Cerebral Visual Impairment Risk in Down Syndrome: Insights from Visual Selective Attention Analysis using Eye Tracking

Master thesis Neuropsychology

Utrecht University

Name: Hesham Elbaz
Student number: 6014011
Date: 29/06/2024

UU supervisor: Marinke Hokken
UU 2nd assessor: Albert Postma

Abstract

Visual impairments frequently occur in children with Down Syndrome (DS). Due to diagnostic overshadowing and unsuitable assessment tools the root of these impairments is left unexplored. Cerebral visual impairment (CVI) is the most prevalent visual function impairment in children and occurs more often in children with intellectual disabilities than neurotypical children. In this study visual search performance (VSP) was investigated in children with DS with suspected CVI (*M* = 114.4 *SD* = 44.1) and non-suspected CVI (M = 167.6, *SD* = 18.7), aiming to test a novel screening tool and give a more comprehensive view on VSP in children with DS. An eye-tracking device was used to record gaze requiring no verbal or motor responses using a novel visual search task. Accuracy (Acc), reaction time (RT) and gaze area (GA) were measured as outcomes for VSP. Additionally, the effects of task type and scene complexity were explored. Overall, the suspected CVI group showed no impaired VSP compared to the non-suspected CVI group. However, as task type difficulty increased the suspected CVI group were observed to have impaired VSP. Furthermore, the suspected CVI group showed impaired VSP on a noisy background. The division of groups using a parent reported questionnaire, significant age differences and a small sample size should be taken into consideration. This research provides an enhanced understanding of higher order visual functions (HOVF) in children with DS and offers an alternative assessment tool suitable for children with DS from an early age.

Keywords: Cerebral visual impairment; Down Syndrome; Visual selective attention; Search task; Eye-tracking

Introduction

Children with Down Syndrome (DS) are at a higher risk of experiencing visual function problems. However diagnostic overshadowing and attribution of visual function problems to common ocular impairments may not give a comprehensive view of the cognitive profile of children with DS (Harvey et al., 2020; Purpurra et al., 2019). Visual function impairments such as low visual acuity, nystagmus and refractive error are a common occurrence in children with DS (Creavin & Brown, 2009; Ugulru & Altinkurt, 2020). However, several visual functions are unexplored, likely due to inappropriate assessments considering the cognitive impairments for children with DS. Therefore, research must be done using suitable assessments for children with DS, while taking the cognitive impairments associated with DS into consideration. The current research investigates higher order visual functions (HOVF), specifically visual search attention (VSA), in DS children with suspected Cerebral Visual Impairment (CVI), using a non-verbal eye tracking task.

CVI is the most prevalent visual function impairment in children in high-income countries (Kong et al., 2012; Pehere et al., 2018; Solebo et al., 2017). CVI is a brain-based visual disorder that is commonly associated with preterm birth, cerebral anoxia (or hypoxia) in the early stages of brain development, affecting the pathways responsible for the processing of visual information (Fazzi et al., 2007; Sakki et al., 2018). CVI presents itself in a heterogeneous fashion across visual functions, varying in severity and areas affected.

Visual functions can be divided into two subcategories: lower order visual functions (LOVF) and HOVF. LOVF consist of sensory and oculomotor functions. Impairments in these functions can be expressed through a diminished sense of visual acuity, visual field loss, disorders in saccades and involuntary eye movements (van Genderen et al., 2012). HOVF are responsible for the processing of the images provided by the LOVF. Impairments in the HOVF can lead to difficulties in visual selective attention, visual memory, and object recognition for example (Friedrichs & Friedrichs. 2022; Zuidhoek, 2020). Although CVI can be the result of impairments in LOVF or a combination of both functions being impaired, CVI most commonly is associated with impairments in HOVF. The fact visual function assessments are often initiated by investigating LOVF, can lead to HOVF impairments being left undiagnosed, as regular visual acuity has been used to rule out CVI in the past. However regular visual acuity does not exclude the possibility of HOVF impairments (Saidkasimova et al., 2007; Sakki et al., 2018; Stiers et al., 2002). This once more emphasises the heterogeneity of CVI and the importance of well-balanced research into visual function impairments.

VSA is a HOVF which determines what information in the visual world is attended to in order to filter out unwanted information. This can be controlled by personal motivations in a top-down manner, for example while looking for a specific item. Contrarily VSA can be abruptly drawn to a stimulus in the outside world due to reflex or automatism in a bottom-up manner, for example due to a loud bang or flash (Hahn et al., 2006; Zuidhoek, 2020). VSA can be divided into two distinctive processing types. Global selective attention is the process of attending to something as a whole figure, this can be compared to a zoomed-out view. Local selective attention is the process which is used when the details of a figure are attended to, a zoomed in view (Förster & Dannenberg, 2010; Treisman, 2013). Global selective attention dysfunction can be expressed through difficulty piecing together visual details creating an overview of a visual scene, such as crossing a street in busy traffic. Local selective attention dysfunction can be manifested through issues such as reading problems or difficulty finding an object in a crowded area, as distinct elements in a scene cannot be separated (Zuidhoek, 2020). VSA dysfunctions are a prevalent impairment in HOVF in children with CVI (Phillip & Dutton, 2014; Zihl et al., 2015).

Early neural damage is often widespread and may affect an array of functions. Neurological disorders or intellectual disabilities are therefore commonly associated with CVI

(Lueck et al., 2019). However, while they are at a higher risk of experiencing impairments related to CVI than neurotypical children, CVI is often overlooked in children with DS. Cognitive deficits in children with DS may cause deficits due to CVI to be attributed to cognitive impairment. Subsequently this may lead to underestimation of cognitive functioning in children with DS (Wilton et al., 2021).

DS, caused by a genetic mutation, is the most prevalent intellectual disability (Coppus, 2013). DS is linked to a variety of traits and observable characteristics such as unique physical and facial features, health problems, atypical ageing, and lower life expectancy. (Krinsky-Mchale et al., 2014). DS is most commonly paired with immense deficits in language and overall slower development in cognitive functions like attention, the performance of motor actions and auditory abilities (Klein & Mervis, 1999; Malak et al., 2013; Roberts et al., 2007). However, due to severity of these language impairments and the overall slower development of cognitive functions, visual function impairments can often be underdiagnosed, as these impairments are not the most prominent impairments in DS. In addition, early comparative research has suggested visual functions are a relative strength in DS, however this is either in comparison with the more severe impairments children with DS endure or compared to other intellectual disabilities (Bellugi et al., 1999; Wang et al., 1995). This can lead to the visual function impairments being left untreated in patients with DS contrary to neurotypical children and children with other intellectual disabilities (Wan et al., 2015).

LOVF are known to be poor in children with DS and are often reported (Postolache., 2019; de Weger et al., 2021; Zahidi et al., 2018) However, the notion that the overall visual function impairments in children with DS cannot only be accounted for by the LOVF, but may also be due to impairments in the higher order visual functions is supported by various studies into visual acuity combined with behavioural assessments (Bosch et al., 2014; Little et al., 2007; Little et al., 2009). Clarification on the HOVF impairments in children with DS is needed. Currently CVI assessments are routinely done by paediatric ophthalmologists more focused on LOVF, which may not deviate from the norm, leading to no further investigation of the visual functions (Pilling et al., 2023). Additionally, the lack of a standardised protocol when it comes to assessing CVI interferes with the diagnostics process (Boonstra et al., 2022; McConnell et al., 2021). Whenever HOVF are investigated the most frequently used methods are observational and neuropsychological tests, such as visual search tasks (Muller & Krummenacher, 2006). However, these tests require verbal instructions and verbal or motor skills, such as pencil and paper search tasks or verbally describing a scene. Because these skills tend to be poor in children with DS, these standard tasks may lead to CVI being regularly underdiagnosed in children with DS. Due to the fact HOVF impairments are often disregarded in children with DS it is of utmost importance to use suitable tests during assessment.

In recent years novel assessment measures have been adopted which seem to avoid the downsides of the current methods. Eye tracking measurements provide an approach in which visual responses can be quantified without the task requiring verbal instructions, verbal, and/or motor responses (Kooiker et al., 2015; Mooney et al., 2021). Furthermore, eye tracking is more suitable for younger children and seems to be appropriate for the assessment of children with intellectual disabilities (Boot et al., 2013; Ithzak et al., 2023; Kooiker et al., 2016a). In addition, the eye tracking research into children with CVI have illustrated search performances which would be expected of children with CVI, showing longer reaction times, less likelihood of finding the target and an overall larger area searched before finding the target compared to neurotypical children (Manley et al., 2022; Zhang et al., 2022, Hokken et al., 2024). It is important to note that thus far the eye tracking studies mentioned above did not include children with DS.

The current study will explore the opportunities of assessing children with DS using this innovative method, possibly applying it for screening in the future. The assessment consists of a feature search task, in which the child will identify a target which is hidden between foils with one common feature. In a feature task global visual search strategies are most commonly applied, as the saliency of the target will make it stand out between the foils. Subsequently, the child will complete a conjunction search task in which the target must be identified hidden between distractors which have multiple common features with the target. In a conjunction task local visual search strategies are most commonly applied as the target is more difficult to find among the similar foils. As children with DS show a global attention bias (Bellugi et al., 1999; Porter & Coltheart, 2006;), this may affect their ability to complete the conjunction task to a greater extent.

Taking the cognitive impairments of children with DS into consideration (verbal, motor, auditory disabilities), the purpose of this study is to test the possibilities of a new CVI screening tool for children with DS while gaining a more in-depth view on their HOVF. DS children will be compared by dividing them into two groups: The suspected CVI group and non-suspected CVI group. This will be done by measuring VSA. The assessment will be done using a non-verbal gaze-based search task. Visual search performance (VSP) was quantified measuring the following aspects: reaction time, gaze accuracy and gaze area. It is hypothesised the suspected CVI group will have more impaired VSP than the non-suspected CVI group. Also, the increase in task demand from the feature to the conjunction task is expected to lead to impaired VSP in the suspected CVI group as the conjunction task is considered a more demanding VSA task (Manley et al., 2023). Finally, an increase in scene complexity is also expected to cause impaired VSP in the suspected CVI group.

Methods

Participants

Data were collected through children recruited at the school of optometry and vision sciences at Cardiff university. The criteria which should be met by participants were the following: a child between the age of 3 and 18 with down syndrome. Visual acuity had to be above 0.1 decimal. The children participating in this study did not have an official CVI diagnosis. An informed consent form was signed prior to the experiment by the parent/carer. Ethical approval was gained through the Ethical Review Board of Social and Behavioural Sciences of Utrecht University, under number 23-1887 and the *Medische Ethische Toetsings Commissie* (METC) of the Erasmus medical centre, under code MEC-2020-0680. The study was in accordance with the declaration of Helsinki (2013) regarding research with human subjects.

Procedure

The assessments took place at the school of optometry and vision sciences at Cardiff university. The experiment was supervised and performed by M. Hokken. Before the assessment started, the child was placed at roughly 60 centimetres from the screen. Parents were requested to not aid the children during the task in order to attain valid measurements. The child was only instructed to keep looking at the screen, no further instructions were given. To calibrate, the infant calibration by Tobii was used (Tobii Prolab, 2019). If the calibration were accurate, a prompt would appear. If the calibration failed on three consecutive trials the experiment was started, regardless of the unsuccessful calibration. Throughout the experiment the assessor kept track of general observations using an observation form for each task. Parents were sent the visual skills questionnaire and Vineland questionnaire after the experiment to obtain further information on the child.

Instruments

The complete test battery consisted of two questionnaires, five eye tracking tasks and two paper-pencil tasks. For this thesis project, the two questionnaires and two eye tracking tasks were assessed and further analysed.

Vineland questionnaire

The Vineland questionnaire (Vineland-3; Sparrow, Cicchetti, & Saulnier, 2016) is a standardized questionnaire which was used to measure the adaptive behaviour of the participants in daily life. The domains measured were Communication, daily tasks and social skills and relationships. The items are scaled on a 3-point Likert scale (0 = never, 1 = sometimes, 2 = usually or most of the time). This resulted in an adaptive behaviour composite (ABC) score. The score was based on the comparison with children the same age. ABC scores were compared in this study to check for differences in adaptive behaviour.

Visual skills questionnaire

The visual skills questionnaire consisted of 70 questions. 15 questions regarding demographic information and medical history, the questions regarding medical history were to be answered using ‘yes’ or ‘no’, when the answer was yes, the parent/carer was asked to elaborate, if possible. Additionally, the questionnaire consisted of 55 questions regarding visual skills of the child which were to be answered on a 5-point scale with the following options: ‘never’, ‘rarely’, ‘sometimes’, ‘often’, ‘always’ and ‘not applicable’. This questionnaire was used to determine whether a child is part of the non-suspected CVI group or the suspected CVI group. This study focussed on the comparison of children with DS with a suspicion factor for CVI (suspected CVI group) and children with DS without this suspicion factor (non-suspected CVI group), the discrepancy between the groups was determined using the visual skills questionnaire. The division of the participants into two groups was done via a 5-question screening tool. The screening tool consisted of 5 questions posed within the questionnaire which had been proven to elicit positive responses mainly in children with CVI (table 1). Furthermore, this screening tool had proven to have a high reliability and validity in previous research (Wilton et al., 2021).

Table 1

Screening questions used to determine two groups

Screening questions
1. Does your child have difficulty walking downstairs?
2. Does your child have difficulty catching a ball?
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?

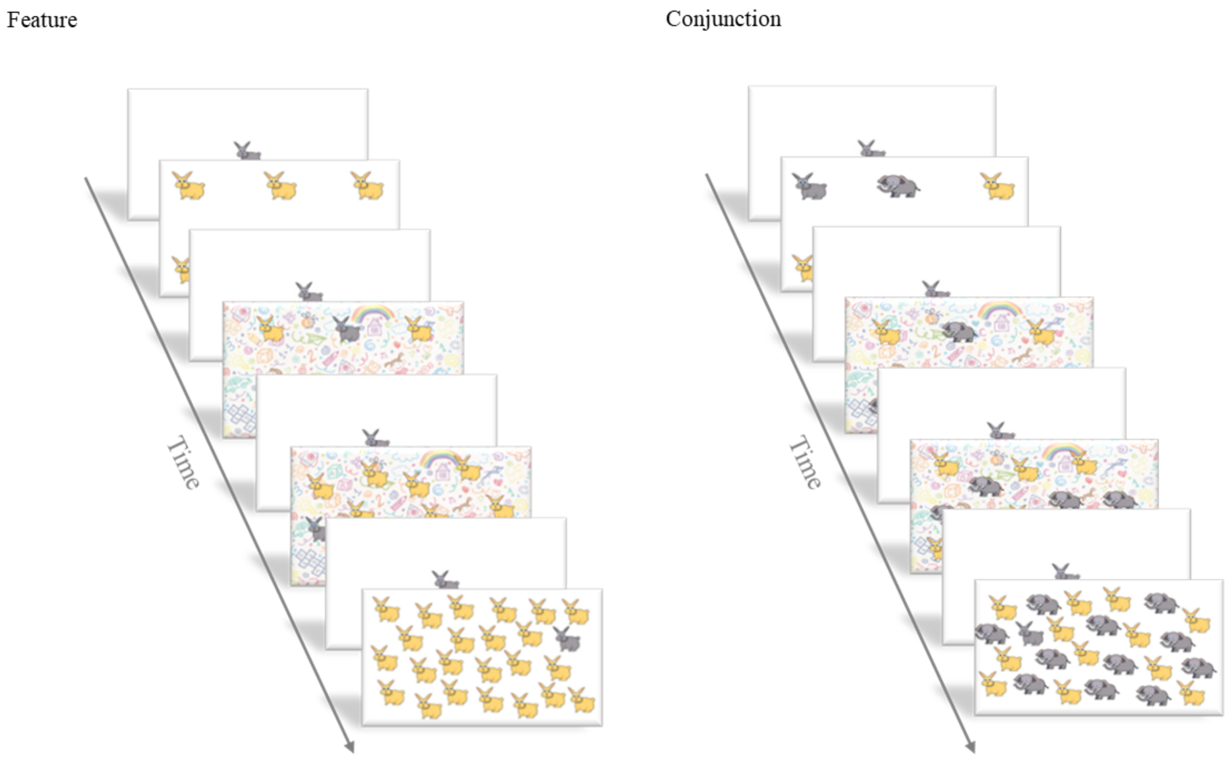
Note: a positive response was a question answered with 'often' or 'always'. The questions were administered through the VSQ.

Animal search task

The animal search task measured visual selective attention by recording eye movements during visual search. The task consists of four subtasks, that were presented in a fixed order: (a) the target grey bunny was shown hidden between yellow bunnies, (b) the target grey bunny was shown hidden between grey elephants, (c) the target grey bunny was shown hidden between different animals, (d) the target grey bunny was shown hidden between yellow bunnies and grey elephants. For this study only subtask A and D were analysed. Each subtask contained 12 trials, both fluctuating in number of distractors (5, 11, 23), presentation (structured or unstructured) and background (calm or noisy). The trials were presented in a fixed order. An overview of each display for both subtasks is given in the appendix A. Prior to the start of both subtasks the children were primed towards the target grey bunny using a cheerful sound and a flickering display of a singular grey bunny. This was followed by two practice trials. During both tasks, each trial was preceded by a display of the target grey bunny making a noise (figure 1). This was followed by the trial which was shown for a maximum of 7 seconds. If fixation on the target had been observed by the assessor before the 7 seconds had passed, the trial was ended. At the end of each trial the target grey bunny flickered within the display.

Figure 1

The feature and conjunction tasks on the animal search task



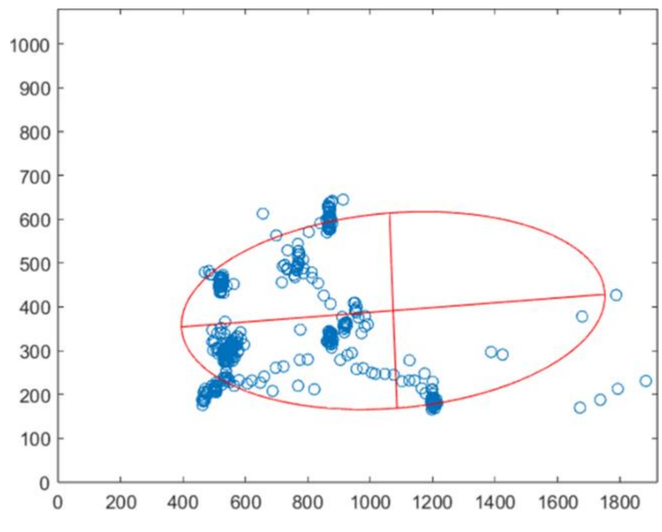
Note: a depiction of the procedure for both tasks showing example trials increasing in scene complexity over time. Between each trial a singular bunny was shown for priming purposes

Data analysis

The animal search task contained targets and distractors of 212 x 212 pixels. An area of interest (AOI) of 408 pixels was drawn around the target bunny. Gaze within this AOI was seen as fixation on the target. The threshold for a valid fixation on the target was set at 150 ms corresponding with similar research into visual search (Hokken et al., 2024). Accuracy (Acc) was measured by accumulating the number of trials a participant fixated on the target, conveyed through a percentage of targets found across the twelve trials within a subtask. Reaction time (RT) was quantified by analysing the amount of time in milliseconds it takes for the child to fixate on the target area. Gaze area (GA) was be measured by drawing an ellipse containing 85% of all gaze measurements following Kooiker et al. (2019). An example ellipse is given in figure 2. GA was then calculated by dividing the area of the ellipse by the resolution of the screen which was 1920 x 1080. This resulted in a percentage of the screen searched by a participant for each trial. The eye tracking data was analysed using MATLAB (Natick, Massachusetts: The MathWorks Inc.) Appendix B shows the script used to form the ellipse.

Figure 2

An ellipse drawn around 85% of valuable gaze points on an example trial



Statistical analysis

The analysis of the data was be done using SPSS version 29.0 (IBM Corporation, Armonk, NY, USA). During data exploration only mild outliers were identified. The outliers were not excluded from the analyses as they were not implausible data. There was one missing value for the conjunction task as a child did not partake in it. Levene's tests for homogeneity of variance and Shapiro Wilk tests for normality were conducted. Independent samples t-tests were performed to analyse participant characteristics and to explore the differences between the groups on valuable gaze samples. Nonparametric analyses were done on eye-tracking data as data was not normally distributed. To compare the suspected CVI group and the non-suspected CVI group on RT, Acc and GA Mann Whitney U tests were used. Wilcoxon's signed rank test was used to measure the effect of task demands within groups. Effect sizes for both tests were measured using effect size *r* (Fritz et al., 2012). Effect sizes were $r = .1$ (small), $r = .3$ (medium) and $r = .5$ (large) (Cohen, 1988). Effects of scene complexity on Acc, RT and GA within the two groups were analysed using a Friedman test for multiple set sizes and a Wilcoxon signed rank's test for structure and background. Wilcoxon's signed rank test was used as a post hoc test for Friedman's test if significance was reached, Bonferroni corrections were then applied for multiple comparisons with an adjusted alpha level of $\alpha = .017$. All other statistical significance levels were set at $p < .05$.

Results

Division into two groups

Two groups were formed using the 5- question screening tool corresponding with previous research by Wilton et al. (2021). Table 2 displays the results of the VSQ. A child was assigned to the suspected CVI group if three or more screening questions had been answered positively.

This method found eight children who had three or more positive answers and eight children with less than three positive responses (Table 2).

Table 2

Overview of the 5- question screening tool and Visual Skills Questionnaire results

Participant number	Screening questions responses	Positive responses (%)	Group
801	1	12,2	Non-suspected CVI
802	3	31,7	Suspected CVI
803	3	32,5	Suspected CVI
804	5	76,5	Suspected CVI
805	2	19,2	Non-suspected CVI
806	1	18,7	Non-suspected CVI
807	4	60,2	Suspected CVI
808	1	8,4	Non-suspected CVI
809	2	20,5	Non-suspected CVI
810	0	7,3	Non-suspected CVI
811	0	16,9	Non-suspected CVI
812	5	38,8	Suspected CVI
813	3	32,9	Suspected CVI
814	3	14,5	Suspected CVI
815	3	33,9	Suspected CVI
816	0	13,8	Non-suspected CVI

Note: Screening question responses are the amount of screening questions of the five answered positively. Positive responses are the percentages of all questions answered with ‘often’ or ‘always’.

Participant characteristics

Table 3 portrays the characteristics of the participants per group. No significant differences were found between the groups on sex (*p* = .619) or on the ABC (*p* = .332). The groups did significantly differ in chronological age as children in the non-suspected CVI group were significantly older than children in the suspected CVI group (*t* (9.430) = 3.144, *p* = .011, *d* = 1.57).

Table 3

Characteristics of the participants in the non-suspected CVI and the suspected CVI group

	Non-suspected CVI (*n* = 8)	**Suspected CVI** (*n* = 8)	**t-test value (df)**	***P*-value**	**Cohen's D**
Age in months (M (SD))	167.6 (18.7)	114.4 (44.1)	3.144 (14)	.011*	1.57
Sex (boys, n (%))	5 (62.5%)	6 (75%)	.509 (14)	.619	.26
Adaptive behaviour compound (ABC)	68.75 (7.25) (*n*=6)	63.17 (13.32)	1.011 (12)	.332	.55

Note: statistical significance levels were set at * $p < 0.05$

Visual search performance

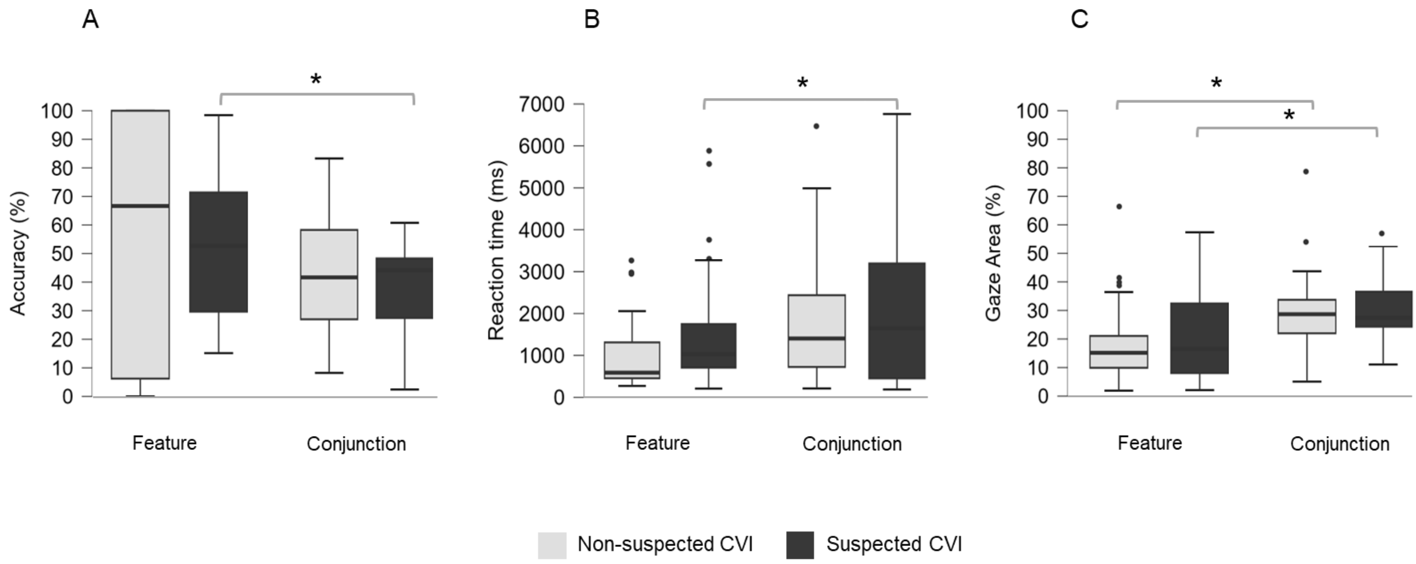
No significant differences were found between the non-suspected CVI group (*M* = 56.8, *SD* = 12.1) and the suspected CVI group (*M* = 42.9, *SD* = 15.0) on valuable gaze samples, *t* (13) = 1.996, *p* = .067.

Figure 3 shows the distribution of the suspected CVI group and the non-suspected CVI group on VSP for the feature and the conjunction task. The suspected CVI group did not show overall impaired VSP in comparison to the non-suspected CVI group. With Acc (U =

24.50, Z= -.406, p = .685), RT (U = 11.00, Z= -1.121, *p* = .262) and GA (U = 5.00, Z= -1.826, *p* = .068). Similarly no significant task specific differences were found between the Non-suspected CVI group and the suspected CVI group for the feature task on Acc (U = 31.50, Z= -.053, p = .958), RT (U = 14.00, Z= -1.291, *p* = .197) and GA (U = 16.00, Z= -1.033, *p* = .302) and the conjunction task there were also no significant differences found between the suspected CVI and the non-suspected CVI group on Acc (U = 23.50, Z= -.528, *p* = .597), RT (U = 12.00, Z= -1.549, p = .121) and GA (U = 11.00, Z= -.053, *p* = .958)

Figure 3

The distribution of the data for both groups for: (A)Accuracy, (B) Reaction Time and (C) Gaze Area for the feature and conjunction task



Note : Significance is depicted using (*) for $p < 0.05$

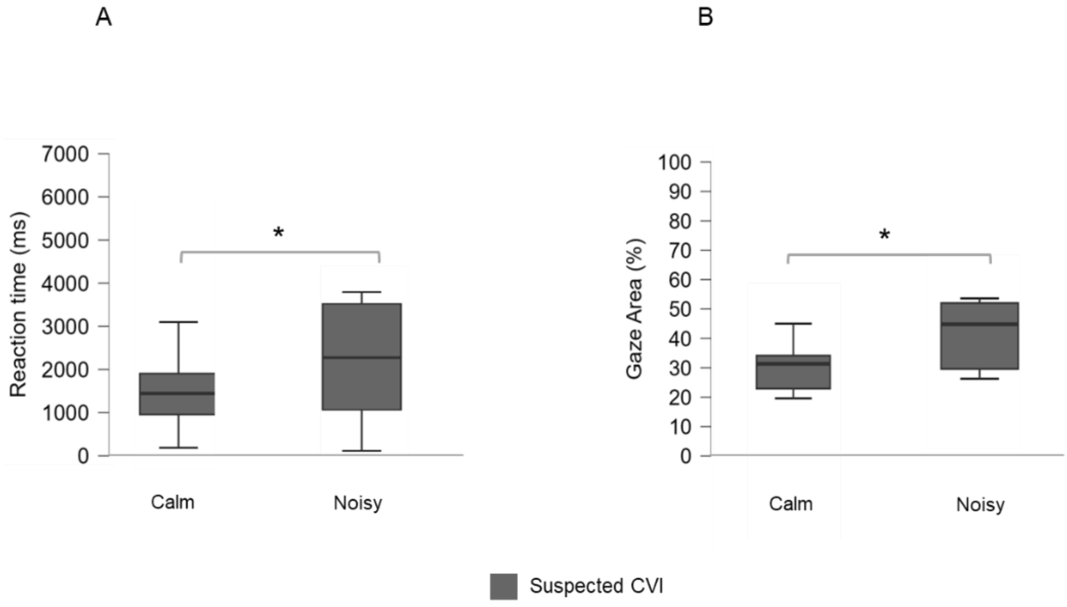
The non-suspected CVI group showed a significantly larger GA on the conjunction task than on the feature task (Z= -2.201, *p* = .028, *r* = .899). No differences were found on Acc (Z = .851, *p* = .395) and RT (Z = -.943, *p* = .345) The suspected CVI group showed overall impaired VSP on the conjunction task compared to the feature task. The suspected CVI group showed less Acc (Z= -2.201, *p* = .028, *r* = .832), had longer RT (Z= -1.992, *p* =

.046, *r* = .813) and had a larger GA (Z= -2.023, *p* = .043, *r* = .905) (figure 3). All effect sizes were large. Full data on the task type effects can be found in appendix C.

Due to increase in scene complexity the suspected CVI group showed a larger RT on the feature task with a noisy background (Z= -2.100, *p* = .036, *r* = .742) and a larger GA on the conjunction task with a noisy background (Z= -2.023, *p* = .043, *r* = .905) showing large effect sizes (figure 4). No effects were found for Acc and GA on the feature task or Acc and RT on the conjunction task due to background for the suspected CVI group. The suspected CVI group showed no effects of increased scene complexity on VSP for set size and structure on the feature and the conjunction task. No effects of set size, structure or background were found for the non-suspected CVI group on VSP on the feature task or the conjunction task. Both groups did initially show significant differences on Acc and RT on the conjunction task, however after post hoc tests significance was no longer met. Appendix D shows full statistics for effects of scene complexity.

Figure 4

Significant effects for scene complexity. (A) RT on the feature task for background, (B) GA on the conjunction task for background



Note : Significance is depicted using (*) for $p < 0.05$

Discussion

In this study a non-verbal eye-tracking based visual search task was used to investigate the differences in VSP between two groups of children with DS: the suspected CVI group and the non-suspected CVI group. The aim of the study was to see whether a discrepancy could be made between the two groups regarding visual search parameters: accuracy, reaction time and gaze area. These parameters were measured on a feature and a conjunction task. Despite DS children being at a higher risk for CVI related impairments than neurotypical children, CVI is often overlooked in children with DS. Due to unsuitable screening methods considering cognitive impairments such as verbal and motor deficits, this study explores the possibilities of a novel screening tool for children with DS and gaining a better understanding of visual impairment in DS.

VSP differences in children with DS

Whilst worse VSP was observed in children with suspected CVI, these differences were not significant. This indicates the suspected CVI group did not find less targets, require more time to find the targets or cover a larger search area to find the targets in comparison to the non-suspected CVI group. These results were discordant with research suggesting a reduced VSP in children with suspected CVI (Manley et al., 2022; Zihl et al., 2024, Hokken et al., 2024).

Interestingly, the suspected CVI group did show significantly more difficulty on the conjunction task compared to the feature task, which was not the case for the non-suspected CVI group. Thus, the suspected CVI group found less targets, took longer to find the target, and searched a larger area on the screen in order to find the target when the target stood out less. An increase in task demands has been associated with impaired search performance in children with CVI (Manley et al., 2023). For the non-suspected CVI group a significant difference was found on gaze area meaning the area searched was larger for the conjunction task than for the feature task. Earlier studies suggest that DS children often show a global attention bias (Bellugi et al., 1999; Porter & Coltheart., 2003). This search tactic would be more suited for the feature task as the target is salient. For the conjunction task however a local search tactic would be best suited to find the target which could explain the significantly larger gaze area for the non-suspected CVI group on the conjunction task.

Additionally, in contrast to the non-suspected CVI group, we found notable findings effects of scene complexity on VSP for the suspected CVI group. The suspected CVI group took longer finding the target on the feature task when the background was noisy, this is in alignment with previous research suggesting children with CVI have difficulty finding relevant information when a visual scene becomes more complex (Dutton et al., 2004; Lam et al., 2010; Zhang et al., 2022; Hokken et al., 2024). This is also coherent with descriptions of certain daily life issues children with CVI experience, such as finding toys on a colourful carpet or a stuffed toy on bed sheets with a pattern. Recommendations to reduce these problems therefore would be to stick to plain interior (Dutton., 2009). Another explanation could be the children were distracted by the background as they simply, found it more interesting. The background contained cars and rainbows which may have caught their attention due to these being objects they are fond of. Furthermore, the suspected CVI group had to search a larger portion of the screen on the conjunction task when the target was presented on a noisy background. This is in concordance with expectations as recent research suggests an increase in complexity and background interference in a scene leads to children with CVI having difficulty finding the target and therefore needing the search a larger proportion of the screen to single out this target (Manley et al., 2022; Walter et al., 2024; Zhang et al., 2022). However, reaction time did not significantly differ due to increase in scene complexity, this could be due to the fact initial reaction times on the feature task were high for the suspected CVI group. Moreover, it is important to note that reaction time was only accounted for if the target was found. If the target had not been found within seven seconds the next trial was started. Longer trials may have led to more targets being found, increasing the targets found and the average reaction time.

VSP differences between the suspected CVI and non-suspected CVI group

Possible explanations were explored as to why no differences were found between the groups, as this was discordant with previous research (Manley et al., 2022; Zihl et al., 2024, Hokken et al., 2024. One possible explanation for this outcome is that in previous studies the CVI group was generally compared to a typically developing control group, highlighting the differences between neurotypical participants and participants with CVI. In turn, the current study does contribute to knowledge on differences between DS children by comparing two groups with DS, indicating the subtle differences between DS children with and without suspected CVI. This could explain the differences within the groups on task type while no differences between the groups were found.

Strengths, limitations, and future directions

Given the lack of research into CVI and HOVF impairments in children with DS and scarcity of suitable diagnostic tools for DS children, the current research introduces a novel paradigm requiring no verbal or motor responses, enabling research into VSP in children with DS while considering deficits which could interfere with assessment. Additionally, no differences were found on valuable gaze samples between the groups, meaning this was of no influence on the findings. However, some limitations need to be addressed. The main limitation in this research was the division of the children into two groups. The five-question screening tool used was derived from previous research using questions which were more likely to elicit positive responses from children with CVI. However as seen in the responses in table 1, a positive response to a screening question is not exclusive to children with suspected CVI. This means children could have been assigned to the non-suspected CVI group while experiencing behavioural symptoms associated with CVI. Considering the current study was specifically researching children with DS the question could be posed whether some questions garnered a positive response due to potential CVI or due to cognitive impairment which can be attributed to DS. (Wilton et al., 2021). Clarity on the official diagnosis for the children participating in the current research would have led to more conclusive findings. However, this emphasises the importance of the current research as it could facilitate in differentiating between DS children with and without CVI.

Second, the non-suspected CVI group was significantly older than the suspected CVI group when looking at chronological age, increasing the expectations and likelihood of finding significant differences between the groups. ABC scores were taken into consideration using the Vineland questionnaire. The ABC scores between the groups did not differ significantly, suggesting development did not influence the results. However, these scores are based on an age matched norm group making the comparison arbitrary across a sample of children with different ages. Therefore, age differences should still be taken into consideration while interpreting the results, as the younger suspected CVI group may have been more affected by the increase in difficulty than the older non-suspected CVI group, leading to the significant findings. In future research age matched groups should be considered, preferably with the addition of a neurotypical group matched for developmental age. Employing this method may give a more complete view of the differences between children with DS with and without CVI, while gaining an overarching understanding of the discrepancies between neurotypical children and children with DS regarding VSP.

Furthermore, a complete overview into the medical and ocular information of each participant including refractive error and visual acuity could have given a better understanding of possible factors which may influence VSP. Refractive error has shown to indicate an increased probability of behaviours associated with CVI (Wilton et al., 2021). As for visual acuity there was a minimal threshold of 0.1 for visual acuity to ensure the participants were able to see the target. Furthermore, no children reported not being able to see the target. However, the variance could have also provided some insight into the differences as low visual acuity has shown to elicit slower reaction times and less accurate search (Barsingerhorn et al., 2018). On the contrary, a near normal visual acuity combined with poor visual functioning strongly indicates issues with HOVF, which are in turn suggestive of CVI (Chandna et al., 2021). This emphasizes the importance of having a comprehensive view of ocular information prior to assessment. This should be taken into consideration in future research, potentially matching participants with the same visual acuity to control for these influences.

The small sample size of just 16 children makes it difficult to generalise the findings of this research. The children were divided into two groups of eight children which led to some analyses being made with effectively less than eight children per group. This was due to the fact the target was not found on all trials by all children. Future research should therefore aim to increase the sample.

Final explorative adjustments in future studies would be to change the order of the assessment to control for mental fatigue as the most conjunction task always follows the feature task in the current study, potentially influencing the performance. This can be controlled by potentially randomizing the trial or to separate testing moments.

Conclusion

To conclude, the results showed no significant difference on visual search performance between the suspected CVI group and the non-suspected CVI group, yet this result could indicate the subtlety of differences between DS children. However, the suspected CVI group showed impaired VSP due to task demands. Furthermore, the suspected CVI group needed more time to find the target on the feature task and searched a larger area of the screen to find the target if the stimuli were presented on a noisy background. Several factors could have led to these results such as the small sample size, age differences or the subtlety in differences between the suspected CVI group and the non-suspected CVI group, shown in the common behavioural features in the five-question screening tool. Nevertheless, although this is a preliminary study, it is a good starting point, possibly leading to the use of an eye-tracking screening tool in clinical practice, as it has proven to be suitable in the assessment of VSP in children with DS. Additionally, the current study has highlighted the extent to which DS children endure HOVF impairment, something which was previously rarely explored. Taking this into consideration, a comprehensive understanding of the visual functions in each individual is essential. This can lead to earlier diagnosis and subsequently more suited education tailored to the needs of DS children. The importance of early diagnosis and suitable treatment is highlighted in several studies, concluding this increases quality of life and prognosis (Fazzi et al., 2021; Idil et al., 2021; Ortibus et al., 2011).

References

Barsingerhorn, A. D., Boonstra, F. N., & Goossens, J. (2018). Symbol discrimination speed in children with visual impairments. *Investigative Ophthalmology & Visual Science*, *59*(10), 3963-3972.

Bellugi, U., Lichtenberger, L., Mills, D., Galaburda, A., & Korenberg, J. R. (1999). Bridging cognition, the brain and molecular genetics: evidence from Williams syndrome. *Trends in neurosciences*, *22*(5), 197-207.

Boonstra, F. N., Bosch, D. G., Geldof, C. J., Stellingwerf, C., & Porro, G. (2022). The multidisciplinary guidelines for diagnosis and referral in cerebral visual impairment. *Frontiers in Human Neuroscience*, *16*, 727565.

Boot, F. H., Pel, J. J. M., Vermaak, M. P., Van der Steen, J., & Evenhuis, H. M. (2013). Delayed visual orienting responses in children with developmental and/or intellectual disabilities. *Journal of Intellectual Disability Research*, *57*(12), 1093-1103.

Bosch, D. G., Boonstra, F. N., Reijnders, M. R., Pfundt, R., Cremers, F. P., & de Vries, B. B. (2014). Chromosomal aberrations in cerebral visual impairment. *european journal of paediatric neurology*, *18*(6), 677-684.

Chandna, A., Ghahghaei, S., Foster, S., & Kumar, R. (2021). Higher visual function deficits in children with cerebral visual impairment and good visual acuity. *Frontiers in Human Neuroscience*, *15*, 711873.

Cohen, J. (1988). Statistical Power Analysis for the Behavioral Sciences. 2nd edn Lawrence Erlbaum: Hillsdale.

Coppus, A. M. (2013). People with intellectual disability: what do we know about adulthood and life expectancy?. *Developmental disabilities research reviews*, *18*(1), 6-16.

Creavin, A. L., & Brown, R. D. (2009). Ophthalmic abnormalities in children with Down syndrome. *Journal of Pediatric Ophthalmology & Strabismus*, *46*(2), 76-82.

Doyle, L., Saunders, K. J., & Little, J. A. (2016). Trying to see, failing to focus: near visual impairment in Down syndrome. *Scientific reports*, *6*(1), 20444.

Dutton, G. N., Saaed, A., Fahad, B., Fraser, R., McDaid, G., McDade, J., ... & Spowart, K. (2004). Association of binocular lower visual field impairment, impaired simultaneous perception, disordered visually guided motion and inaccurate saccades in children with cerebral visual dysfunction—a retrospective observational study. *Eye*, *18*(1), 27-34.

Fazzi, E., Micheletti, S., Calza, S., Merabet, L., Rossi, A., Galli, J., ... & Semeraro, F. (2021). Early visual training and environmental adaptation for infants with visual impairment. *Developmental Medicine & Child Neurology*, *63*(10), 1180-1193.

Fazzi, E., Signorini, S. G., Bova, S. M., La Piana, R., Ondei, P., Bertone, C., ... & Bianchi, P. E. (2007). Spectrum of visual disorders in children with cerebral visual impairment. *Journal of child neurology*, *22*(3), 294-301.

Förster, J., & Dannenberg, L. (2010). GLOMOsys: A systems account of global versus local processing. *Psychological inquiry*, *21*(3), 175-197.

FRCOPHTH, G. N. D. M. (2009). 'Dorsal stream dysfunction'and'dorsal stream dysfunction plus': a potential classification for perceptual visual impairment in the context of cerebral visual impairment?. *Developmental medicine and child neurology*, *51*(3), 170.

Friederichs, E., & Friederichs, P. (2022). Approaching New Clinical Horizons: The Case of Cerebral Visual Impairment (CVI). *Medical Research Archives*, *10*(8).

Fritz, C. O., Morris, P. E., & Richler, J. J. (2012). Effect size estimates: current use, calculations, and interpretation. *Journal of experimental psychology: General*, *141*(1), 2.

van Genderen, M., Dekker, M., Pilon, F., & Bals, I. (2012). Diagnosing cerebral visual impairment in children with good visual acuity. *Strabismus*, *20*(2), 78-83.

Harvey, H., Ashworth, M., Palikara, O., & Van Herwegen, J. (2020). The underreporting of vision problems in statutory documents of children with Williams syndrome and Down syndrome. *Journal of Autism and Developmental Disorders*, *50*(12), 4553-4556.

Hahn, B., Ross, T. J., & Stein, E. A. (2006). Neuroanatomical dissociation between bottom–up and top–down processes of visuospatial selective attention. *Neuroimage*, *32*(2), 842-853.

Hokken, M. J., Krabbendam, E., van der Zee, Y. J., & Kooiker, M. J. (2023). Visual selective attention and visual search performance in children with CVI, ADHD, and Dyslexia: a scoping review. *Child Neuropsychology*, *29*(3), 357-390.

Hokken, M. J., Stein, N., Kooiker, M. J., & Pel, J. J. (2024). A novel gaze-based visual search task for children with CVI: A twin study. *British Journal of Visual Impairment*, 02646196241247973.

İdil, Ş. A., Altınbay, D., Şahlı, E., Kızıltunç, P. B., Timlioğlu-İper, H. S., Turan, K. E., ... & Bektaş, F. M. (2021). Ophthalmologic approach to babies with cerebral visual impairment. *The Turkish Journal of Pediatrics*, *63*(1), 1-10.

Jarrold, C., & Baddeley, A. (2001). Short-term memory in Down syndrome: Applying the working memory model. *Down syndrome research and practice*, *7*(1), 17-23.

Itzhak, N. B., Kooiker, M. J. G., Pel, J. J. M., & Ortibus, E. (2023). Including visual orienting functions into cerebral visual impairment screening: Reliability, variability, and ecological validity. *Research in Developmental Disabilities*, *132*, 104391.

Klein, B. P., & Mervis, C. B. (1999). Contrasting patterns of cognitive abilities of 9-and 10-year-olds with Williams syndrome or Down syndrome. *Developmental neuropsychology*, *16*(2), 177-196.

Kong, L., Fry, M., Al-Samarraie, M., Gilbert, C., & Steinkuller, P. G. (2012). An update on progress and the changing epidemiology of causes of childhood blindness worldwide. *Journal of American Association for Pediatric Ophthalmology and Strabismus*, *16*(6), 501-507.

Kooiker, M. J., Pel, J. J., & van der Steen, J. (2015). The relationship between visual orienting responses and clinical characteristics in children attending special education for the visually impaired. *Journal of child neurology*, *30*(6), 690-697.

Kooiker, M. J., Pel, J. J., Verbunt, H. J., de Wit, G. C., van Genderen, M. M., & van der Steen, J. (2016a). Quantification of visual function assessment using remote eye tracking in children: validity and applicability. *Acta ophthalmologica*, *94*(6), 599-608.

Kooiker, M. J., Verbunt, H. J., van der Steen, J., & Pel, J. J. (2019). Combining visual sensory functions and visuospatial orienting functions in children with visual pathology: a longitudinal study. *Brain and Development*, *41*(2), 135-149.

Krinsky-McHale, S. J., Silverman, W., Gordon, J., Devenny, D. A., Oley, N., & Abramov, I. (2014). Vision deficits in adults with Down syndrome. *Journal of Applied Research in Intellectual Disabilities*, *27*(3), 247-263.

Lam, F. C., Lovett, F., & Dutton, G. N. (2010). Cerebral visual impairment in children: a longitudinal case study of functional outcomes beyond the visual acuities. *Journal of Visual Impairment & Blindness*, *104*(10), 625-635.

Little, J. A., Woodhouse, J. M., Lauritzen, J. S., & Saunders, K. J. (2007). The impact of optical factors on resolution acuity in children with Down syndrome. *Investigative ophthalmology & visual science*, *48*(9), 3995-4001.

Little, J. A., Woodhouse, J. M., Lauritzen, J. S., & Saunders, K. J. (2009). Vernier acuity in Down syndrome. *Investigative ophthalmology & visual science*, *50*(2), 567-572.

Lueck, A. H., Dutton, G. N., & Chokron, S. (2019, October). Profiling children with cerebral visual impairment using multiple methods of assessment to aid in differential diagnosis. In *Seminars in pediatric neurology* (Vol. 31, pp. 5-14). WB

Malak, R., Kotwicka, M., Krawczyk-Wasielewska, A., Mojs, E., & Szamborski, W. (2013). Motor skills, cognitive development and balance functions of children with Down syndrome. *Annals of Agricultural and Environmental Medicine*, *20*(4).

Manley, C. E., Bennett, C. R., & Merabet, L. B. (2022). Assessing higher-order visual processing in cerebral visual impairment using naturalistic virtual-reality-based visual search tasks. *Children*, *9*(8), 1114.

Manley, C. E., Bauer, C. M., Bex, P. J., & Merabet, L. B. (2023). Impaired visuospatial processing in cerebral visual impairment revealed by performance on a conjunction visual search task. *British Journal of Visual Impairment*, 02646196231187550.

Manley, C. E., Walter, K., Micheletti, S., Tietjen, M., Cantillon, E., Fazzi, E. M., ... & Merabet, L. B. (2023). Object identification in cerebral visual impairment characterized by gaze behavior and image saliency analysis. *Brain and Development*, *45*(8), 432-444.

McConnell, E. L., Saunders, K. J., & Little, J. A. (2021). What assessments are currently used to investigate and diagnose cerebral visual impairment (CVI) in children? A systematic review. *Ophthalmic and Physiological Optics*, *41*(2), 224-244.

Mooney, S. W., Alam, N. M., & Prusky, G. T. (2021). Tracking-based interactive assessment of saccades, pursuits, visual field, and contrast sensitivity in children with brain injury. *Frontiers in Human Neuroscience*, *15*, 737409.

Müller, H. J., & Krummenacher, J. (2006). Visual search and selective attention. *Visual Cognition*, *14*(4-8), 389-410.

Ortibus, E., Laenen, A., Verhoeven, J., De Cock, P., Casteels, I., Schoolmeesters, B., ... & Lagae, L. (2011). Screening for cerebral visual impairment: value of a CVI questionnaire. *Neuropediatrics*, *42*(04), 138-147.

Pehere, N., Chougule, P., & Dutton, G. N. (2018). Cerebral visual impairment in children: Causes and associated ophthalmological problems. *Indian journal of ophthalmology*, *66*(6), 812-815.

Philip, S. S., & Dutton, G. N. (2014). Identifying and characterising cerebral visual impairment in children: a review. *Clinical and Experimental Optometry*, *97*(3), 196-208.

Pilling, R. F., Allen, L., Bowman, R., Ravenscroft, J., Saunders, K. J., & Williams, C. (2023). Clinical assessment, investigation, diagnosis and initial management of cerebral visual impairment: a consensus practice guide. *Eye*, *37*(10), 1958-1965.

Porter, M. A., & Coltheart, M. (2006). Global and local processing in Williams syndrome, autism, and Down syndrome: perception, attention, and construction. *Developmental Neuropsychology*, *30*(3), 771-789.

Postolache, L., Monier, A., & Lhoir, S. (2021). Neuro-ophthalmological manifestations in children with Down syndrome: current perspectives. *Eye and Brain*, 193-203.

Postolache, L. (2019). Abnormalities of the optic nerve in Down syndrome and associations with visual acuity. *Frontiers in neurology*, *10*, 460112.

Purpura, G., Bacci, G. M., Bargagna, S., Cioni, G., Caputo, R., & Tinelli, F. (2019). Visual assessment in Down Syndrome: The relevance of early visual functions. *Early human development*, *131*, 21-28.

Roberts, J. E., Price, J., & Malkin, C. (2007). Language and communication development in Down syndrome. *Mental retardation and developmental disabilities research reviews*, *13*(1), 26-35.

Saidkasimova, S., Bennett, D. M., Butler, S., & Dutton, G. N. (2007). Cognitive visual impairment with good visual acuity in children with posterior periventricular white matter injury: a series of 7 cases. *Journal of American Association for Pediatric Ophthalmology and Strabismus*, *11*(5), 426-430.

Sakki, H. E., Dale, N. J., Sargent, J., Perez-Roche, T., & Bowman, R. (2018). Is there consensus in defining childhood cerebral visual impairment? A systematic review of terminology and definitions. *British Journal of Ophthalmology*, *102*(4),424- 432.

Solebo, A. L., Teoh, L., & Rahi, J. (2017). Epidemiology of blindness in children. *Archives of disease in childhood*, *102*(9), 853-857.

Sparrow, S. S., Cicchetti, D. V., & Saulnier, C. A. (2016). *Vineland Adaptive Behavior Scales, (Vineland-3) --Complete Kit*. PsychCorp.

Stiers, P., Vanderkelen, R., Vanneste, G., Coene, S., De Rammelaere, M., & Vandenbussche, E. (2002). Visual–perceptual impairment in a random sample of children with cerebral palsy. *Developmental medicine and child neurology*, *44*(6), 370-382.

Treisman, A. (2013). How the deployment of attention determines what we see. In *Progress in Psychological Science around the World. Volume 1 Neural, Cognitive and Developmental Issues.* (pp. 245-277). Psychology Press.

Ugurlu, A., & Altinkurt, E. (2020). Ophthalmologic manifestations and retinal findings in children with down syndrome. *Journal of Ophthalmology*, *2020*(1), 9726261.

Walter, K., Manley, C. E., Bex, P. J., & Merabet, L. B. (2024). Visual search patterns during exploration of naturalistic scenes are driven by saliency cues in individuals with cerebral visual impairment. *Scientific Reports*, *14*(1), 3074.

Wan, Y. T., Chiang, C. S., Chen, S. C. J., Wang, C. C., & Wuang, Y. P. (2015). Profiles of visual perceptual functions in Down syndrome. *Research in Developmental Disabilities*, *37*, 112-118.

Wang, P. P., & Bellugi, U. (1994). Evidence from two genetic syndromes for a dissociation between verbal and visual-spatial short-term memory. *Journal of clinical and experimental Neuropsychology*, *16*(2), 317-322.

de Weger, C., Boonstra, F. N., & Goossens, J. (2021). Differences between children with Down syndrome and typically developing children in adaptive behaviour, executive functions and visual acuity. *Scientific Reports*, *11*(1), 7602.

Wilton, G. J., Woodhouse, R., Vinuela-Navarro, V., England, R., & Woodhouse, J. M. (2021). Behavioural features of cerebral visual impairment are common in children with down syndrome. *Frontiers in human neuroscience*, *15*, 673342.

Zahidi, A. A., Vinuela-Navarro, V., & Woodhouse, J. M. (2018). Different visual development: norms for visual acuity in children with Down's syndrome. *Clinical and Experimental Optometry*, *101*(4), 535-540.

Zhang, X., Manley, C. E., Micheletti, S., Tesic, I., Bennett, C. R., Fazzi, E. M., & Merabet, L. B. (2022). Assessing visuospatial processing in cerebral visual impairment using a novel and naturalistic static visual search task. *Research in developmental disabilities*, *131*, 104364.

Zihl, J., Dutton, G. N., Zihl, J., & Dutton, G. N. (2015). Visual disorders. *Cerebral Visual Impairment in Children: Visuoperceptive and Visuocognitive Disorders*, 61-115.

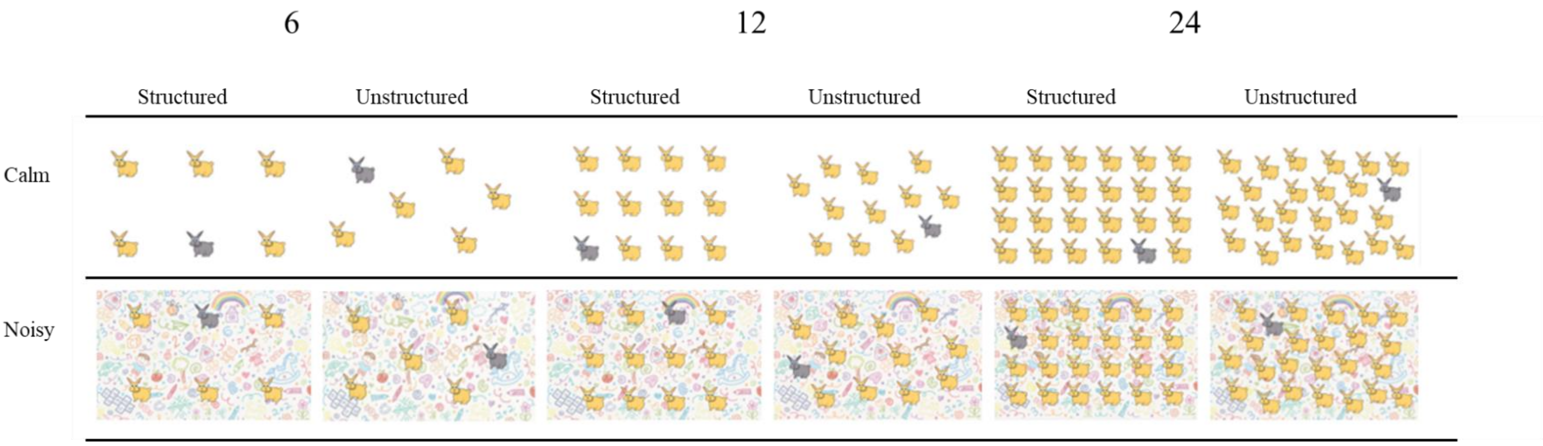
Zihl, J., Unterberger, L., & Lippenberger, M. (2024). Visual and cognitive profiles in children with and without cerebral visual impairment. *British Journal of Visual Impairment*, *42*(2), 557-576.

Zuidhoek, S. (2020). CVI in the Picture. *When the Brain Is the Cause of Visual Impairment in Children. Huizen: Visio*.

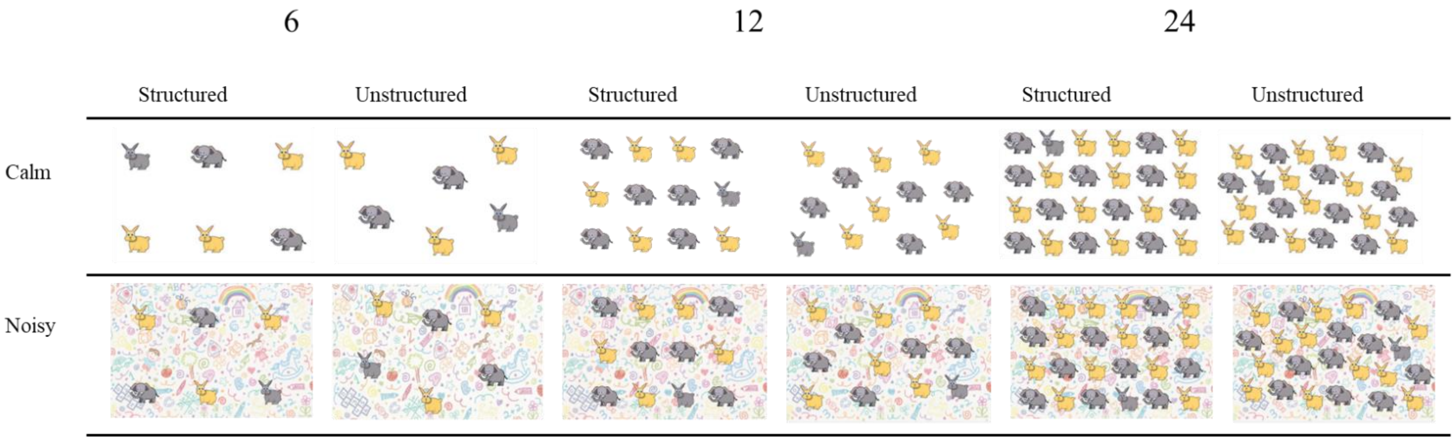
Appendix A

All trials of the feature and conjunction animal search task

Feature task



Conjunction task



Note: a depiction of all different trials within each task showing different set sizes, structures and backgrounds

Appendix B

```
function CorrectScriptEllipse

close all;

% Define the x and y coordinates of the points
data = readtable("");

x = data.X;
y = data.Y;


% Calculate the ellipse parameters
ellipseData = fit_ellipse(x, y);

% Extract the ellipse parameters
xCenter = ellipseData.X0;   % x-coordinate of the ellipse center
yCenter = ellipseData.Y0;   % y-coordinate of the ellipse center
semiMajorAxis = ellipseData.long_axis/2;   % semi-major axis
semiMinorAxis = ellipseData.short_axis/2;  % semi-minor axis
rotationAngle = ellipseData.phi;   % rotation angle in radians
area = pi * semiMajorAxis * semiMinorAxis;                  % area

% Print the ellipse parameters
fprintf('Center: (%f, %f)\n', xCenter, yCenter);
fprintf('Semi-major axis: %f\n', semiMajorAxis);
fprintf('Semi-minor axis: %f\n', semiMinorAxis);
fprintf('Rotation angle: %f radians\n', rotationAngle);
fprintf('Area: %f\n)', area);

function ellipse_t = fit_ellipse( x,y,~ )
%
% fit_ellipse - finds the best fit to an ellipse for the given set of points.
%
% Format:   ellipse_t = fit_ellipse( x,y,axis_handle )
%
% Input:    x,y         - a set of points in 2 column vectors. AT LEAST 5 points
are needed !
%           axis_handle - optional. a handle to an axis, at which the estimated
ellipse
%                         will be drawn along with it's axes
%
% Output:   ellipse_t - structure that defines the best fit to an ellipse
%                       a           - sub axis (radius) of the X axis of the non-
tilt ellipse
%                       b           - sub axis (radius) of the Y axis of the non-
tilt ellipse
%                       phi         - orientation in radians of the ellipse (tilt)
%                       X0          - center at the X axis of the non-tilt ellipse
%                       Y0          - center at the Y axis of the non-tilt ellipse
%                       X0_in       - center at the X axis of the tilted ellipse
%                       Y0_in       - center at the Y axis of the tilted ellipse
%                       long_axis   - size of the long axis of the ellipse
%                       short_axis  - size of the short axis of the ellipse
%                       status      - status of detection of an ellipse
%
% Note:     if an ellipse was not detected (but a parabola or hyperbola), then
```

```
%           an empty structure is returned
%
=================================================================================
===
%                  Ellipse Fit using Least Squares criterion
%
=================================================================================
===
% We will try to fit the best ellipse to the given measurements. the mathematical
% representation of use will be the CONIC Equation of the Ellipse which is:
%
%    Ellipse = a*x^2 + b*x*y + c*y^2 + d*x + e*y + f = 0
%
% The fit-estimation method of use is the Least Squares method (without any
weights)
% The estimator is extracted from the following equations:
%
%    g(x,y;A) := a*x^2 + b*x*y + c*y^2 + d*x + e*y = f
%
%    where:
%       A   - is the vector of parameters to be estimated (a,b,c,d,e)
%       x,y - is a single measurement
%
% We will define the cost function to be:
%
%   Cost(A) := (g_c(x_c,y_c;A)-f_c)'*(g_c(x_c,y_c;A)-f_c)
%            = (X*A+f_c)'*(X*A+f_c)
%            = A'*X'*X*A + 2*f_c'*X*A + N*f^2
%
%   where:
%       g_c(x_c,y_c;A) - vector function of ALL the measurements
%                        Each element of g_c() is g(x,y;A)
%       X              - a matrix of the form: [x_c.^2, x_c.*y_c, y_c.^2, x_c, y_c
]
%       f_c            - is actually defined as ones(length(f),1)*f
%
% Derivation of the Cost function with respect to the vector of parameters "A"
yields:
%
%   A'*X'*X = -f_c'*X = -f*ones(1,length(f_c))*X = -f*sum(X)
%
% Which yields the estimator:
%
%
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
%       |  A_least_squares = -f*sum(X)/(X'*X) ->(normalize by -f) = sum(X)/(X'*X)
|
%
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
%
% (We will normalize the variables by (-f) since "f" is unknown and can be
accounted for later on)
%
% NOW, all that is left to do is to extract the parameters from the Conic
Equation.
% We will deal the vector A into the variables: (A,B,C,D,E) and assume F = -1;
%
%    Recall the conic representation of an ellipse:
```

```
%
%       A*x^2 + B*x*y + C*y^2 + D*x + E*y + F = 0
%
% We will check if the ellipse has a tilt (=orientation). The orientation is
present
% if the coefficient of the term "x*y" is not zero. If so, we first need to remove
the
% tilt of the ellipse.
%
% If the parameter "B" is not equal to zero, then we have an orientation (tilt) to
the ellipse.
% we will remove the tilt of the ellipse so as to remain with a conic
representation of an
% ellipse without a tilt, for which the math is more simple:
%
% Non tilt conic rep.:  A`*x^2 + C`*y^2 + D`*x + E`*y + F` = 0
%
% We will remove the orientation using the following substitution:
%
%   Replace x with cx+sy and y with -sx+cy such that the conic representation is:
%
%   A(cx+sy)^2 + B(cx+sy)(-sx+cy) + C(-sx+cy)^2 + D(cx+sy) + E(-sx+cy) + F = 0
%
%   where:      c = cos(phi)    ,   s = sin(phi)
%
%   and simplify...
%
%       x^2(A*c^2 - Bcs + Cs^2) + xy(2A*cs +(c^2-s^2)B -2Ccs) + ...
%           y^2(As^2 + Bcs + Cc^2) + x(Dc-Es) + y(Ds+Ec) + F = 0
%
%   The orientation is easily found by the condition of (B_new=0) which results
in:
%
%   2A*cs +(c^2-s^2)B -2Ccs = 0  ==> phi = 1/2 * atan( b/(c-a) )
%
%   Now the constants   c=cos(phi)  and  s=sin(phi)  can be found, and from them
%   all the other constants A`,C`,D`,E` can be found.
%
%   A`  = A*c^2 - B*c*s + C*s^2                  D`  = D*c-E*s
%   B`  = 2*A*c*s +(c^2-s^2)*B -2*C*c*s = 0      E`  = D*s+E*c
%   C`  = A*s^2 + B*c*s + C*c^2
%
% Next, we want the representation of the non-tilted ellipse to be as:
%
%       Ellipse = ( (X-X0)/a )^2 + ( (Y-Y0)/b )^2 = 1
%
%       where:  (X0,Y0) is the center of the ellipse
%               a,b     are the ellipse "radiuses" (or sub-axis)
%
% Using a square completion method we will define:
%
%       F`` = -F` + (D`^2)/(4*A`) + (E`^2)/(4*C`)
%
%       Such that:    a`*(X-X0)^2 = A`(X^2 + X*D`/A`  + (D`/(2*A`))^2 )
%                     c`*(Y-Y0)^2 = C`(Y^2 + Y*E`/C`  + (E`/(2*C`))^2 )
%
%       which yields the transformations:
%
```

```
%           X0  =   -D`/(2*A`)
%           Y0  =   -E`/(2*C`)
%           a   =   sqrt( abs( F``/A` ) )
%           b   =   sqrt( abs( F``/C` ) )
%
% And finally we can define the remaining parameters:
%
%   long_axis   = 2 * max( a,b )
%   short_axis  = 2 * min( a,b )
%   Orientation = phi
%
%
% initialize
orientation_tolerance = 1e-3;
% empty warning stack
lastwarn( '' );
% prepare vectors, must be column vectors
x = x(:); X_data = x;
y = y(:); Y_data = y;
% remove bias of the ellipse - to make matrix inversion more accurate. (will be
added later on).
mean_x = mean(x);
mean_y = mean(y);
x = x-mean_x;
y = y-mean_y;
% the estimation for the conic equation of the ellipse
X = [x.^2, x.*y, y.^2, x, y ];
a = sum(X)/(X'*X);
% check for warnings
if ~isempty( lastwarn )
    disp( 'stopped because of a warning regarding matrix inversion' );
    ellipse_t = [];
    return
end
% extract parameters from the conic equation
[a,b,c,d,e] = deal( a(1),a(2),a(3),a(4),a(5) );
% remove the orientation from the ellipse
if ( min(abs(b/a),abs(b/c)) > orientation_tolerance )

    orientation_rad = 1/2 * atan( b/(c-a) );
    cos_phi = cos( orientation_rad );
    sin_phi = sin( orientation_rad );
    [a,~,c,d,e] = deal(...
        a*cos_phi^2 - b*cos_phi*sin_phi + c*sin_phi^2,...
        0,...
        a*sin_phi^2 + b*cos_phi*sin_phi + c*cos_phi^2,...
        d*cos_phi - e*sin_phi,...
        d*sin_phi + e*cos_phi );
    [mean_x,mean_y] = deal( ...
        cos_phi*mean_x - sin_phi*mean_y,...
        sin_phi*mean_x + cos_phi*mean_y );
else
    orientation_rad = 0;
    cos_phi = cos( orientation_rad );
    sin_phi = sin( orientation_rad );
end
% check if conic equation represents an ellipse
test = a*c;
```

```
% switch (1)
% case (test>0),  status = '';
% case (test==0), status = 'Parabola found';  warning( 'fit_ellipse: Did not
locate an ellipse' );
% case (test<0),  status = 'Hyperbola found'; warning( 'fit_ellipse: Did not
locate an ellipse' );
% end
% if we found an ellipse return it's data
%if (test>0)

    % make sure coefficients are positive as required
    if (a<0), [a,c,d,e] = deal( -a,-c,-d,-e ); end

    % final ellipse parameters
    X0          = mean_x - d/2/a;
    Y0          = mean_y - e/2/c;
    F           = 1 + (d^2)/(4*a) + (e^2)/(4*c);
    [a,b]       = deal( sqrt( F/a ),sqrt( F/c ) );
    long_axis   = 2*max(a,b);
    short_axis  = 2*min(a,b);
    % rotate the axes backwards to find the center point of the original TILTED
ellipse
    R           = [ cos_phi sin_phi; -sin_phi cos_phi ];
    P_in        = R * [X0;Y0];
    X0_in       = P_in(1);
    Y0_in       = P_in(2);

    % pack ellipse into a structure
    ellipse_t = struct( ...
        'a',a,...
        'b',b,...
        'phi',orientation_rad,...
        'X0',X0,...
        'Y0',Y0,...
        'X0_in',X0_in,...
        'Y0_in',Y0_in,...
        'long_axis',long_axis,...
        'short_axis',short_axis,...
        'status','' );
% else
%     % report an empty structure
%     ellipse_t = struct( ...
%         'a',[],...
%         'b',[],...
%         'phi',[],...
%         'X0',[],...
%         'Y0',[],...
%         'X0_in',[],...
%         'Y0_in',[],...
%         'long_axis',[],...
%         'short_axis',[],...
%         'status',status );
% end
% check if we need to plot an ellipse with it's axes.
%if (nargin>2) & ~isempty( axis_handle ) & (test>0)

    % rotation matrix to rotate the axes with respect to an angle phi
    R = [ cos_phi sin_phi; -sin_phi cos_phi ];
```

```
    % the axes
    ver_line        = [ [X0 X0]; Y0+b*[-1 1] ];
    horz_line       = [ X0+a*[-1 1]; [Y0 Y0] ];
    new_ver_line    = R*ver_line;
    new_horz_line   = R*horz_line;

    % the ellipse
    theta_r         = linspace(0,2*pi);
    ellipse_x_r     = X0 + a*cos( theta_r );
    ellipse_y_r     = Y0 + b*sin( theta_r );
    rotated_ellipse = R * [ellipse_x_r;ellipse_y_r];

    % draw
%     hold_state = get( axis_handle,'NextPlot' );
%     set( axis_handle,'NextPlot','add' );
    plot(X_data,Y_data,'o'); hold on;
    plot( new_ver_line(1,:),new_ver_line(2,:),'r' );
    plot( new_horz_line(1,:),new_horz_line(2,:),'r' );
     plot( rotated_ellipse(1,:),rotated_ellipse(2,:),'r' );
    axis([0 1920 0 1080]);
%     set( axis_handle,'NextPlot',hold_state );
%end
```

Appendix C

Wilcoxon's Signed Rank test for reaction time, gaze accuracy and gaze area within groups for the feature vs the conjunction task

Group	**Variable**	**Feature**		**Conjunction**		**Z**	***P*-value**	***r***
		Mdn	*IQR*	*Mdn*	*IQR*			
Non-suspected CVI								
	Acc (%)	66.65	97.93	41.70	43.80	.851	.395	.301
	RT (ms)	869.42	858.07	1635.53	734.79	-.943	.345	.385
	GA (%)	16.67	3.04	25.62	8.03	-2.201	.028*	.899
Suspected CVI								
	Acc (%)	54.20	58.38	41.70	33.33	2.201	.028*	.832
	RT (ms)	1287.75	800.84	2081.13	1179.07	-1.992	.046*	.813
	GA (%)	20.98	8.47	31.70	9.97	-2.023	.043*	.905

Note: Significance levels for Wilcoxon's signed rank test were set at * $p < 0.05$

Appendix D

Friedman's test and Wilcoxon's signed rank's test to measure VSP differences between set size, background and structureon the feature and the conjunction task

			Set size			Structure			Background		
Group	**Task**		χ^2 (2)	*p*-value	Kendall's W	Z	*p*-value	*r*	Z	*p*-value	*r*
Non-Suspected CVI	Feature	Acc (%)	1.000	.607	.063	-1.000	.317	.354	-.447	.655	.158
		RT (ms)	.400	.819	.040	-.944	.345	.422	-.135	.893	.060
		GAr (%)	2.800	.247	.280	-1.483	.138	.663	-1.483	.138	.663
	Conjunction	Acc (%)	7.280	.026	.455	-.333	.739	.118	-.108	.914	.038
		RT (ms)	6.500	.039	.813	-1.183	.237	.447	-1.352	.176	.511
		GAr (%)	4.500	.105	.563	-.676	.499	.256	-1.183	.237	.447
Suspected CVI	Feature	Acc (%)	3.391	.183	.212	-.378	.705	.133	-.966	.334	.341
		RT (ms)	1.000	.607	.083	-.338	.735	.128	-2.100	.036*	.742
		GAr (%)	5.333	.069	.444	-1.521	.128	.575	-.700	.484	.247
	Conjunction	Acc (%)	6.700	.035	.479	-.707	.480	.267	-1.633	.102	.730
		RT (ms)	6.500	.039	.813	-.944	.345	.422	-.135	.893	.060
		GAr (%)	3.000	.223	.223	-.674	.600	.301	-2.023	.043*	.904

Note: Friedman's test adjusted significance level using a Bonferroni correction was set at * $p < 0.17$. Significance levels for Wilcoxon's signed rank test were set at * $p < 0.05$