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Research Article

Step VEP visual acuity in a pediatric neuro-ophthalmological cohort

Alison M Mackay*

Faculty of Biology, Medicine and Health, University of Manchester, UK

Abstract

Steady-state VEPs, have been used to estimate visual acuity since the 1970s and allow responses to a range of stimulus sizes to be collected rapidly- with particular utility in infants. However, the assessment of children with cortical visual impairment is a bigger challenge that lead to the development of the Step VEP. Its initial evaluation revealed that accuracy and precision were poorer for pediatric patients than for optically degraded normal adults and that it was not necessarily successful in every child.

Statistical models generated the equations: $VA_O = 0.56\ VA_{Step}$ ($r^2 = 0.75$, $F = 60.93$, $p = 0.000$) and $VA_{PL} = 0.45\ VA_{Step}$ ($r^2 = 0.82$, $F = 156.85$, $p = 0.000$), supported by a recent a systematic review of VA comparisons showing that recognition VA (optotypes) agrees more closely than discrimination VA (PL) with VEP VA.

In combination, Step VEPS and subjective tests allowed complete assessment in 96% of patients, with incomplete Step VEPS much more likely to be partially successful than not, and more likely to be partially successful than incomplete subjective tests. This supports the rationale that Step VEPs maintain attention by limiting the time spent stimulating away from an individual's threshold of spatial resolution. For the small number of patients in whom VA cannot be estimated, alternative stimuli and methods of presentation are proposed.

More Information

***Address for Correspondence:**
Alison M Mackay, Faculty of Biology, Medicine, and Health, University of Manchester, UK,
Email: alisonmackay@live.co.uk

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ORCiD: https://orcid.org/0000-0002-6652-1154

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Abbreviations: BA: Bland Altman; CVI: Cortical Visual Impairment; DR: Direction Reversal; FVL: Functional Visual Loss; GAC: Glasgow Acuity Cards; ISCEV: International Society for the Clinical Electrophysiology of Vision; K: Koniocellular; LRM: Logistic Regression Model; M: Magnocellular; MRM: Multiple Regression Model; O: Optotypes; OR: Orientation Reversal; P: Parvocellular; PL: Preferential Looking; SF: Spatial Frequency; SL: Spatial Luminance; SLO: Scanning Laser Ophthalmoscope; TL: Temporal Luminance; VA: Visual Acuity; VI: Visual Impairment

Introduction

Steady-state Visual Evoked Potentials (ssVEPs) have been used to assess Visual acuity (VA) since the 1970s [1,2], with either critical check size (CCS) [3] or extrapolation of the spatial frequency- amplitude function used to express exact threshold following sweep [2] or transient [4] VEP recordings. The automated presentation aspect of the Sweep VEP allowed responses to a range of stimulus sizes to be collected quickly, facilitating studies of the natural course of visual development in term-born and preterm infants [5-7].

SsVEP research in pediatric ophthalmology then diversified to study patient cohorts [8-10], older normal volunteers [11-13] and methodology improvements [14-19]. However, measurement of VA in children with cortical visual impairment (CVI) remained a challenge (Bill Good Personal Communication) instigating the development of the Step VEP [20]. Its success in clinical pediatric VA estimation [21] was attributed to a short test duration compared to transient VEPS [22] and an algorithm that minimized the presentation of stimuli away from an individual's spatial resolution threshold [20]. Moreover, the relationship between Step VEP VA with gold standard subjective tests was consistent across the whole range of VA in optically degraded adults [23] revealing that it was uniquely suited to clinical assessment in those of unknown prior ability or less likely to engage with other tests.

Initial analysis suggested a different relationship between Step VEP and subjective VA for pediatric patients and found the test was occasionally unsuccessful. The aim of this study is primarily to derive an equation to express the Step VEP threshold in terms that all clinicians would understand- subjective test VA. In addition, the reasons why tests were unsuccessful will be considered.

Materials and methods

Children attending Neuro-ophthalmology clinics wore any optical correction they had been prescribed and had their VA measured using Step VEPs and a subjective test appropriate

to their age and ability. All parameters of the Step VEP methodology have been published previously [idem], and they met or exceeded the contemporaneous ISCEV technical standards [24]. The etiology of visual impairment (VI) was categorized according to the anatomical location of primary damage, or suspicion of Functional Visual Loss (FVL) [25]. For all tests success was expressed dichotomously.

For the subgroup of patients succeeding at both tests, and without FVL, Multiple regression modeling (MRM) was used to investigate the influence of age, subjective VA, subjective test modality, and aetiological group on the relationship between subjective and Step VEP VA. More specifically, the subjective tests were Cardiff Cards, Keeler Cards, Snellen Charts, and Sheridan-Gardiner Optotypes. Multiple regression required variables to be normally distributed, assumes a linear relationship between independent and dependent variables, assumes the data was measured reliably and without error, and that homoscedasticity (consistent variance of errors over the whole range) is present [26]. The modeling process comprised of univariate tests to identify individual influences followed by a multivariate regression including influential parameters and their interactions with each other.

The data from all successful subjective tests were entered in a logistic regression model (LRM) of influences on Step VEP success, and similarly, data from successful Step VEPs were used to model subjective test success. Logistic regression requires that independent variables are not collinear [27], and interactions between variables were also considered [28].

Bland-Altman analysis (BA-A) is a quantification of the agreement between two methods of measuring the same thing [29] and requires the mean VA for an individual assessed by two different methods to be plotted against the difference between the two methods in that individual. Results across a group are expressed in terms of the accuracy (the mean difference between two measurements), precision (the width of the confidence limits around the mean difference), and bias (the deviation of the regression line from horizontal) in the relationship between VA measurement methods. According to our published methodology [23], in the absence of bias, a simple linear regression equation can be derived to describe the relationship between tests.

Results

Data was collected for 100 children aged one month to thirteen years. 85 children completed each test, but not the same 85 children. 59 children successfully completed both Step VEP and subjective VA assessments and were judged to have organic vision loss. Age, VA, and etiological grouping did not influence the VA relationship between the two methods. However, subjective test modality was a factor, and so the dataset was stratified accordingly and reanalyzed. The following two equations were generated: $VA_0 = 0.56\ VA_{Step}$ ($r^2 = 0.75$, $F = 60.93$, $p = 0.000$) $VA_{PL} = 0.45\ VA_{Step}$ ($r^2 = 0.82$, $F = 156.85$, $p = 0.000$). BA-A confirmed that the relationship between tests was consistent over the range of VA in each group. During LRM, poor VA was the only limit found on the success of Step VEPs, with no specific limit identified for subjective testing.

Discussion

The high success rate of Step VEPs [20,21] created a large dataset for the derivation of equations expressing outcome in terms of subjective VA allowing clear clinical interpretation. Our group with mixed ability and a range of ages and VA created a dynamic range with which to perform regression analyses to identify influences on success and the VA relationship between methods..

Comparisons of subjective and VEP VA have been published periodically, but rarely verify the degree of success of either assessment- those that the author is aware of are included in Table 1. Including underestimations of VA from partially complete tests in analyses will increase variation in the relationship between test results. Excluding them, however, should be explicit and allows the test success rate to be quantified and interpreted. This parsing of the data means the clinician can be sure that any VA disparity results from anatomical and physiological factors.

Previously published work [idem] infers that attempting both Step VEP and subjective VA assessment in pediatric patients improves the chance of success over just one test. Also, unsuccessful Step VEPS were likely to be partially successful allowing 'VA better than ... ' to be expressed. This high partial success rate for Step VEPs compared to subjective tests supports the rationale that the technique maintains attention by limiting the time spent stimulating too far above and below an individual's threshold of spatial resolution. However, the dynamic nature of the stimulus may also play a part. Even so, these advantages did not help the least able children who may also have difficulties with higher processing and motor function. Alternative methods of presenting the stimulus should address this.

A Scanning Laser Ophthalmoscope (SLO) has been used to present VEP stimuli [30] and circumvents any refractive error. However, persuading children who are unable to engage with Step VEPs to sit completely still and hold their heads in the same position for minutes may not be realistic. In recent years, headsets and glasses have been employed very effectively to direct the stimulus onto the retina [31,32]. Where the poor vision is known to be secondary to CVI, lower luminance can facilitate testing [33] and a recumbent position and background music have positively influenced completion [34].

A larger LRM with additional patient factors could provide more insight into the limits on subjective test success. Considering the different visual pathways following monochromatic stimulation of the striate cortex (V1): the Magnocellular (M) pathway responds to temporal luminance

Table 1: Reports on the degrees of Success of Visual Acuity Estimation including VEPS.

First Author	Year	Clinical Group	Age range
Sokol [a]	1983	Paediatric Patients	Four months to ten years
Orel-Bixler [b]	1989	Multiply Handicapped	Three to 33 years
Bane [c]	1992	Moderate to Severe Visual Impairment	Four months to nine years
Mackie [d]	1995	Multiply Handicapped	Five months to 16 years
Saunders [e]	1995	Rett Syndrome	One to 24 years
Mackay [f]	2003	Neuro-Ophthalmological	One month to 13 years
Costa [g]	2004	Cerebral Palsy	Six months to four years
Ghasia [h]	2009	Cerebral Palsy	One to 19 years
Costa [i]	2012	Cerebral Palsy	Six months to four years
Mackay [21]	2012	Neuro-ophthalmological	One month to 13 years

a. Sokol S, Hansen VC, Moskowitz A. Evoked Potential and Preferential Looking Estimates of Visual Acuity in Pediatric patients. Ophthalmology 1983; 90(3):552-562.
b. Orel-Bixler D, Haegerstrom-Portnoy G, Hall A. Visual assessment of the multiply handicapped patient. Optom Vis Sci 1989; 66: 530–536.
c. Bane MC, Birch EE. VEP Acuity, FPL Acuity, and Visual Behaviour of Visually Impaired Children. J Paediatr Ophthalmol Strabismus. 1992; 29(4):202-209.
d. Mackie RT, McCulloch DL, Saunders KJ. Relation between neurological status, refractive error, and visual acuity in children: a clinical study. Dev Med Child Neurol. 1998; 40:31–37.
e. Saunders KJ, McCulloch DL, Kerr AM. Visual function in Rett syndrome. Dev Med Child Neurol. 1995; 37: 496–504.
f. Mackay AM. Estimating Children's Visual Acuity with Steady State VEPs. Ph.D. Thesis. University of Glasgow. 2003.
g. Costa MF, Saloma˜o SR, Berezovsky A. Relationship between vision and motor impairment in children with spastic cerebral palsy: new evidence from electrophysiology. Behav Brain Res. 149:145–150.
h. Ghasia F, Brunstom J, Tychsen L (2009) Visual acuity and visually evoked responses in children with cerebral palsy: Gross Motor Function Classification Scale. Br J Ophthalmol. 93:1068–1072.
i. Costa MF, Ventura DF. Visual impairment in children with spastic cerebral palsy measured by psychophysical and electrophysiological grating acuity tests. Dev Neurorehabil. 2012; 15:414-424.

contrast, while parvocellular (P) fibers respond to spatial luminance contrast [3]. Static subjective tests generate an exclusively P response which abates at a smalller check size than the M response, and so it is unsurprising that no outcome is achieved in profoundly impaired patients. In the same patients, VEP responses may be present via the M pathway. The contributors to a VEP should be identifiable by latency and morphology but will be obscured by higher processing problems associated with CVI.

In this study, a range of different subjective tests was available to the orthoptist and the VA relationship with Step VEPs was much more variable than the Adult study employing exclusively Glasgow Acuity Cards (GACs). Optotypes (O) such as GACs and Snellen charts (SC) are an identification task, whereas Preferential Looking cards (PL) represent a discrimination task. A recent review of VA comparisons showed that recognition VA agreed more closely with VEP VA than discrimination VA, with smaller inter-and intra-subject variation [35], explaining why the regression coefficient is closer to one (perfect agreement) for optotypes than PL cards in this study.

Processing beyond the primary V1/V2 response occurs via M, P, and Koniocellular (K) pathways which then input the dorsal and ventral streams in different proportions [36]. These streams go on to modulate occipital electrical activity. A range of new technologies used alongside the ssVEP [37] will enhance our understanding of the relationship between the stimulus, the brain's response to it, and the VEP recording. The 2016 study by Marcar and Jäncke used a dartboard stimulus as opposed to checkerboard reversals and they advocate the study of the phasic and tonic aspects of its VEP spatial frequency (SF) response, rather than separate temporal luminance (TL) and spatial luminance (SL) response functions [38].

The presence and morphology of evoked responses to orientation-reversal (OR) and direction reversal (DR) stimuli have been reported to show differences between those with and without perinatal brain injuries [39] and so automated presentation of these stimuli could provide further clinical specificity.. Also, a set of expanding and contracting concentric rings caused less fatigue during ssVEP VA assessment than other stimuli and is worth considering in children whose tests are incomplete [40].

Other recent methodological developments include the use of Gaussian functions during extrapolation of the sweep VEP spatial frequency-amplitude function [41], ISCEV's publication of an extended protocol for estimation of VA using VEPs [42] and using the difference between VA scores in an individual as a marker of CVI [43]. The latter idea requires further mathematical consideration, while a protocol provides a useful starting point for clinicians and researchers applying this technology for the first time, so long as it isn't so restrictive it deters the development of new tests.

Conclusion

By attempting both subjective tests and Step VEPs, most children attending neuro-ophthalmology clinics can now have their VA measured. Where Step VEPs are the only VA assessment a child can complete, equations have been derived to express the results in terms familiar to all clinicians. The MRM, LRM and BA-A described here could be attempted on other large datasets of VEP and subjective VA in specific cohorts.

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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).

We had local ethical committee approval for the work and conducted it according to the tenets of the declaration of Helsinki.

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