Validity and reliability of CVI Range assessment for Clinical Research (CVI Range-CR): a longitudinal cohort study

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ABSTRACT
Introduction  Cortical visual impairment (CVI) is the leading cause of paediatric visual impairment in developed countries. Children with CVI exhibit visual behaviours that differ from those with ocular causes of visual impairment. Currently, there is no standard method of assessing these visual characteristics. We have developed a modified version of the CVI Range, a functional vision assessment, suitable for use in clinical research (CVI Range–Clinical Research (CVI Range-CR)). The purpose of this study is to assess the reliability and validity of this instrument in children with CVI.

Methods and analysis  This is a prospective cohort study of 45 children with CVI. A neuro-ophthalmologist will grade visual acuity using the six-level Visual Behaviour Scale (VBS). A neuropsychologist will administer the CVI Range-CR, which will be recorded. The neuropsychologist and two external graders will review and score recorded assessments. These procedures will be performed at baseline and 12 months. We will calculate the intraclass correlation coefficient to assess inter-rater reliability at baseline and follow-up. Additionally, we will correlate CVI Range-CR scores to VBS scores.

INTRODUCTION  Cortical visual impairment (CVI), also known as cerebral or brain-based visual impairment, is the leading cause of paediatric visual impairment in high-income countries and is increasing in low-income nations, accounting for an estimated 20%–48% of cases.2–4 CVI is diagnosed in children with visual deficits due to damage to postgeniculate visual pathways in the brain, rather than the eye.5 Common causes include hypoxic-ischaemic encephalopathy, prematurity with periventricular leukomalacia, hydrocephalus, trauma, seizures, structural brain abnormalities and genetic syndromes.1 6 Although children with CVI may have ocular comorbidities, the visual dysfunction is worse than expected for the degree of ocular pathology. Traditionally, decreased visual acuity and visual field deficits are required for diagnosis of CVI, but some practitioners diagnose CVI in patients with higher-level visual processing abnormalities only.

Because of involvement of central visual pathways, children with CVI frequently exhibit characteristic visual behaviours and deficits that differ from children with ocular causes of visual impairment.2,9 These behaviours were first described by Jan et al in 1987 and include variable visual function (dependence on environmental factors, fatigue, illness, etc), staring at lights, and decoupled visual and motor functions (looking away while reaching), in addition to decreased visual acuity and visual field deficits.8 Colour vision may be relatively preserved.9 Later investigators have described other visual deficits, such as difficulties with recognising faces (prosopagnosia) or objects, depth perception, multiple objects (simultanagnosia), motion perception and visuospatial orientation.7 10 Because of the myriad of abnormalities of visual behaviours and deficits displayed by children with CVI, no single test has been universally accepted to characterise CVI severity.11 However, a
method of quantifying visual function and functional vision in CVI is necessary for both clinical practice and research. In clinical practice, such a measure would enable longitudinal assessments of a child’s progress and could potentially inform vision services and accommodations. In clinical research, a measure of CVI severity is needed to demonstrate the efficacy of proposed interventions in a controlled trial. Currently, there is no standard treatment for children with CVI.1 Vision services are region-dependent, and children with CVI often receive generic accommodations designed for patients with ocular causes of visual impairment.

Psychophysical measures of visual function in CVI include preferential looking tests and sweep visual evoked potentials (VEPs). Due to neurological deficits and developmental delays, many children with CVI are unable to cooperate with optotype acuity testing.11 In these children, visual acuity may be estimated using preferential looking methods, such as Teller acuity.12 Electrophysiology, particularly sweep VEP, may also estimate visual acuity in non-verbal children with CVI.13 However, these measures do not capture the breadth of deficits in visual functioning exhibited by children with CVI.

More comprehensive measures of visual function in CVI include neuropsychological tests and eye tracking. Neuropsychological tests of visual perception, such as the Children’s Visual Impairment Test (CVIT) 3–6, are rigorously developed and tested but may be applicable to a limited subset of children with CVI who are able to understand and respond to questions (CVIT 3–6 is indicated for children between developmental ages of 3 years and 6 years).14 15 Eye tracking shows promise as an objective method of quantifying multiple aspects of visual function in children with CVI, but research is still ongoing to validate this technique.16 17

The CVI Range is a behavioural assessment of functional vision (the ability to interpret and react to visual information) administered by certified examiners, typically teachers for the visually impaired.18 Through a combination of observation, parent interview and direct assessment, the examiner grades the child on 10 characteristics of CVI (box 1), which function as subscales or domains of the total CVI Range score. There are two methods of calculating the CVI Range score: across-CVI and within-CVI Characteristics. CVI Range scores range from 0 to 10, with 10 indicating the best functional vision. The scores are further divided into three phases (phase I: 0–3, phase II: 4–7 and phase III: 8–10; figure 1). The reliability of the CVI Range was evaluated in a thesis by Newcomb.19 Of 104 children included in the study, 27 underwent CVI Range testing by two different examiners to assess inter-rater reliability, and 20 underwent CVI Range testing twice by the same examiner (within 14 days) to assess test–retest reliability. All 104 children were included in the analysis of internal consistency. Newcomb reported excellent test–retest reliability (Pearson’s r=0.99) and inter-rater reliability (r=0.98) of the within-CVI characteristics method of scoring the CVI Range. Internal consistency was also excellent (Cronbach’s α=0.962). There was excellent agreement between the across-CVI and within-CVI characteristics methods of scoring (κ=0.88). However, this study was judged to be poor quality by the Consensus-based Standards for the Selection of Health Measurement Instruments criteria,20 21 likely due to lack of masking and standardisation of test administration, as the children were variably evaluated at home or school.

The purpose of this study is to evaluate the reliability and validity of the CVI Range in a clinical research environment (CVI Range–Clinical Research (CVI Range–CR)). This modified version of the CVI Range is a semistructured assessment that can be administered in a controlled setting using a defined set of materials.

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**Box 1** Ten characteristics evaluated on the CVI Range

- Colour preference.
- Need for movement.
- Visual latency.
- Visual field preferences.
- Difficulties with visual complexity.
- Need for light.
- Difficulty with distance viewing.
- Atypical visual reflexes.
- Difficulty with visual novelty.
- Absence of visually guided reach.

Figure 1 Scoring line for CVI Range–Clinical Research. Scores range from 0 to 10, with increasing numbers indicating more typical functional vision. The scores are divided into three phases, shown below the line.
The CVI Range-CR is designed to enable remote grading by video recordings and therefore may be applicable to multicentre clinical trials requiring a centralised remote grader.

METHODS AND ANALYSIS

Patient population and recruitment

In this prospective cohort study, we will recruit children diagnosed with CVI by an ophthalmologist based on the following criteria: reduced visual acuity or visual field defect with normal eye exam or visual acuity worse than expected based on the degree of ocular pathology (such as optic atrophy). Children will be required to have a known risk factor for damage to the postgeniculate visual pathway (eg, hypoxic–ischaemic encephalopathy). Children with pure CVI (ie, no intraocular comorbidities) must have normal pupillary responses, normal oculaructions and normal fundus examination for diagnosis.

Children between the ages of 12 months and 8 years will be included. We will exclude patients with ocular motor apraxia, ophthalmoplegia or any eye condition that may preclude accurate assessment of functional vision based on visual behaviour. Additionally, we will exclude families who are not fluent in English because the interview will be conducted in English.

Patients will be recruited from the paediatric neuroophthalmology clinics at our hospital. We recognise that there may be a selection bias towards children with more severe disease at our tertiary care clinic. Therefore, we will distribute flyers to other providers of children with CVI in our state. The flyers provide information for families to contact study personnel if they are interested in participating in the study. Diagnosis of CVI in participants referred from outside our clinics will be confirmed by medical record review and repeat ophthalmological assessment.

Study procedures

All participants will be evaluated at baseline and 12 months. In the intervening time, they will continue standard of care vision services through the regional centre or local school district.

See figure 2 for the flowchart of study procedures at baseline and 12 months.

Ophthalmological examination and assessment of visual behaviour

All patients will undergo complete ophthalmological examination to ensure they meet the diagnostic criteria for CVI, as detailed previously. Additionally, a paediatric neuro-ophthalmologist will complete the Visual Behaviour Scale (VBS), a six-level scale of visual behaviour specific for CVI that has been used in prior publications (online supplemental table 1). The ophthalmological examination and VBS will be repeated at 12 months.

Questionnaires

At each visit, the parent or legal guardian will complete two questionnaires. At baseline, the intake form and Vineland Adaptive Behaviour Scale, Third Edition (VABS-III) parent/caregiver questionnaire will be administered. At 12 months, the parent will complete the 12-month questionnaire and repeat the VABS-III.

The intake questionnaire collects data on baseline demographics and medical history. The 12-month questionnaire requests families to report on the type and frequency of vision interventions that the child has received since the baseline visit, in addition to updating demographics and medical history.

Figure 2 Flowchart of study procedures at baseline and 12 months.
The VABS-III is a validated measure of adaptive behaviour. Three domains are assessed: communication, daily living skills and socialisation, in addition to an optional motor function domain that will be included in this study. An adaptive behaviour composite score is also provided. The scores are reported as standard scores (mean 100, SD 15) and percentiles.

**CVI Range-CR**

The CVI Range was developed by Dr Christine Roman-Lantzy as a tool for understanding a child’s functional vision and applying targeted interventions. For the purpose of this study, we created the CVI Range-CR, a semistructured assessment with a defined set of materials and activities. We designed the CVI Range-CR to be replicable at multiple institutions with different examiners to facilitate its use in future multicentre clinical research studies. Moreover, the CVI Range-CR was developed to enable remote grading of assessments by examiners watching video recordings.

The CVI Range-CR was refined over a period of 1 year; a research-trained neuropsychologist conducted CVI Range assessments on 11 children with CVI, while the feasibility of recording and scoring each activity by video was continually evaluated by the research team. The final version of the CVI Range-CR that will be used in this study is described further.

**Administration**

The CVI Range assessment includes three parts: interview, observation, and direct assessment. The observation period occurs in a child’s natural environment (home or school). Due to the need for standardisation, the observation period is omitted in the CVI Range-CR. However, examiners will observe a child’s visual behaviour and interaction with pictures and objects placed in a standard format in the examination room (figure 3) during the interview and direct assessment.

**Interview**

The in-person examiner will conduct the interview while seated with the parent and child around a table. The questions will be directed toward the parent, but the child may participate, depending on communication ability. A list of 24 standard questions (online supplemental table 2) will be asked of the parent, with follow-up questions if the parent wishes to elaborate on any of the responses.

**Direct assessment**

The in-person examiner will lead the child through a series of activities designed to assess functional vision. The materials required for the activities are listed in box 2. In general, the examiner presents visual targets to the child under a variety of conditions (eg, different distances, ambient lighting, isolated or in an array) and notes whether there is a visual response (looking toward the object). Whenever a visual response is generated, the examiner also observes the time to response (visual latency). The order of the activities may be adjusted based on the child’s level of functioning and interest in the objects presented.

**Description of activities**

1. **Reflexes.** The examiner will assess blink to threat and blink to touch. Visual threat is evaluated by quickly moving one hand towards the child’s face while spreading the fingers open. Blink to touch is assessed by quickly touching the child on the forehead with an index finger between the eyebrows, three times in a row. Reflexive response to visual threat is considered...
Box 2  Materials used for direct assessment in the CVI Range–Clinical Research

- Flashlight with red light.
- Brightly coloured strings of beads of various colours (‘Mardi gras’ beads).
- Translucent neon Slinky toys.
- Clear plastic coloured blocks.
- A dozen plastic animals (approximately 1-inch height).
- Two stuffed animals (10-inch height): red Elmo and yellow Big Bird.
- Musical toy (eg, Fisher-Price BeatBo).
- Black tray.
- Colourful patterned fabric.
- Picture book (see description in text).
- Light box.
- CVI Complexity Sequence Cards (American Printing House, Louisville, Kentucky, USA).
- iPad with apps (Tap-N-See Now, CVIHumanFace).
- Handheld mirror (8.5x11.0 inches).
- Dimmable floor lamp.

abnormal if there is a diminished blink response to threat while blink to touch is preserved. Reflexes are performed throughout the assessment at least three times.

2. Visual field preference. Rather than assessing formal perimetry, the CVI Range evaluates the binocular response to a projected light source from the right, left, upper and lower visual fields. A red flashlight is directed towards the child’s face from various angles. A positive response is recorded when the child looks in the direction of the red light. After assessing the response peripherally, the examiner sweeps the red light horizontally across the face over both eyes to confirm that the child generates a response to the red light (typically blink or grimace). A reaction to the red light is required to grade peripheral responses.

3. Response to overhead light. Throughout the interview and assessment, the examiner notes whether the child stares at the overhead lights in the room.

4. Response to moving and stationary objects. The examiner presents a string of brightly coloured beads or a coloured Slinky toy in the child’s preferred field of vision. The object is presented both with and without movement (shaking beads or bouncing Slinky).

5. Response to objects in light and dark. A clear plastic coloured toy block is presented to the child with the room lights on. If there is no visual response, the room lights are turned off and a floor lamp is turned on to the dimmest setting. The block is illuminated with a light box or flashlight, and the child is observed for a visual response.

6. Response to electronic images. Various apps are available that display moving objects on a plain background that the child is asked to look at and touch. For this study, we will use the Tap-N-See Now app on a 10-inch iPad (Apple, Cupertino, California, USA). If the examiner judges the child’s functional vision to be more advanced, we will use the CVIHumanFace app.

7. Response to mirror. A mirror (8.5x11.0 inches) is held in front of the child’s face and moved back and forth horizontally. The examiner notes whether the child fixates and follows his or her own reflection in the mirror.

8. Visually guided reach. The examiner chooses a toy seen by the child in activity 4 or 5. If the child has sufficient motor control of arms and hands, the examiner encourages the child to reach for the toy (‘Can you get it?’).

9. Distance of object fixated. The examiner selects a stuffed animal based on preference relayed by the parent. The toy is held in front of the examiner’s body (a plain dark-coloured shirt is worn to provide a simple background) while the examiner stands across the room from the child. The parent is advised not to prompt the child to look at the toy. The examiner slowly walks closer to the child until the child looks at the toy. The distance at which a visual response is generated is recorded.

10. Auditory distraction. The examiner presents a large toy with a switch for music or noise (BeatBo (Fisher-Price, El Segundo, California, USA) will be used in this study). If the child looks at the toy under silent conditions, the music or noise will then be turned on. The child is observed for a visual response in the presence of auditory distraction.

11. Complexity. A variety of activities may be used to assess complexity, based on the child’s level of functional vision. The activities are listed in order of least to greatest functional vision required. The examiner may skip the final two activities if the child’s functional vision is not sufficient to participate.

a. Array. A single small toy (for this study, we will use plastic animals) is placed on a black tray. If the child looks at it, the examiner removes it then places an array of three similar objects, including the original object, on the tray. The child is asked to find the original object. If this is accomplished, progressively more items are added to the array until the child no longer looks at the original object. The process is repeated with the array placed on a complex, patterned fabric background.

b. Book. A picture book with a recurring character depicted in both simple and visually complex settings is chosen. For this study, we will use Grumpy Monkey (Lang, Suzanne. New York, Random House, 2018). The child is asked to look at the recurring character (‘Find the monkey. Where’s the monkey?’)

c. Complexity cards (phases II and III). The CVI Complexity Sequence Cards (American Printing House, Louisville, Kentucky) are a series of illustrations beginning with a single object (eg, toothbrush) on a plain white background. Over the sequence of eight cards, more objects are progressively added to increase the complexity of the image. The child
is presented with the cards in order, from simplest to most complex, and asked to find the original object. The child may respond by pointing to or looking at the item.

d. Scavenger hunt (phases II and III). Five to 10 objects from box 1 are placed in the hallway outside the assessment room. The child is guided down the hallway (either walking or in his or her own wheelchair) while the examiner observes whether the child looks at any of the target objects without prompting.

Recording

Video recording will be accomplished by two iPads (Apple) positioned at 90° angles from the participant. A research assistant will adjust the iPads as needed during the assessment to accommodate various activities. The two videos will be synced in iMovie (Apple), with the image showing the child in profile displayed as an inset of the larger video focused directly on the child’s face. Videos will be manually edited and zoomed in on salient portions of the examination, such as assessment of reflexes. Editing will also be required to prevent release of protected health information. The videos will be uploaded to a secure data-sharing website for review.

Scoring

The neuropsychologist administering the CVI Range assessments will score all evaluations. Two external graders, both teachers for the visually impaired certified in CVI Range administration, will also provide scores based on review of videos. At baseline, only one of the two external graders will score each assessment (assignments will be alternated). At 12 months, both external graders will score all assessments. This allows for one masked grader at 12 months for each participant.

The scoring for the CVI Range-CR is identical to the original CVI Range, with the exception that some characteristics may be left blank if the graders are unable to determine the response on the video recording. Blank responses will be removed from consideration for the final CVI Range scores. Graders will complete scoring sheets for the across-CVI characteristics and within-CVI characteristics methods of scoring (online supplemental worksheets). In the across-CVI characteristics method, visual functioning is assessed across five blocks (1–2, 3–4, 5–6, 7–8, and 9–10) of characteristic behaviours that represent increasing levels of functioning. Starting with block 1–2, the grader indicates whether the behavioural characteristic is resolved (R), currently present (+), partially present (+/−) or not present (−). If all of the characteristics are graded as R or +, then the grader progresses to the next block. Once a characteristic is graded as +/− or −, the grader completes the current block and is not required to grade any subsequent blocks. The score and phase are determined based on the number of characteristics exhibited in each block, as indicated by online supplemental table 1 and figure 1.

In the within-CVI characteristics method, the grader assigns scores for each of 10 functional domains in quarter-point increments. Scores on each domain are summed to produce the second CVI Range score.

For the CVI Range-CR, the scoring sheets will be input into our electronic Research Electronic Data Capture (REDCap) database, hosted at University of Southern California. This REDCap database has been programmed to automatically calculate the CVI Range score and phase for each participant using both scoring methods.

Release of information to families

After each CVI Range assessment, families will be informed of the child’s phase on the CVI Range by verbal and written report.

Statistical analysis

The primary outcome of this study is inter-rater reliability of the CVI Range-CR. We will calculate inter-rater reliability of both scoring methods at baseline and at 12 months. At baseline, scores will be generated by the in-person examiner and one remote grader. At 12 months, both remote graders will score all videos, so there will be three scores per participant at follow-up. We will assess inter-rater reliability using the intraclass correlation coefficient (ICC); the corresponding 95% CI for precision of the point estimate will also be reported. An ICC will be calculated for the across-CVI characteristics score, for the total score derived from the within-CVI characteristics method, and for each of the 10 characteristics rated on the within-CVI characteristics scale (ie, 10 ICC point estimates for 10 domains).

A secondary outcome is the validity of CVI Range-CR scores, as compared with ophthalmological assessment of visual behaviour using the six-level VBS. The scores derived from the CVI Range across-CVI characteristics and within-CVI characteristics methods will be correlated to VBS scores using Spearman’s correlation, the non-parametric equivalent of Pearson’s r correlation appropriate for both ordinal and continuous data. Additionally, bivariate analyses will be performed to assess potential confounding by the subject’s age, VABS-III scores, frequency of vision services and other variables. The association between the CVI Range-CR and the VBS will then be re-evaluated with adjustments for confounding variables using ordinary least squares regression models.

An additional secondary outcome is the longitudinal change in CVI Range-CR scores after 12 months of standard vision services. For both scoring methods, we will compare baseline and 12 months’ CVI Range scores using paired t-tests, or the Wilcoxon signed-rank test if data are not normally distributed. Because there are three graders (in-person examiner, unmasked remote grader who will assess both baseline and 12-month videos, and masked remote grader who will assess only the 12-month video), there will be three analyses:
Sample size
In order to detect an ICC as low as 0.68, with 80% power and 5% probability of α type I error, 36 children with CVI will be required. In order to meet this recruitment goal, we will aim to enrol 45 children with CVI to account for up to 20% attrition.

Patient and public involvement
Although patients were not directly involved in the design of this research study, they will be critical to disseminating the results. Through the Paediatric Cortical Visual Impairment Society, the authors are in close communication with families of children with CVI. These parents plan to advocate for funding of future clinical trials of interventions for CVI, with the CVI Range-CR as an outcome measure if shown to be reliable and valid.

Contributors
MC contributed to the study design, monitored the data collection, edited study recordings, and drafted and revised the manuscript. CR-L developed the original version of the instrument used in this study (CVI Range), provided training during practice sessions, contributed to the final study design and edited the manuscript. SHO’N was responsible for data collection (performing CVI Range-Clinical Research assessments), adjustment of study design and editing of the manuscript. MWR designed the statistical analysis plan and edited the manuscript. MSB conceived the study design and led adjustments to the study protocol (including preparation of the protocol paper).

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Competing interests
CR-L received royalty payments for textbooks associated with the topic of interest. She also received consulting fees from the Miami Lighthouse for the Blind, Perkins School for the Blind and Berwick Area School District. She also received research funding from the National Eye Institute (R01EY023163) and the University of Miami (CIT01422). She also received training and travel grants from the Ingerman Foundation and New York University. She also receives research funding from the Foundation Fighting Blindness and the Optometry and Vision Science of the University of Houston.

Patient and public involvement
Patients and/or the public were involved in the design, conduct, reporting or dissemination plans of this research. Refer to the Methods and analysis section for further details.

Patient consent for publication
Not applicable.

Ethics approval
This study has been approved by the local institutional review board and will adhere to the tenets of the Declaration of Helsinki and the US Health Insurance Portability and Accountability Act of 1996. Informed consent will be obtained from the parent or legal guardian of all participants.

Provenance and peer review
Not commissioned; externally peer reviewed.

Data availability statement
No data are available. No data included in this protocol paper.

Supplemental material
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