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Research Article

VEP visual acuity in children with cortical visual impairment

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Abstract

Given improvements in neonatal care and the increased survival rates of infants born pre-term, Cortical Visual Impairment (CVI) is now the leading cause of visual impairment (VI) in the developed world. In this study, Step VEPS, transient VEPS and Vernier Sweep VEPs all demonstrated unbiased relationships with Preferential looking (PL) cards over the whole range of Visual Acuity (VA) in children with CVI, allowing equations for clinical use to be derived. The results also suggested that a slower, vernier steady-state stimulus of 80% contrast and presented with the Step VEP algorithm could further improve VA agreement with PL and optimise developmental sensitivity.

An eye tracking device has proved very useful in the clinical assessment of this cohort. It is also now known that children can have good VA and CVI, and that sweep VEPS can highlight higher processing deficits. As well as negative findings, compensatory neuroplasticity is thought to occur during maturation and it is now realistic to study this mechanism, and other age-related changes across VI with functional tests and neuroimaging (including VEPS). A cross-sectional study of adults would highlight CVI's ultimate functional limitations.

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Introduction

Cerebral Visual Impairment and Cortical Visual Impairment (CVI) are slightly different terms for pre-perinatal hypoxic damage to the post-chiasmal visual pathway causing a reduction in Visual Acuity (VA) and other functions [1,2]. Terminology in the literature has been governed by geography [3] and the work that the scientific researcher is exposed to. Given improvements in neonatal care and the increased survival rates of infants born pre-term, CVI is now the leading cause of visual impairment in the developed world [4]; in 2000, 197 diagnoses of CVI were made among 483 children born with Severe Visual Impairment (SVI) in the UK [5].

Table 1 ranks the visual manifestations of CVI according to prevalence; the majority of patients have impaired visual perception, reduced VA, altered smooth pursuit, strabismus, and nystagmus. In Cerebral Palsy (CP), the proximity of lesions to the motor pathways (i.e. periventricular leukomalacia) to the visual pathways means that CP and CVI often co-occur [6]. In children with CP, the severity of Visual Impairment (VI) and motor deficits (MD) tends to correlate [7], and vision is known to improve with age given maturation of the visual system and adaptive neuroplasticity [8].

MD can make any assessment difficult [9,10] and solutions proposed for directing VEP stimuli onto the retina given poor VA [11] are highly relevant. Projection of the stimulus onto three walls of a room may also help, however, ISCEV field size requirements would be exceeded [12,13]. Historically, t-VEPS were used to test children and other challenging cohorts such as those with CVI, and extrapolation of the spatial frequency-amplitude function was used to establish a threshold [14]. However, given its apparent ability to provide complete VA assessment of all patients, the sweep VEP dominated the academic literature from the mid-eighties, with different tests emerging after the Millenium [15]. Equations were derived to express Step VEP VA in terms of subjective VA in a broad Neuro-Ophthalmological cohort [11] and optically degraded normal adults [16], providing a metric that was easy for all

Table 1: Functional Deficits in Children with CVI ranked by prevalence [2].

	%
Impaired Visual Perception	89
Reduced Visual Acuity	87
Altered Smooth Pursuit	79
Strabismus	73
Nystagmus	73
Reduced Contrast Sensitivity	48
Altered Fixation	48
Abnormal Ocular Movements	36
Altered Saccades	34
Visual Field Deficits	6

clinicians to interpret. Publication of this methodology meant that similar formulae could be calculated by workers using commercial VEP systems.

A recent systematic review [17-19] presented results from just four studies of VA in CVI where both sweep VEPs and PL were measured successfully, and these results will be considered alongside locally collected data using t-VEPs and Step VEPs. The aim of the study is to investigate the relationship between VEP and subjective VA in children with CVI.

Methods

Prospective patients referred to a pediatric neuro-ophthalmological clinic had VA assessed with Preferential Looking cards and either t-VEPs or Step VEPs. The VA comparison of PL and Step VEPs in the whole cohort using has been published previously [11]. However, further consideration of the complete clinical work-up allowed a small proportion of these children to be sub-categorized as having CVI. The uniqueness of this study, enabled by the technical development of the Step VEP, meant that a-priori power calculations for the comparisons was not possible. An equivalent group of children receiving t-VEPs were also identified [15] and this thesis also provides details of the stimulation and recording parameters of VEPs, which met with contemporaneous ISCEV technical standards [20]. Children wore any prescribed refractive correction for all modalities of assessment. Separate analyses were performed on successful pairs of t-VEPs and PL, Step VEPS and PL, and sweep VEP vs PL from the work of Good, et al. [19], Lim, et al. [20] and Watson, et al. [21].

The agreement and relationship between methods were investigated using Bland-Altman Analysis (BA-A) [22] and regression, according to our published methodology [16]. If BA-A revealed an absence of bias in the agreement between tests across all VA, then the relationship was expressed using a regression equation.

Results

31 children successfully underwent Step VEPs and PL and had a mean age of 2.8 years (SD 3.20) and a mean VA of 0.70 LogMAR (0.51). 19 children successfully underwent t-VEPs and PL and had a mean age of 2.47 years (4.20), with a mean VA of 1.08 LogMAR (0.58). While the ages are matched, the difference in VA is both clinically and statistically significant (0.38 poorer for the t-VEP group). WHO definitions of visual impairment (Table 2) place the t-VEP and Step VEP groups in the 'severe' and 'moderate' categories respectively.

The key parameters of BA-A and regression analyses are given in Table 3 and exclude the data of two patients in the Step VEP group that were classed as outliers. This does not prevent the resulting equations being applicable to all children with CVI completing the test. BA-A revealed that no bias was present across the range of VA for either group in this study and so regression equations were derived (Table 4). A post-hoc power calculation demonstrated that these analyses have 100% power. Bias was also absent in the vernier sweep VEP data of Watson, et al. [21] allowing an additional equation was derived. All these equations required a constant term to fulfil the mathematical requirement of homoscedasticity [23].

Discussion

The first finding is that CVI with VA in WHO's 'Moderate Visual Impairment' category is just as common as 'Severe Visual Impairment'. Moreover, two recent publications [24,25] found near normal VA alongside higher processing deficits and a diagnosis of CVI.

Adequate BA-A test statistics for Step VEPS and the Vernier sweep VEPs of Watson, et al. [21] suggest the vernier offset stimulus, and the real-time analysis and presentation are more suited to these children than swept vertical sine-wave gratings. The longer trajectory to maturation for vernier than sinusoidal grating sweep VEP VA (four years vs one year) [26] contributes to the explanation. Incidentally, this duration is doubled for psychophysical VA employing static versions of the same stimuli [27] emphasizing the effect of temporal modulation. The normal maturation of Step VEP VA has yet to be studied, but we do know that suprathreshold pattern-onset VEPs show latency [28] and morphological changes [29] into adulthood.

Table 2: World Health Organisation Classifications of Visual Impairment (VI) [5].

WHO VI category	Snellen VA range	Decimal VA Min	Decimal VA Max	LogMAR VA Min	LogMAR VA Max
mild	6/12 - 6/18	2	3	0.30	0.48
moderate	6/18 - 6/60	3	10	0.48	1.00
severe	6/60 - 3/60	10	20	1.00	1.30
Blind	> 3/60		> 20		> 1.3

Table 3: BA-A and regression parameters in comparisons of VEP and PL VA in CVI.

Author	Year	VEP modality	Stimulus	N	Bias	r^2	F	P
Mackay	2022f	Step	Checkerboard 7.78Hz reversal	29	No	0.42	14.28	0.001
Mackay	2022f	Transient	Checkerboard 1Hz reversal	21	No	0.92	36.44	< 0.001
Good	2001	Sweep	Vertical sinusoidal grating 5Hz onset	23	yes			
Watson	2009	Sweep	Vertical sinusoidal grating 7.5Hz reversal	29	yes			
Watson	2009	Sweep	Vertical vernier offsets 5Hz	29	No	0.33	12.78	0.001
Lim	2005	Sweep	Grating	19	yes			

Table 4: Equations expressing Step VEP VA in terms of subjective VA.

Equation	Subjects	First Author	Year of publication
$VA_{PL}=0.59VA_{STEP}-0.19$	Pediatric CVI	This study	
$VA_{PL}=0.94VA_{t\text{-}VEP}-0.79$	Pediatric CVI	This study	
$VA_{PL}=0.75VA_{vernier\ sweep}-0.19$	Pediatric CVI	Watson	2009

The relatively large test statistics for the t-VEP stimulus in this study reflect consistent results between patients, suggesting that a slower stimulus rate is suited to children with CVI. These consistently good agreements between tVEPS and PL parallels larger step VEPS studies in adults [16] and pediatric patients [11]. Also, a recent sweep VEP study [30] used a slower reversal rate for grating VA and contrast sensitivity measurement in this cohort.

Low luminance has now been proven to work well in sweep VEP VA assessment of CVI [31] but technical nuances require expert ophthalmological and scientific input at all times. In the 2012 Smith-Kettlewell study [30], the electrophysiological contrast sensitivity function has a larger dynamic range across patient ability than the spatial-frequency amplitude function, making it distinctively useful in monitoring individual progression over time. Performing VEPs at the peak of an individual contrast sensitivity function (typically 80%) may improve SNR (Gordon Dutton personal communication) and make the test more sensitive to anatomical and physiological development.

Sweep VEP VA (the outcome rather than the whole spatial frequency-amplitude function) has demonstrated improvement over time in children with CVI [32], and complementary functional assessments (Table 5; [33]) and neuroimaging could give further insights into the temporal processing limitations of these patients, and the effect of feedback from the dorsal and ventral streams on VEPs [34]. Functional neuroimaging would also be useful in the investigation of the neuroplastic compensatory processes [25].

The discovery of complex motion processing deficits in the absence of significant VA loss in CVI [24] highlights the limitations of the WHO definitions of VI. In the same demographic, other dorsal stream deficits were detected by the Higher Visual Function Question Inventory (HVFQI-51) [25] and there is clearly much left to learn about this condition.

Theoretically, the functional deficits of CVI should affect PL scores of VA more than VEPs given their need for eye movement. However, that did not prevent us finding good agreement between them in our study and one published experiment. These factors may, however, have contributed to poorer agreements during historical comparisons of sweep VEP and PL VA [19,20]. An eye tracking device presenting gratings agreed well with PL in pediatric CVI [35] and could become clinically useful in this cohort.

Table 5: Assessment types identified by a recent systematic review [35].

	Assessments utilised in children with CVI
1.	Medical History
2	Vision Assessment/Ophthalmologic Exam
3	Neuroimaging
4	Visual Behaviour/Direct Observations
5	Structured History Taking
6	Visual Perception Tests
7	Ocular Movement and Posture Assessment
8	Intelligence/IQ Assessment
9.	Clinical Electrophysiology
10	Neurodevelopmental Tests

Conclusion

Knowledge of the normal maturation of Step VEPs should aid its interpretation in children, and for those with CVI, agreement with PL could be enhanced by employing a slower, Vernier stimulus. Consideration of the spatial-frequency-amplitude function may provide further insights to development, and a longitudinal, functional study including VEPs would reveal detail about maturation in CVI including compensatory neuroplasticity. An adult study may also be required to understand the ultimate functional limitations of this condition.

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Declarations

The data were collected at the Royal Hospital for Sick Children in Glasgow, UK under the guidance of a Neuro-Ophthalmologist (GD) and a Clinical Scientist (MB).

The research followed the tenets of the declaration of Helsinki.

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