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Early Visual Evoked Potential Acuity and Future Behavioral Acuity in Cortical Visual Impairment

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Abstract

Purpose—Cortical Visual Impairment (CVI) is bilateral visual impairment caused by damage to the posterior visual pathway. Both preferential looking (PL) and sweep visual evoked potential (VEP) can be used to measure visual acuity. The purpose of this study was to determine if an early VEP measure of acuity is related to a young patient's future behavioral acuity.

Methods—The visual acuity of 33 patients with CVI was assessed using the sweep VEP and a behavioral measure on two occasions. The median age of the patients at the initial visit was 4.8 years (range: 1.3–19.2 years), and they were followed for an average of 6.9 years (SD: 3.5 years).

Results—The mean initial VEP acuity was 20/135 (0.735 logMAR), and the mean initial behavioral acuity was 20/475 (1.242 logMAR). The average difference between the two initial measures of acuity was 0.55 log unit, with the behavioral measure reporting a poorer visual acuity in all patients. However, the mean final behavioral acuity was 20/150 (0.741 logMAR), and the average difference between the initial VEP acuity and the final behavioral acuity was only 0.01 log unit. Therefore, the initial VEP measure was not statistically different from the final behavioral measure ($t=0.11$; $df=32$; $p=0.45$).

Conclusions—Even though the initial VEP measure was much better than the initial behavioral measure, the initial VEP measure was similar to the behavioral visual acuity measured approximately 7 years later. Sweep VEP testing can be used as a predictive tool for at least the lower limit of future behavioral acuity in young patients with CVI.

Keywords

cortical visual impairment; cerebral visual impairment; sweep vep acuity; behavioral acuity; visual acuity

Cortical visual impairment, also known as cerebral visual impairment or CVI, is a neurological disorder that results in bilateral visual impairment caused by damage to the posterior visual pathways^{1–5}. Clinically, it manifests as a bilateral reduction in visual acuity with normal ocular structures and normal pupil response^{1–5}. The most common etiology for CVI is hypoxic brain injury^{1,2,6}. Other causes of CVI include head injury (such as shaken baby syndrome), infection, hydrocephalus, and metabolic disorders^{2,6,7}.

The most common clinical finding of CVI is reduced visual acuity, often associated with reduced contrast sensitivity, visual field defects, and ocular motility abnormalities^{8–12}. The severity of vision loss in patients with CVI is variable. Furthermore, the potential for recovery is also variable. Interestingly, some patients with CVI improve over time while

others show no change in vision function^{8,13}. It is currently thought that the prognosis for patients with CVI may depend on the etiology, age of onset, and severity of brain damage². Additionally, patients with periventricular leukomalacia and subsequent damage to the optic radiations may have a poorer prognosis than patients with isolated cortical damage^{3,8}.

Both preferential looking (PL) and the sweep visual evoked potential (VEP) can be used to measure visual acuity¹⁴⁻¹⁹. Both techniques have been shown to be reliable measures of visual acuity in patients with CVI^{10,17,18}. The VEP is an electrophysiological technique that provides general information about the occipital response to visual stimuli¹⁹. Because the VEP represents a neural response, it is possible to obtain a visual acuity measure for a child who is not verbal and/or unable to generate an oculomotor response to communicate what they see. Even though the ability of the VEP to provide a measurement of vision without the influence of motor ability offers several advantages for the CVI population, a behavioral measure of vision may be more helpful in describing the patient's vision function in their natural environment.

Some studies report that children with vision impairment show lower visual acuity on behavioral measures of acuity compared to VEP measures^{10,17,20}. Furthermore, the difference between sweep VEP acuity and behavioral acuity increases with poorer visual acuity²¹ and in patients with developmental disabilities¹⁰. At an initial exam, the sweep VEP is often the only testable method of visual acuity, especially in young children with multiple disabilities. As the child matures over time, behavioral measures of vision function often become possible and/or more accurate. Some think of VEP acuity as a measure of the integrity of the neural substrate used for vision processing and the behavioral measure of acuity as the level of vision the patient is able to access. So even though the sweep VEP measure may suggest vision function better than what the child shows behaviorally at the initial exam, the child's behavioral acuity might improve over time to reach the acuity that was initially found with the sweep VEP. If true, it would be helpful to the child's parents and educators to know a general level of visual impairment that can be expected for the child in the future.

A previous study found that sweep VEP grating acuity is predictive of future recognition acuity in children with albinism²². In this study, 5 of 13 patients had final recognition acuity within 1 Snellen line of initial sweep VEP acuity; and five additional patients had final recognition acuity that surpassed the initial sweep VEP acuity by 2 to 3 lines. They found that the mean duration for recognition acuity to reach the initial VEP acuity was 5.4 years. Another study reported that while grating acuity measured by either VEP or PL is predictive of future recognition acuity in low birth-weight children, abnormal VEP grating acuity is a stronger indicator of a long-term deficit than PL acuity²³. Furthermore, Thompson and colleagues²⁴ evaluated the correlation of recognition acuity to sweep VEP acuity in patients aged 4 to 16 years who underwent lensectomy for congenital cataracts at a young age. They reported a strong correlation between VEP estimation and later recognition acuity in the patients studied.

To date, there is no study in the literature comparing sweep VEP acuity with future behavioral visual acuity in young patients with CVI. The purpose of this study is to determine the relationship between early sweep VEP visual acuity and future behavioral acuity in patients with CVI. If predictive, early sweep VEP acuity measurements could be a guide for the potential of vision function development in patients with CVI. The initial sweep VEP may serve as a realistic expectation of future vision function for the parents and teachers of young patients with CVI.

METHODS

A retrospective study was performed on 33 young patients (13 female and 20 male) with CVI. The research study was approved by the UC Berkeley Committee for the Protection of Human Subjects and informed consent was obtained from the patients and/or the patients' parent prior to being included in the study. Sweep VEP testing was performed at the first visit as part of a comprehensive eye examination. A behavioral measure of visual acuity (either preferential looking cards or single symbols, depending on the patient's cognitive and motor ability) was also measured. The patients were then followed over time and retested at a later date. Significant refractive error was corrected prior to acuity testing. Patients with ocular pathology or whose reduction in vision could be attributed to a condition other than CVI were excluded. The median age of the patients at the initial visit was 4.8 years (range: 1.3–19.2 years). The study participants were then followed for an average of 6.9 years (SD: 3.5 years). At the final exam, behavioral acuity was retested as part of another comprehensive eye exam.

A summary of the study participants and etiology of CVI is listed in Table 1. The presumed causes of CVI are as follows: birth asphyxia (n=8), acute episode of hypoxia (n=4), infection (n=4), PVL (n=3), trauma (n=2), static encephalopathy (n=2), hydrocephalus (n=1), multiple complications (n=3), and six cases with an unknown origin.

VEP Technique

The patients were presented with high contrast (80% Michelson) sinusoidal luminance vertical gratings on a high-resolution video display monitor with an average luminance of 80 cd/m². Over a period of 10 seconds, the spatial frequency of the reversing grating was incremented logarithmically in 19 steps, spanning a 10 to 1 range of spatial frequencies expressed in cycles/degree. Testing was performed under binocular viewing with proper refractive error correction.

The gratings were modulated at a rate of 12 contrast reversals per second. The second harmonic component of the response at 12Hz is extracted by a Discrete Fourier Transform (DFT) and compared to an adjacent frequency band at 14 Hz, which did not contain any visual evoked activity. The adjacent frequency measurements were used to estimate the noise background during the trial and reject portions of the record with muscle spikes or movement artifacts. Sweep VEP acuity was estimated by the method described by Norcia and Tyler²⁵. Determination of visual acuity was based on the linear decline of the VEP amplitude and the increase in the implicit time near the acuity threshold²⁵. The extrapolation technique took into account the signal-to-noise ratio and phase statistics. Multiple sweeps were recorded and the trial yielding the highest spatial frequency that met scoring criteria was used for the visual acuity estimate²⁵. VEP grating acuity (in cyc/deg) was converted into logMAR for data analysis, using the conversion that 1 cyc/deg is mathematically equivalent to 20/600 (logMAR = 1.477) and 30 cyc/deg is mathematically equivalent to 20/20 (logMAR = 0).

Behavioral Acuity Technique

Berkeley Grating Acuity Cards²⁶, a clinical variation of the Teller Acuity Card procedure was used to measure forced choice preferential looking (PL) acuity. The patient was presented with a rectangular card that had two targets positioned on a gray homogenous background. One target matched the gray background and the other target contained a grating pattern. If the patient responded by turning his/her eyes or head in the direction of the grating pattern, then the patient's response was interpreted as an ability of the patient to see the target. Threshold visual acuity was determined by observing the finest grating to

which the patient reliably oriented their gaze for a minimum of three out-of four presentations (75% correct).

The acuity cards were presented either horizontally or vertically to minimize the effects of visual field defects and either lateral to or central to the gaze direction to minimize the effects of oculomotor abnormalities. The acuity cards were presented in sequential order from lower to higher spatial frequencies. Each card was presented as many times as necessary to decide whether the patient could resolve the grating on the card. The examiner was masked to the absolute frequency of the grating on the card and to the location of the grating on each card. As with VEP acuity, the PL grating acuity (in cyc/deg) was converted into logMAR for data analysis.

Lea single symbols cards were used for the patients who were capable of performing a recognition acuity task. The patient was presented with a pair of 10cm square cards. One card had the Lea house (or arrow) symbol and the other card had the Lea apple (or heart) symbol positioned in the center of the card. The size of the symbols varied logarithmically between one pair of cards and the next. For each card pair, the patient was asked to either “point to the apple (or heart)” or “point to the house (or arrow)”. Always starting at a size level where the recognition was easy for the patient and moving to smaller sized targets, the acuity was determined by a three out-of four (75% correct) criteria following a forced-choice procedure.

Data Analysis

As previously stated, a primary goal of this study is to assess the relationship between the initial sweep VEP acuity and a later behavioral acuity in young patients with CVI. The initial sweep VEP acuities will first be compared to the initial behavioral acuities and then compared to the final behavioral acuities graphically and with a repeated measures t-test. Factors such as the age of the child, the duration between measures, and the etiology of CVI will also be examined as potential confounders for a patient’s visual outcome. Additionally, three individual cases will be briefly described.

RESULTS

Sweep VEP testing was possible in all study participants at the first visit. A behavioral measure of visual acuity was possible in 31 of 33 patients at the first visit. Twenty-one of the patients were tested with preferential looking cards and the remaining 12 patients were tested with single symbols. Every participant was measured with the same behavioral test at both the initial and final exam. VEP data from the final exam was not available for many of the participants; therefore any change in VEP acuity over time was not included in this analysis.

All of the participants had substantial visual impairment. The mean initial VEP acuity was 20/94 (0.67 logMAR), and the mean initial behavioral acuity was 20/475 (1.38 logMAR). The average difference between the two measures of acuity was 0.55 log unit, with the behavioral measure reporting a poorer visual acuity in all patients. Therefore, at the initial test, the behavioral measure of acuity was significantly worse than the VEP measure of acuity ($t=9.68$; $df=30$; $p<0.0001$). Figure 1 graphically displays a comparison between VEP acuity and behavioral acuity at the initial exam. All of the points fall above the 1:1 line, showing that all patients had better visual acuity measured with the VEP than measured behaviorally.

The mean time between the initial sweep VEP testing and the final behavioral testing was 6.9 years (SD: 3.5 years). At the final visit, a behavioral measure of acuity was possible for

all 33 patients. The mean final behavioral acuity was 20/150 (0.88 logMAR). The average difference between the initial VEP acuity and the final behavioral acuity was 0.01 log unit. The initial VEP measure was not statistically different from the final behavioral measure ($t=0.11$; $df=32$; $p=0.45$). Figure 2 graphically displays a comparison between the initial VEP acuity and the later behavioral acuity.

Twenty-six of the patients tested (79%) had a final behavioral acuity within 0.1 log unit (approx 1 chart line) or better than their initial VEP acuity. Twenty-seven (82%) had a final behavioral acuity within 0.2 log unit (approx 2 chart lines) or better than their initial VEP acuity.

The age of the child was not significantly correlated with the degree of agreement between the final behavioral acuity and the initial VEP acuity ($r=0.082$; $df=31$; $p=0.65$). The six patients whose behavioral acuity did not improve to within 0.2 log unit of the initial VEP were essentially the same age as those who did improve (mean: 5.4 years vs. 5.7 years; $t=-0.58$; $df=31$; $p=0.28$). Furthermore, in this study population, there was no significant relationship between the etiology of CVI and whether the child behaviorally met the acuity level measured by the initial sweep VEP ($\chi^2=0.65$; $df=32$; $p=ns$). Because the insult occurred within 3 months of birth for 89% of the participants with a known etiology, there was not enough statistical power to adequately assess the influence of the age of the insult on recovery.

The duration of time between acuity measures was correlated with the degree of final agreement of the two measures ($r=0.400$; $df=31$; $p<0.05$). The six participants whose behavioral acuity did not improve to within 0.2 log unit of the initial VEP were followed for a slightly shorter duration when compared to those who did improve to meet their initial VEP acuity ($t=-1.36$; $df=31$; $p=0.09$). The average duration of follow-up for those who did not improve to the acuity level of the initial sweep VEP acuity was 5.2 years (SD: 2.6 years). The average duration of follow-up for those who did improve to meet the initial VEP acuity was 7.3 years (SD: 3.6 years). Additionally, the average difference between the initial VEP measure and the initial behavioral measure of acuity was larger for those who did not behaviorally meet the initial VEP acuity value ($r=0.493$; $df=31$; $p<0.01$). These two findings (a larger difference between the initial values of acuity and a shorter duration of follow-up) may suggest that if given more time, the children who did not behaviorally meet the acuity measured with the initial VEP might continue to improve to eventually meet the level of acuity measured by the initial VEP. However, as described below, further analysis revealed that a third component, rate of behavioral acuity improvement, was also different between the two groups.

There is a significant difference in the rate of behavioral acuity improvement between the two groups ($t=2.27$; $df=29$; $p=0.01$). The average rate of change for those who did improve to their initial VEP acuity was 0.11 log unit per year (approximately one chart line per year). Whereas the average rate of change for those who did not improve to their initial VEP acuity was only 0.03 log unit per year. The significantly slower rate of improvement for the patients who have not yet met their initial VEP acuity suggests that it will take much longer for them to do so, if they ever do. Furthermore, this finding suggests that the difference in duration of follow-up and the difference in initial discrepancy between the two measures for this study population are not solely responsible for the difference between the two groups. The few participants who did not behaviorally meet their initial VEP acuity are improving at a much slower rate than the majority of the patients tested.

Figure 3A is a graphical representation of one of the 18 patients whose final behavioral acuity met the initial VEP acuity. At the initial exam, this patient was 3.8-years-old and had

a 0.70 log unit difference between his VEP acuity and his behavioral acuity. However, over the course of 11.7 years, his behavioral acuity improved to become very similar to his initial VEP acuity (0.48 log unit vs. 0.41 log unit). Behavioral data was collected three times for this patient and this is shown graphically. However, only the first and last measures are included in the data analysis.

Figure 3B and 3C are graphical representations of the 6 patients who did not behaviorally meet their initial sweep VEP acuity. The pattern seen in Figure 3B is an example of the majority of patients (4 of the 6) who did not meet the initial VEP acuity. This child was first seen at 5.5 years of age. At this initial exam, there was a 0.90 log unit difference between her VEP and behavioral acuity. When she was seen again 8 years later, her behavioral acuity remained approximately the same as that reported at her initial exam. Her average behavioral acuity rate of change was only 0.01 log unit per year. The rates of change for the other three patients with a similar outcome ranged from 0.00–0.02 log unit per year.

Figure 3C is an example of a patient who did not behaviorally meet the initial VEP acuity, but if the current trend continues, the child is likely to behaviorally meet the initial VEP acuity value in the future. This pattern was seen in two of the six patients who did not behaviorally meet their initial VEP. The example patient was first seen at 4.4 years of age and there was a 1.1 log unit difference between the two measures of acuity. Nine years later, a 0.45 log unit difference remains. However, if the trend continues, the child is likely to behaviorally meet the initial VEP acuity value in the near future. As previously mentioned, only two of the patients followed this pattern where there was a sizable improvement in their behavioral acuity and if given more time it is conceivable that they will behaviorally meet their initial VEP acuity value. The average rate of change for both of these patients was 0.07 log unit per year.

DISCUSSION

Because CVI is often associated with global cognitive and motor disabilities, the assessment of visual acuity in patients with CVI can be challenging. Assessment of vision function with behavioral measures is often not possible for patients with severe CVI or for young infants with CVI. Sweep VEP is a technique that can be used to assess visual acuity in infants and children with severe CVI. However, considerable discrepancies in threshold visual acuity have been noted between behavioral and electrophysiological techniques. As seen in this data set, the discrepancy between the two measures can be quite large.

In this study, the behavioral measure of acuity was worse than the sweep VEP measure of acuity in all study participants at the initial examination (mean: 20/110 vs. 20/475). However, even though the initial VEP measure was much better than the initial behavioral measure, the VEP measure was statistically similar to the behavioral visual acuity measured on average 6.9 years later.

Our study demonstrates that sweep VEP testing can be used as a predictive tool for at least the lower limit of future behavioral acuity in patients with CVI. 82% of the patients studied either met or surpassed the visual acuity measured by the initial sweep VEP. In four of the six patients whose behavioral acuity did not improve to the level of their initial VEP acuity, it appears unlikely that they will improve behaviorally to meet their initial VEP acuity in the near future. This is because their rate of improvement (average of 0.03 log unit per year) is far below that of the other study participants (average of 0.11 log unit per year).

Despite the fact that CVI is the leading cause of bilateral visual impairment in industrialized nations, there have been very few longitudinal evaluations of vision function in patients with CVI to date. Therefore, there is a pressing need for more research quantifying and

evaluating the various aspects of vision loss in patients with CVI. Quantitative information about a patient's condition will not only be useful clinically, but will also be extremely valuable in enabling better information about the patient's visual capabilities to be provided to the young patient's educators and family. Currently the prognosis of vision function potential in patients with CVI is unknown. If predictive, an early sweep VEP acuity measurement could be a guide for the potential of vision function development in young patients with CVI. An early VEP may provide a conservative estimation of future behavioral vision function in young patients with CVI. Even though there may be a large discrepancy between VEP and behavioral acuity measures at initial exam, parents and teachers of young patients with CVI can be informed that it is likely that their child's vision function will improve to at least the level of the initial VEP.

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Figure 1.

The initial behavioral acuity value (in logMAR form) is plotted as a function of the initial sweep VEP acuity value (also in logMAR form). The dashed black line is the 1:1 line. If a point is on the dashed line, the patient's initial behavioral visual acuity was the same as their initial VEP acuity. A higher point on the vertical axis and a point to the right on the horizontal axis indicate a worse visual acuity. If a point is above the 1:1 line, the patient's initial behavioral acuity was worse than their initial sweep VEP acuity.

Figure 2.

The final behavioral acuity value (in logMAR form) is plotted as a function of the initial sweep VEP measure of acuity (also in logMAR form). The dashed black line is the 1:1 line. Points above the 1:1 line indicate the behavioral acuity did not improve to reach the initial VEP acuity. Points below the line show patients whose final behavioral acuity was better than their initial VEP acuity.

Figure 3.

(A) Initial sweep VEP acuity (solid symbol) and behavioral acuity (open symbols) is plotted as a function of age for a patient whose final behavioral acuity met their initial VEP acuity. Visual acuity is expressed in terms of logMAR on the left vertical axis. A higher point the vertical axis indicates a worse visual acuity. (B) Initial sweep VEP acuity (solid symbol) and behavioral acuity (open symbols) is plotted as a function of age for a patient whose final behavioral acuity did not meet their initial VEP acuity. (C) Initial sweep VEP acuity (solid symbol) and behavioral acuity (open symbols) is plotted as a function of age for another patient whose final behavioral acuity did not meet their initial VEP acuity.

Table 1

Summary of participants (age, etiology of CVI, and the duration of time followed).

Subject	1st Age	Etiology of CVI	Duration of F/U (years)
1	19.2	Infectious	3.5
2	7.8	Birth Asphxia	7.7
3	5.0	Hydrocephalus	9.3
4	6.7	Birth Asphxia	3.5
5	5.5	PVL	5.1
6	3.3	Static Encephalopathy	10.0
7	2.3	Infectious	2.3
8	1.3	Birth Asphxia	9.1
9	6.6	Birth Asphxia	5.0
10	3.2	Acute Episode of Hypoxia	3.1
11	4.1	Multiple	3.4
12	8.0	Birth Asphxia	8.2
13	5.3	Infectious	7.2
14	4.6	Multiple	2.7
15	5.9	Trauma	1.7
16	3.8	Unknown	11.7
17	3.8	Unknown	10.3
18	11.1	Acute Episode of Hypoxia	3.2
19	3.2	Infectious	11.8
20	1.6	Birth Asphxia	2.7
21	4.8	Acute Episode of Hypoxia	4.3
22	4.3	PVL	12.1
23	7.5	Birth Asphxia	9.8
24	4.4	Unknown	9.0
25	3.8	Multiple	3.5
26	7.8	Unknown	6.3
27	10.0	Unknown	7.5
28	2.9	Birth Asphxia	3.3
29	6.1	Unknown	11.5
30	4.1	Trauma	13.2
31	6.8	Acute Episode of Hypoxia	8.1
32	1.3	Static Encephalopathy	11.1
33	5.6	PVL	8.7