which is present both in the global motion detection CVIT 3-6 subtest as well as the global motion stimulus in the eye tracking paradigm. However, the nature of the tasks may be too different, the CVIT 3-6 subtest requires both detection and identification of the direction of moving dots, whereas the ET paradigm only requires detection of the origin of the movement of the dots and integrating the dots into an expansion.

Strengths and limitations

One limitation of the study was that some data were missing, as the VP dimensions were calculated from retrospective data. Therefore, future studies should strive for complete and standardized measurements inclusive of VP testing of different dimensions at the same moment as VOF measurement. Nevertheless, this exploratory study demonstrated that the wide variety of collected results is beneficial in profiling both VOF and higher-order perception of children with (suspected) CVI.

6. Conclusion

The present study showed the added value in including an eye tracking paradigm that measures VOF in the clinic. If basic processing is not intact this could lead to greater deficits in the higher-order stages of vision as shown by the present study’s found associations. There is potential to use the eye tracking VOF paradigm in the assessment of CVI, as it adds information complementary to mid- and higher-order perception, but further research is needed to study the specificity and sensitivity with and without eye tracking on the accuracy of a CVI diagnosis. Certainly in conditions with a large heterogeneity in vision and perceptual functions such as autism spectrum disorder (Chokron et al., 2020) and cerebral palsy (Philip et al., 2020), the diagnostic procedure could benefit from multiple assessments at differing levels of the visual hierarchy. Finally, this study may provide a shared ‘vocabulary’ between parents and clinicians to discuss the visual challenges that a child experiences in daily life, and researchers can train clinicians to approach the child with CVI from a more holistic perspective and communicate on the same ‘functional’ level with parents so that the child optimally benefits from multidisciplinary care.

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Tables and Figures

Appendix A

Comparison of eye tracking results between children with cerebral visual impairment and children without cerebral visual impairment.

Stimulus [N CVI; N No CVI]	ET outcome parameters	Children with CVI Median (IQR)	Children without CVI Median (IQR)	Mann-Whitney U test	P-value	Effect size *(r)*
Cartoon [33; 10]	#stimuli seen	11 (9 to 12)	10 (8 to 12)	160	0.559	0.08
	#RTs	9 (5 to 11)	7 (5 to 12)	153	0.437	0.11
	RTF	-3.18 (-6.88 to -2.17)	-2.47 (-7.08 to -1.94)	141	0.490	0.10
	FD	-0.84 (-2.31 to 0.37)	0.64 (-1.59 to 1.71)	110	0.114	0.24
	GFA	-4.61 (-5.91 to -3.43)	-3.02 (-5.02 to -1.95)	110	0.117	0.23
Contrast [30; 10][a]	#stimuli seen	4 (2.5 to 4)	4 (2 to 4)	180	0.976	0.00
	#RTs	3 (2 to 4)	2 (2 to 3)	147	0.334	0.14
	RTF	-2.72 (-5.71 to -1.69)	-1.83 (-3.80 to -0.59)	98	0.104	0.25
Form [26; 9]	#stimuli seen	3 (2 to 4)	2 (1 to 3)	179	0.944	0.01
	#RTs	2 (1 to 4)	2 (1 to 3)	178	0.923	0.01
	RTF	-3.16 (-7.13 to -0.94)	-0.50 (-1.63 to 0.02)	404	0.016*	0.40
Local motion [27; 9]	#stimuli seen	3 (1 to 4)	3 (1 to 4)	169	0.737	0.05
	#RTs	2 (1 to 3)	2 (1 to 4)	161	0.580	0.18
	RTF	-3.28 (-6.64 to -1.68)	-0.84 (-4.67 to 0.17)	65	0.039*	0.34

Global motion [25; 8]	#stimuli seen	3 (2 to 4)	2 (1 to 4)	135	0.199	0.19
	#RTs	2 (0.5 to 3)	1 (0 to 3)	172	0.802	0.03
	RTF	-0.05 (-1.81 to 0.71)	-0.37 (-2.01 to 0.10)	92	0.737	0.05
Colour [11; 6]	#stimuli seen	0 (0 to 2.5)	1 (0 to 2)	176	0.874	0.02
	#RTs	0 (0 to 1)	1 (0 to 2)	155	0.411	0.12
	RTF	-0.66 (-2.32 to -0.09)	-0.25 (-2.53 to 0.089)	90	0.366	0.21

Notes. #stimuli seen and #RTs include all 44 children, while all other presented z-score results are calculated only for children who had reliable data. [a]One extreme outlier participant was excluded for contrast stimuli as their RT was ~300ms slower than the other participants. Effect size was calculated using $r = \frac{Z}{\sqrt{N}}$ (Fritz et al., 2016). ET: Eye tracking. RTs: Individual reaction times. RTF: Average reaction time to fixation. FD: Fixation duration. GFA: Gaze fixation area. CVI: Cerebral visual impairment. IQR: Interquartile range. Significant *p*-values are marked as $^{*}< 0.05$, $^{**}< 0.01$, $^{***}< 0.001$.

Appendix B

Comparison of eye tracking results between children with strabismus and children without strabismus.

Stimulus [N strabismus; N No strabismus]	ET outcome parameters	Children with strabismus Median (IQR)	Children without strabismus Median (IQR)	Mann-Whitney U test	P-value	Effect size (r)
Cartoon [29; 14]	#stimuli seen	10 (8.5 to 12)	11 (9 to 12)	187	0.446	0.11
	#RTs	7 (5 to 10.5)	9 (6 to 10)	195	0.636	0.07
	RTF	-3.87 (-8.09 to -2.21)	-2.62 (-4.55 to -1.78)	140	0.103	0.24
	FD	-1.39 (-2.13 to 0.29)	0.37 (-2.19 to 1.71)	149	0.162	0.21
	GFA	-5.30 (-6.72 to -3.77)	-2.86 (-4.03 to -1.83)	53	<0.001***	0.59
Contrast [27; 13]	#stimuli seen	3 (2 to 4)	4 (3 to 4)	169	0.184	0.20
	#RTs	2 (2 to 3.5)	3 (2 to 4)	181	0.357	0.13
	RTF	-2.19 (-5.39 to -1.66)	-2.18 (-4.63 to -0.90)	152	0.497	0.10
Form [22; 13]	#stimuli seen	3 (1.5 to 4)	4 (3 to 4)	149	0.079	0.26
	#RTs	2 (0.5 to 3)	3 (1 to 4)	164	0.179	0.20
	RTF	-2.58 (-6.03 to -0.47)	-1.52 (-5.15 to -0.39)	123	0.495	0.11

Local motion [23; 13]	#stimuli seen	2 (1 to 3)	4 (3 to 4)	127	0.021*	0.34
	#RTs	2 (1 to 3)	4 (2 to 4)	103	0.004**	0.43
	RTF	-5.04 (-6.64 to -2.58)	-1.68 (-3.14 to -0.34)	84	0.031*	0.35
Global motion [22; 11]	#stimuli seen	2 (1.5 to 3)	3 (1 to 4)	176	0.296	0.15
	#RTs	2 (0.5 to 2)	2 (0 to 3)	182	0.373	0.13
	RTF	-0.87 (-2.54 to 0.23)	0.32 (-0.04 to 1.21)	62	0.024*	0.39
Colour [8; 9]	#stimuli seen	0 (0 to 2)	1 (0 to 3)	156	0.084	0.21
	#RTs	0 (0 to 1)	1 (0 to 2)	169	0.184	0.26
	RTF	-0.42 (-1.91 to 0.14)	-1.13 (-2.76 to 0.69)	79	0.847	0.04

Notes. #stimuli seen and #RTs include all 44 children, while all other presented z-score results are calculated only for children who had reliable data. [a]One extreme outlier participant was excluded for contrast stimuli as their RT was ~300ms slower than the other participants. Effect size was calculated using $r = \frac{Z}{\sqrt{N}}$ (Fritz et al., 2016). ET: Eye tracking. RTs: Individual reaction times. RTF: Average reaction time to fixation. FD: Fixation duration. GFA: Gaze fixation area. IQR: Interquartile range. Significant *p*-values are marked as $^{*}< 0.05$, $^{**}< 0.01$, $^{***}< 0.001$.

Appendix C

Comparison of eye tracking results between children with nystagmus and children without nystagmus.

Stimulus [N nystagmus; N No nystagmus]	ET outcome parameters	Children with nystagmus Median (IQR)	Children without nystagmus Median (IQR)	Mann-Whitney U test	P-value	Effect size (r)
Cartoon [14; 29]	#stimuli seen	10 (8.75 to 12)	11 (8.75 to 12)	203	0.856	0.02
	#RTs	8 (5 to 11)	9 (5.75 to 10)	202	0.839	0.03
	RTF	-4.76 (-8.13 to -2.19)	-2.66 (-6.57 to -2.12)	146	0.140	0.22
	FD	-1.72 (-2.65 to 0.18)	-0.43 (-2.00 to 1.21)	146	0.140	0.22
	GFA	-5.47 (-7.28 to -4.22)	-3.96 (-5.28 to -2.37)	101	0.008**	0.40
Contrast [13; 27]	#stimuli seen	3.5 (2.75 to 4)	4 (2 to 4)	206	0.911	0.01
	#RTs	3 (2 to 3)	3 (2 to 4)	196	0.715	0.05
	RTF	-2.19 (-6.38 to -1.70)	-2.18 (-4.68 to -1.25)	146	0.394	0.13
Form [9; 26]	#stimuli seen	3.5 (1 to 4)	3 (2 to 4)	195	0.703	0.05
	#RTs	2 (0 to 4)	2 (1 to 3.25)	198	0.757	0.04
	RTF	-1.51 (-9.44 to -0.05)	-1.94 (-4.73 to -0.49)	116	0.970	0.00

Local motion [11; 25]	#stimuli seen	3 (1 to 3.25)	3 (1 to 4)	178	0.412	0.12
	#RTs	2 (0.75 to 2.25)	2.5 (1 to 4)	176	0.382	0.13
	RTF	-6.64 (-11.99 to -3.28)	-2.63 (-4.74 to -0.70)	53	0.004**	0.48
Global motion [9; 24]	#stimuli seen	3 (1.75 to 4)	2 (1 to 4)	197	0.736	0.05
	#RTs	1.5 (0 to 3)	2 (1 to 3)	180	0.445	0.11
	RTF	-1.36 (-2.14 to 0.19)	-0.01 (-1.58 to 0.77)	84	0.332	0.16
Colour [5; 12]	#stimuli seen	0 (0 to 2)	1 (0 to 2.25)	177	0.383	0.13
	#RTs	0 (0 to 1)	0 (0 to 2)	197	0.708	0.05
	RTF	-0.71 (-5.27 to -0.63)	-0.16 (-2.32 to 0.52)	19	0.246	0.28

Notes. #stimuli seen and #RTs include all 44 children, while all other presented z-score results are calculated only for children who had reliable data. [a]One extreme outlier participant was excluded for contrast stimuli as their RT was ~300ms slower than the other participants. Effect size was calculated using $r = \frac{Z}{\sqrt{N}}$ (Fritz et al., 2016). ET: Eye tracking. RTs: Individual reaction times. RTF: Average reaction time to fixation. FD: Fixation duration. GFA: Gaze fixation area. IQR: Interquartile range. Significant *p*-values are marked as $^{*}< 0.05$, $^{**}< 0.01$, $^{***}< 0.001$.

Appendix D

Survey items rated by a high percentage (≥52%) of experts as related to the eye tracking paradigm.

Survey subpart	Item (item number; factor[a])	Percentage of total experts[b]	Specific eye tracking stimuli in experts who find an item associated[c]
FCVIQ	Cannot focus on persons or objects (#2; F1)	76%	Cartoon (100%), contrast (81%), colour (63%)
	Often stares at light sources e.g., lights or open windows (#4; NA)	62%	Cartoon (70%)
	Falls frequently over clearly visible objects (#5; F4)	52%	Cartoon (82%), contrast (82%), form (73%), local motion (64%)
	Does not find his/her toy when he/she drops it (#6; F3)	67%	Form (100%), colour (71%), contrast (64%), cartoon (57%)
	Pays attention only to objects in the centre of his/her visual field (#8; F1)	81%	Cartoon (76%), global motion (76%), local motion (76%), contrast (71%), colour (71%)
	Cannot keep looking at objects or persons (#9; NA)	81%	Cartoon (94%), local motion (65%), colour (65%), global motion (59%), form

		(53%)
Needs more time than you would expect to look at an object (#12; F2)	86%	Cartoon (78%), contrast (78%), colour (72%), form (67%), global motion (61%), local motion (61%)
Does not look spontaneously at an object, does not explore the room spontaneously (#13; NA)	67%	Cartoon (93%), contrast (93%), form (86%), colour (86%), local motion (71%), global motion (57%)
More toys perturb visual attention (#15; NA)	52%	Form (73%), global motion (64%), colour (64%), local motion (55%)
Does not see level differences e.g., stairs (#27; NA)	52%	Cartoon (91%), global motion (64%), form (55%)
Has no interest for simple pictures (#30; F2)	76%	Cartoon (81%), contrast (75%)
Has no interest for complex pictures (#31; F2, F5)	52%	Form (82%), local motion (82%), colour (82%), global motion (73%), cartoon (73%)

	Cannot find his/her teddy bear (or equal) amongst other cuddly animals (#33; F1)	52%	Form (91%), colour (73%)
	A moving object/person attracts more attention than a stationary one (#38; F2)	100%	Local motion (86%), global motion (76%), cartoon (71%)
	I often wonder: Does he not want to look at things or is he not able to? (#46; NA)	81%	Cartoon (88%), contrast (88%), form (88%), global motion (82%), local motion (82%), colour (82%)
VP dimensions	Motion perception	100%	Global motion (95%), local motion (95%)
	Figure-ground perception	90%	Contrast (89%), local motion (74%), colour (74%), form (68%), cartoon (53%)
	Visual spatial perception	62%	Global motion (85%), local motion (77%), form (77%)
CVIT 3-6	Global motion detection	95%	Global motion (95%), local motion (55%)
	Kinematic object segmentation	90%	Local motion (89%), global motion (74%)

Object recognition	76%	Cartoon (81%)

Notes. [a]Refers to the factor to which the FCVIQ item belongs, F1: Object and face processing impairments, F2: Visual (dis)interest, F3: Clutter and distance viewing impairments, F4: Moving in space impairments, F5: Anxiety-related behaviours, and NA: Not applicable, as these items did not fall into any factor in the original factor analysis. [b]Percentage of total experts refers to the percentage of experts out of 21 who think an item is related to the eye tracking paradigm in general. [c]The percentage of experts who find an item associated refer to the number of experts who said 'yes' in level I and not the total 21 experts who filled out the survey. FCVIQ: Flemish cerebral visual impairment questionnaire. VP: Visuoperceptual. CVIT 3-6: Children's visual impairment test for 3- to 6-year olds.