Tests of Functional Vision in CVI: Evidence Based Approaches

1:30-3pm

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What Makes a "Good" Assessment?

- Measures what it is supposed to
- Doesn't measures what it says it doesn't
- Repeatable
- Same result regardless of who gives the assessment (consistent)
- Other factors??

COSMIN Standards

COnsensus-based Standards for the selection of health status Measurement INstruments

COSMIN standards

- Internal Consistency – Does the test measure what it is meant to?
- Reliability – Does the test provide stable, consistent results?
  - Over time, between administrators, across items in the test
- Measurement Error – Difference between the measured value and its true value
- Content Validity – How well the test measures the behavior for which it is intended
  - Correspondence between test items and symptoms
- Structural Validity – How well the questionnaire score reflects the construct being measured
- Hypothesis Testing – Test the size and direction of effect in a random sample
- Cross-cultural Validity – Can the test be used in different populations and cultural groups
- Criterion Validity – How well the tool measurements compare to the 'gold standard'
- Responsiveness – The ability of the tool to detect change over time in the measured construct

BMC Med Res Methodol. 2010; 10: 22

Reliability

- "The degree to which the result of a measurement, calculation, or specification can be depended on to be accurate."
- Internal Reliability
  - Consistency of results across items within a test
- External Reliability
  - Extent to which a measure varies from one use to another
  - Test re-test: stability of test over time
  - Inter-rater: consistent results across different independent raters
  - Inter-method reliability: consistent results with other tests/instruments used
- Reliability does not equal validity

How to Evaluate Reliability

- Internal reliability/consistency – Cronbach's alpha
  - Used to determine if the designed test accurately measures the variable of interest
- Reliability (correlation) coefficient – correlation between 2 or more variables
  - 0.9-1.0 – excellent reliability
  - 0.8-0.9 – good reliability
  - 0.7-0.8 – acceptable reliability
  - 0.6-0.7 – questionable reliability
- Test-re-test – correlation between two or more separate occasions
- Inter-rater – correlation between scores from two or more administrators
  - Note: high correlation does not ensure the test is administered correctly, only that the test is being measured the same
- The more items in the test, the larger the sample needed

Validity

- "The extent to which a test accurately measures what it is supposed to measure"
- Content Validity
  - Measures what it was designed to measure
    - E.g. a comprehensive math test would lack content validity if good scores depended mainly on knowledge of English or if it only contained algebra questions
- Face Validity
  - Ability of an instrument to be understandable and relevant for the targeted population
- Criterion-related Validity
  - Useful for predicting a person's performance on an external criterion measure
    - E.g. score on test A predicts scores in test B
- Construct Validity
  - The degree to which a test measures what it claims to be measuring
  - The appropriateness of the inferences made on the basis of observations or measurements
  - Content Validity – The degree to which an assessment is relevant to or representative of the targeted construct it is designed to measure
    - Enables instrument to make meaningful and appropriate inferences/decisions based on the scores
  - Concurrent Validity - Measures how consistent the results are compared to other already validated tests
  - Predictive Validity - The extent to which test predicts score on some criterion measure

How do we Determine Validity

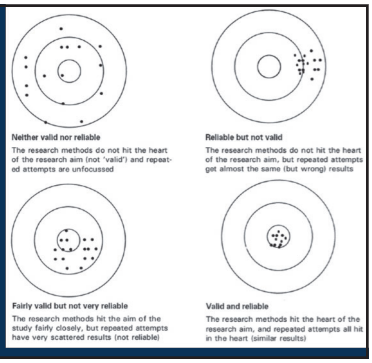
- "The extent to which a test accurately measures what it is supposed to measure"
- Concurrent Validity: Correlation with existing test measuring same construct
- Content Validity: Expert Opinion, Cronbach's alpha
- Predictive Validity: Correlation with predicted outcome
- Need to make sure that you have a large enough sample

Relationship between Validity and Reliability

- If a test is unreliable, it cannot be valid
- For a test to be valid, it must be reliable
- Just because a test is reliable, does not mean it will be valid
- Reliability is a necessary but not sufficient condition for validity
- High alpha does not guarantee construct of interest is being measured or that important concepts are not missing
- High test-retest reliability does not imply that all items are relevant or that important concepts are not missing

Examples:

- Every day for the past year, your scale at home says that you weigh 200 lbs. At the doctor's office, you weigh 150 lbs.
- Is your home scale reliable?
- Is your home scale valid?



Examples:

- You and a colleague are testing a new device to measure temperature. You each take temperatures with the new device and the "gold standard" thermometer.
- You get different values than your colleague and the values you obtain change on the same person between week 1 and week 2
- Does the new test have good external reliability? Internal reliability? Test-retest reliability? Inter-rater reliability?
- Is this new measurement for temperature valid?

Reliability and Validity: What's the Big Deal?

- Validity is important because if the test does not measure what it is intended to, then the results cannot be used to answer that question
  - The results cannot be used to generalize the findings
  - Ensures that results can be used effectively
- Reliability is important because if the results are inconsistent across time or administrators, then changes in the test result cannot be trusted – uncertain if change in outcome due to test or actual change

Sensitivity & Specificity

- Measures of classification accuracy
- Sensitivity: True positive rate
  - Proportion of actual positive that are correctly identified as such
- Specificity: True negative rate
  - Proportion of actual negatives that are correctly identified as such
- Positive Predictive Value
  - Percentage of patients with a positive test who actually have the condition
- Negative Predictive Value
  - Percentage of patients with a negative test who do not have the condition

Evaluating Sensitivity & Specificity

- Want high sensitivity and high specificity
- Sensitivity = true positive / (true positive + false negative)
- Specificity = true negative / (true negative + false positive)
- PPV = true positive / (true positive + false positive)
- NPV = true negative / false negative + true negative)

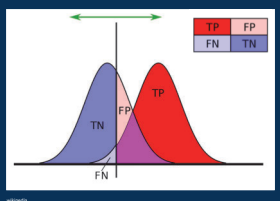
	Gold standard disease present	Gold standard disease absent	
Test positive	True positives (TP): a	False positives (FP): b	Total test positives: a+b
Test negative	False negative (FN): c	True negatives (TN): d	Total test negatives: c+d
	Total diseased: a+c	Total normal: b+d	Total population: a+b+c+d

Indian J Ophthalmol. 2008 Jan-Feb; 56(1): 45–50.

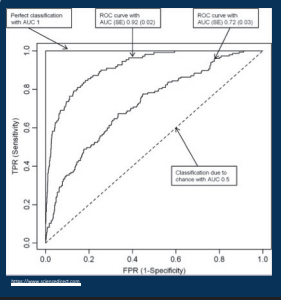
	Disease present	Disease absent
Test positive	a (TP)	b (FP)
Test negative	c (FN)	d (TN)
	Sensitivity: a/ (a+c)	Specificity: d/ (b+d)

TP: True positive, FP: False positive, FN: False negative, TN: True negative

Sensitivity and Specificity



wikipedia



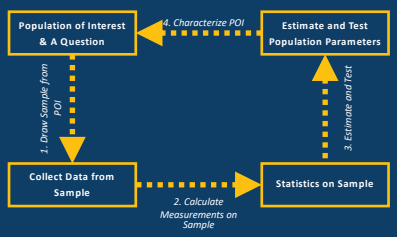
Sensitivity and Specificity: Why Do They Matter?

- If a test claims 100% sensitivity, it may not be very specific and provide a large number of false positives
- Tests and screening tools should be as accurate as possible, particularly when it governs who gets intervention or treatment

The Importance of Good Study Design

Factors to Keep in Mind in your Own Studies

Process of Research Inference

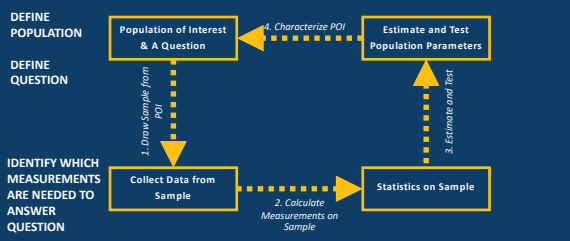


POI = population of interest

Study Design Basics

- Multiple types of study designs
  - All aimed at answering some sort of specific topic or question
- Study design will depend on the question you want to ask and the type of data you will be collecting or have already
  - Question needs to be clearly defined
  - Outcome needs to be measurable
- Each type of study design has strengths and limitations
  - Vary in terms of bias and overall strength

Study Design



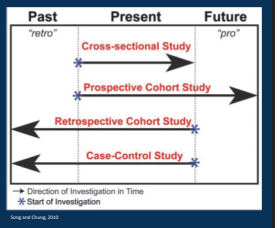
POI = population of interest

Types of Study Design

- Classified broadly based on two characteristics:
  1. Time period in which the data is collected
  2. Employ an experimental treatment

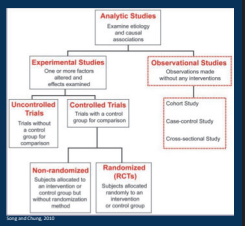
Study Design

- Prospective – subjects recruited and data collected on subsequent events
- Retrospective – subjects recruited and data is collected on prior events or exposures
- Cross-Sectional – subjects recruited and data collected at a single fixed time point, rather than multiple time points



Study Design

- Experimental – impose a treatment/intervention and collect information on responses.
  - Aims to determine if treatment affects response
  - Can only be done prospectively
- Observational – observe the individuals and collect variables of interest
  - Do not impose any condition on the subjects
  - Can be prospective, retrospective, or cross-sectional



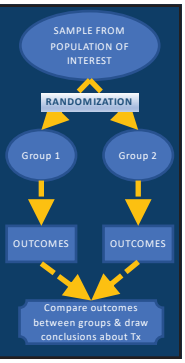
Key Concepts

"Any proof of effectiveness cannot be obtained from a non-randomized study"
Norum et al., 2012

- Bias - any influence that acts to make the observed results not actually representative of the true results. Can occur in te design, conduct, or interpretation of the study.
  - E.g. In an study involving patient interviews, could bias the results by asking leading questions or changes in tone of voice that might influence the response
    - "Do you have difficulty finding your mom in the supermarket?" vs.
    - "You sometimes have difficulty finding your mom in the supermarket, don't you?"
- Variability – spread of outcomes between or within individuals
  - High variability can make it difficulty to draw conclusions because it can mask the differences between groups
- Randomization - participants are randomly assigned to groups
  - E.g. heads or tails
- Blinding – mask the identity of the assigned group/intervention
  - Helps avoid bias
  - E.g. in a clinical trial, usually the patient and the physician are not aware which group that individual is assigned to
- Placebo effect – beneficial response produced by a placebo that are due to the patient's belief in the treatment, rather than the treatment/placebo itself
  - E.g. controls for Drug A given a sugar pill, but still improve in symptoms

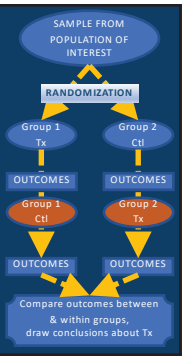
Experimental Study: Randomized Control Trial (RCT)

- Gold Standard in study design
  - Reduces bias (affects accuracy)
  - Reduces variability (affects precision)
- Sample from population is ***randomly assigned*** to groups
  - e.g. treatment and control, treatment 1 and 2, etc.
- Randomization is very important!
  - Helps ensures that potentially confounding effects are balanced between the groups
  - Can more safely assume that difference in outcomes attributed to treatment
  - Enables cause and effect relationship to be drawn
- Prospective, randomized, and comparison group



Experimental Study: Cross-Over Design

- In Cross-Over Design, each subject receives all treatments
  - Enables comparisons within and between groups
  - Subject can serve as their own control because they are part of *both* groups
- Repeated measures: measure outcomes before and after the switchover
- Sometimes unethical for one group not to receive the treatment
- *OR* want each subject to serve as their own control



Observational Study Types

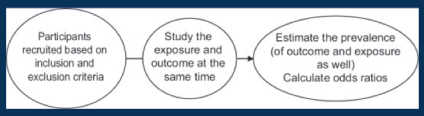
- Ecological
- Cross-Sectional
- Cohort
- Case-control

Observational Study Types: Ecological Design

- At least 1 variable measured at a population or group level, rather than at the individual level
  - E.g. Relationship between per capita preterm birth and prevalence of visual impairments across regions in the USA
  - Per capita preterm birth: ecological variable
    - Cases of visual impairment per 1,000 within the region is group data because region, rather than individual information
- Often used to monitor population health
- can make large-scale comparisons (e.g. between countries, states, provinces)
- Can study relationship between population-level exposure to risk factors and disease

Observational Study Types: Cross-sectional Design

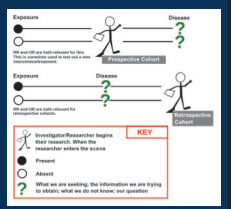
- Measure outcome and the exposure in the participants at the same time at a single time point
  - Assessing prevalence of condition
  - Population-based surveys
  - Calculate odds ratios (e.g. males have a higher odds of having a beard)



Setia, 2016

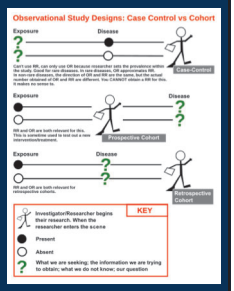
Observational Study Types: Cohort Design

- Evaluate the effect of exposure (e.g. exposure to radiation, presence of a genetic factor, etc.) on the outcome of interest (e.g. incidence of cancer)
- Prospective: Recruit subjects and collect baseline exposure data *before* any subjects have developed the outcome of interest
  - E.g. Framingham Heart Study, Nurses Health Study
- Retrospective: Recruit subjects and collect data after exposure and compare outcome of interest
  - E.g. Comparing the incidence of cancer in the Smith family between those with and without genetic factor



Observational Study Types: Case-Control Design

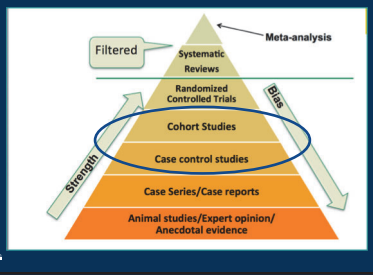
- Compare a group of subjects with condition and those without the condition and compare the level of exposure to factors of interest
  - Suggests an association between the level of exposure and the condition of interest
- E.g. Recruit group of patients with cancer and those without and evaluate differences in lifestyle factors between the groups that may be associated with cancer (e.g. smoking)



Summary

Design	Type	Strengths	Limitations
Randomized Control Trial	Experimental, Prospective	Randomized Comparison Group, can apply different treatment designs	Can be time consuming and expensive, not ethical for all situations
Ecological	Observational	Useful for hypothesis generation	Findings for group may not apply to individual
Cross-Sectional	Observational	Faster and less expensive than cohort studies	Cannot determine trends over time
Cohort	Observational, Prospective	Can asses temporal changes	Difficult for rare diseases or long latency periods
Case-Control	Observational, Retrospective	Useful for rare outcomes	Could be recall or misclassification bias

Study Design Overview



Summary of Things to Keep in Mind When Evaluating the Results of Studies

- Association is not causation
- Importance of reproducibility
- Isolating effects with control and experimental groups
- Learning effects (doing anything twice will likely make you better)
- Unbiased, "blinded" assessment – staying objective
- The power of a big 'n' (large sample sizes matter)

Tools for CVI

Applying a Critical Eye to CVI:
Questions to Ask Yourself When Evaluating a Study or New Tool

Does this study use:

- Treatment *AND* control groups?
- Controlled interventions?
- Adequate statistical analysis?
- Evidence-based approaches?
- Clear and measurable outcomes?

Does this tool have

- Clear and measurable outcomes?
- Evidence-based design?
- Reliability?
  - Are the results consistent over time, between administrators, across items
- Content Validity?
  - Does it measure what it is intended to
- Structural Validity?
  - Do the questions reflect the construct being measured
- Cross-cultural validity?
  - Is it appropriate to use in my population?
- Criterion validity?
  - How does it compare against the "gold standard"
- Responsiveness
  - It is able to detect meaningful change over time without influence of bias
- Can it be used to test a hypothesis?

The Challenge with CVI…

Before we can gauge the efficacy of an intervention on a specific skill, we first need to *empirically* determine the baseline level of function. Otherwise, it is unclear whether there was actual (rather than perceived) improvement

- Need sensitive and specific empirical tests
- Need targeted interventions ***or*** compensatory strategies for different aspects of visual processing
- Outcomes cannot be the same as the intervention

- But, we need effective tools and intervention strategies now (or *n* years ago)

CVI Range

- "Designed to evaluate the degree of effect of the unique visual and behavioral characteristics [of CVI]" (Roman Lantzy and Lantzy, JVIB, 2010)
- Has been used to "monitor changes in functional vision status" (Roman Lantzy and Lantzy, JVIB, 2010)
- 10 characteristics found to be descriptive of brain-based rather than ocular-based visual impairment in infants and young children
  - Color 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

The 5 Questions

- 5 questions from the CVI Inventory, found to be particularly discriminating, while screening of CVI

1. Does your child have difficulty walking down stairs?
2. Does your child have difficulty seeing things which are moving quickly, such as small animals?
3. Does your child have difficulty seeing something which is pointed out in the distance?
4. Does your child have difficulty locating an item of clothing in a pile of clothes?
5. Does your child find copying words or drawings time-consuming and difficult?

RESEARCH ARTICLE

Towards population screening for Cerebral Visual Impairment: Validity of the Five Questions and the CVI Questionnaire

Fiona Gorrie[1*], Karen Goodall[1*], Robert Rush[2], John Ravenscroft[3*]

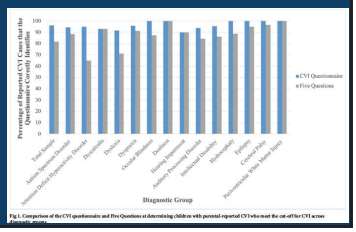
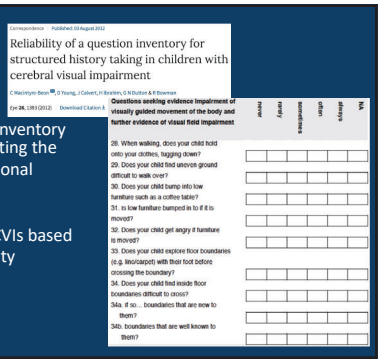


Fig 1. Comparison of the CVI questionnaire and Five Questions at determining children with parental-reported CVI who meet the cut-off for CVI across

CVI Inventory

- Structured history taking inventory of 51 questions for evaluating the presence of specific functional visual impairments
- Good predictive value for identifying children with CVIs based on sensitivity and specificity



Reliability of a question inventory for structured history taking in children with cerebral visual impairment

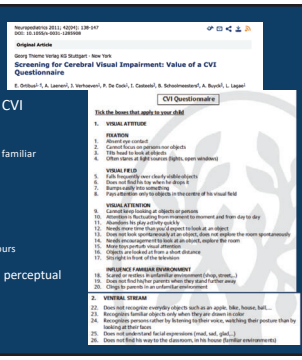
C Macintyre-Beon, D Young, J Calvert, H Brekkn, G N Dutton & R Bowman

Eye 26, 1393 (2012) Download Citation

Questions seeking evidence impairment of visually guided movement of the body and further evidence of visual field impairment	never	rarely	sometimes	often	always	NA
28. When walking, does your child hold onto your clothes, tagging down?						
29. Does your child find uneven ground difficult to walk over?						
30. Does your child bump into low furniture such as a coffee table?						
31. Is low furniture bumped in to if it is moved?						
32. Does your child get angry if furniture is moved?						
33. Does your child explore floor boundaries (e.g. linoleum) with their foot before crossing the boundary?						
34. Does your child find inside floor boundaries difficult to cross?						
34a. If so... boundaries that are new to them?						
34b. boundaries that are well known to them?						

CVI Questionnaire

- Screening tool for identifying potential CVI
- 47 questions covering:
  - Visual Attitude
    - Fixation, fields, visual attention, influence of familiar environment
  - Ventral Stream
  - Dorsal Stream
  - Complex Problems
  - Other Senses
  - Associated Characteristics
    - E.g. memory, anxiety, compensatory behaviours
  - Good sensitivity and specificity
  - Good agreement with other tests of visual perceptual tasks
    - E.g. L-94, TVPS-R, and VP subtask



Neuropediatrics 2011; 42(04): 139-147

Original Article

Georg Thieme Verlag KG Stuttgart · New York

Screening for Cerebral Visual Impairment: Value of a CVI Questionnaire

E. Ortibaul-T, A. Laurent, J. Verhoeven, P. De Cock, I. Casteels, B. Schoolmeesters, A. Buyck, L. Lagae

CVI Questionnaire

Tick the boxes that apply to your child

1. VISUAL ATTITUDE

FIXATION

1. Absent eye contact
2. Cannot focus on persons nor objects
3. Only looks at bright objects
4. Often stares at light sources (lights, open windows)

VISUAL FIELD

5. Falls frequently over clearly visible objects
6. Does not find his toy when he drops it
7. Bumps easily into something
8. Pays attention only to objects in the centre of his visual field

VISUAL ATTENTION

9. Cannot stop looking at objects or persons
10. Attention is fluctuating from moment to moment and from day to day
11. Needs more time to look at objects
12. Needs more time than you'd expect to look at an object
13. Does not look spontaneously at an object, does not explore the room spontaneously
14. Needs encouragement to look at an object, explore the room
15. More than normally visual attention
16. Objects are looked at from a short distance
17. Sits right in front of the television

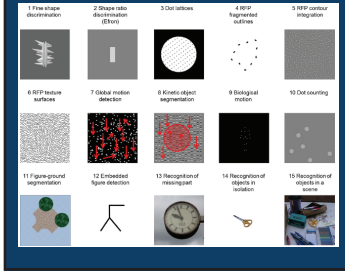
INFLUENCE FAMILIAR ENVIRONMENT

18. Scared or restless in unfamiliar environment (shop, street,...)
19. Does not find his/her parents when they stand further away
20. Clings to parents in an unfamiliar environment

2. VENTRAL STREAM

22. Does not recognize everyday objects such as an apple, bike, house, hat,...
23. Recognizes familiar objects only when they are shown in color
24. Recognizes persons rather by listening to their voice, watching their posture than by looking at their faces
25. Does not understand facial expressions (mad, sad, glad,...)
26. Does not find his way to the classroom, in his house (familiar environments)

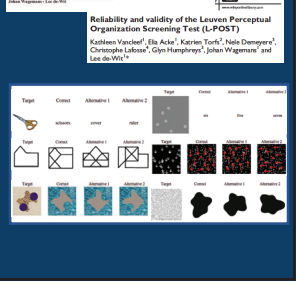
L-POST



The Leuven Perceptual Organization Screening Test (L-POST), an online test to assess mid-level visual perception

Katrien Torfs · Kathleen Vancleef · Christophe Lafosse ·

Johan Wagemans · Lee de Wit

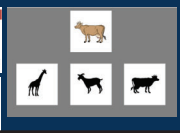


Reliability and validity of the Leuven Perceptual Organization Screening Test (L-POST)

Kathleen Vancleef[1], Ella Acke[1], Katrien Torfs[2], Nele Demeyere[3], Christophe Lafosse[2], Glyn Humphreys[3], Johan Wagemans[1] and Lee de-Wit[1]*

CVIT 3-6: Children's Visual Impairment Test for 3-6 y/o

- 14 subtests across 4 domains of visual perception
  - Object Recognition
  - Degraded Object Recognition
  - Motion Perception
  - Global-Local Processing



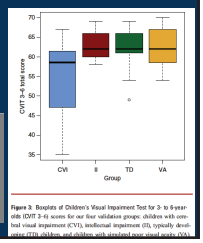
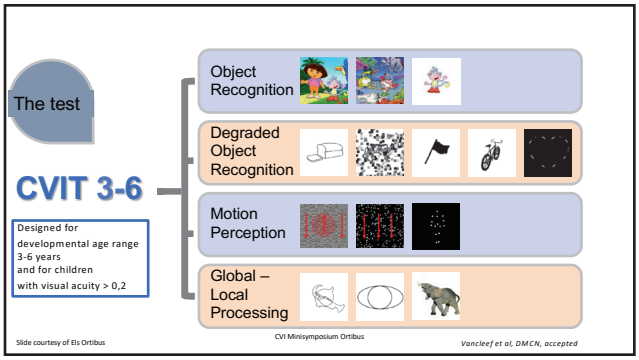
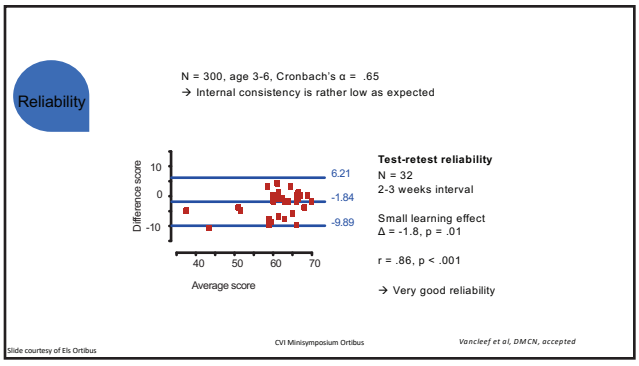
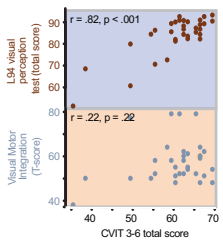


Figure 3: Boxplots of Children's Visual Impairment Test for 3- to 6-year-olds (CVIT 3-6) scores for our four validation groups: children with cerebral visual impairment (CVI), intellectual impairment (II), typically developing (TD) children, and children with simulated poor visual acuity (VA).

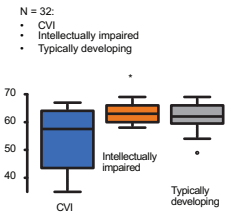




Validity



High correlation with visual perceptual skills on L94
Low correlation with the VMI



Group differences indicate specificity of CVIT 3-6

Vancleef et al, DMCN, 2019

Slide courtesy of Els Ortibus

CVIT 3-6 summary

- The CVIT-3-6 is a scientifically sound tool for identifying visual perceptual/ 'higher vision' difficulties in children with a developmental age 3- 6 years;
- It does not involve motor skills and could be used with a wide group of children including those with cerebral palsy
- It is an online tool, fun and easy to use in the clinic (https://psytests.be/clinicians/test-centrum/cvi-t.php)
- It potentially assesses and identifies children who would be in Sakki et al **Cluster subtype A1 and Cluster subtype A2**

Slide courtesy of Els Ortibus

Teach CVI

TEACH ERAVS MUSI+

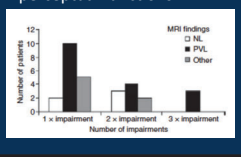
- teachCVI is a European partnership that aims to create collaborative tools for teachers and healthcare professionals that will help bridge the gap between teachers/educators and healthcare professionals so that they can work together to benefit the target group: children with CVI

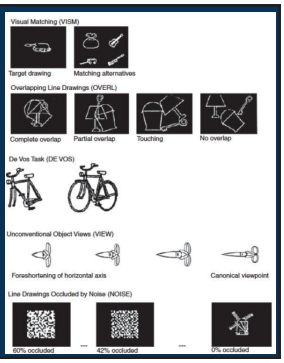
- **Aims of the project:**
- Making a tool for healthcare professionals and educators to screen for CVI
- Creating a common database of tools for CVI detection
- Producing resources for teachers to support their work in the assessment of CVI
- Making teaching methodologies to enable the child's access to literacy, this includes training and teaching materials for teachers/educators of children with CVI

- https://www.teachcvi.net
- Series of assessments, screening tools, and other helpful resources

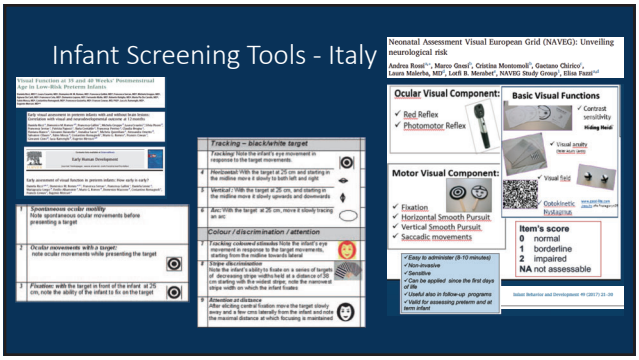
L-94

- Perceptual battery created in Leuven, Belgium in 1994
- Shows correlation with MRI and agreement with other tests of visual perceptual functions





Infant Screening Tools - Italy

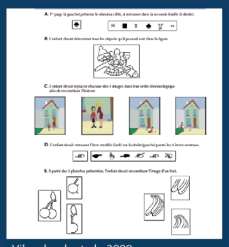


Screening tools for VI in schools - UK

- Non-verbal children:
  - Lea Gratings
  - Cardiff Cards
  - Puppet Face
  - Hiding Heidi (contrast)
- Young Children (ability to match)
  - BUST (near and distance)
  - Kay Picture test
  - Sonksen-Silver Visual Acuity System
  - Colour Vision Made Easy
  - PV 16 Colour Test
  - Lea Symbols high/low contrast test
- Older Children
  - MacLure Reading Type for Children (near)
  - Kays Crowded LogMAR letter test
  - Snellen Chart
  - Pelli Robson Chart (Contrast Sensitivity)
  - Precision Vision Colour Test as above
  - Ishihara

Varies Across districts and countries

Screening tools for VI in schools - France



Vilayphonh et al., 2009

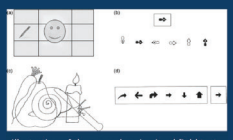


Illustration of the procedure in visual field test (a), and examples of items used in the visual memory (b) with the target to be memorized at the top, in the embedded figures (c), and in the matching (d) tasks. Cavezian et al., 2010

Visual Skills Inventory: 4-8, 9-12 y/o

- Structured clinical history taking inventory
- Home and School strategies

- https://www.ulster.ac.uk/research/topic/biomedical-sciences/research/optometry-and-vision-science-research-group/vision-resources/resources-for-professionals/cerebral-visual-impairment-assessment

How can we increase our knowledge of CVIs to improve patient care?

- Rigorous scientific evaluations
- Large studies with diverse populations or multiple replications
- Significant and sustained effects

Evidence-Based Principles

- "A systematic approach to clinical problem solving which allows the integration of the best available research evidence with clinical expertise and patient values"
  - *Masic et al., 2008*
- " we would be better to base our decisions on the collective experience of thousands of clinicians treating millions of patients, rather than on what individuals have seen and felt"
  - *Greenhalgh*

The Big Picture

Use neuroscience to determine the anatomical substrate of visual dysfunctions associated with CVI

In turn, this can help inform the definition, diagnosis, and treatment of CVIs

- For example, CVI initially defined mainly on acuity and visual field loss and from "damage to the visual system between the lateral geniculate nucleus and the cortex"
  - *Steendam 1989*

We now know that CVIs extend to include many perceptual functions and that it can be caused by injury to other parts of the brain involved with visual processing, not just to the primary visual pathway

- "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*


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

Hanna E.A. Sakki,[1] Naomi J. Dale,[1,2] Jenefer Sargent,[2] Teresa Perez-Roche,[3] Richard Bowman[1,4]

"The benefits of evidence-based medicine, when properly applied, are obvious. We can use test characteristics and results to make better diagnoses. We can use evidence from treatments to help people make better choices once diagnoses are made. We can devise research to give us the information we are lacking to improve lives. And, when we have enough studies available, we can look at them together to make widespread recommendations with more confidence than we'd otherwise be able."

Aaron E. Carroll
TheUpshot, The New York Times
Dec. 27, 2017