

# Predicting potential acuities in amblyopes

## Predicting post-therapy acuity in amblyopes

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### Abstract

**Purpose** Amblyopic patients, or their parents, often want to know the potential for success before committing to treatment. Recent reports have indicated that the pattern visual evoked potential (pVEP) can be used as a predictor of the success of amblyopia therapy. Unfortunately, these studies did not determine if acuity estimates from pVEPs could accurately predict the acuity post-treatment. Furthermore, pVEPs are not always practical to obtain because of the time necessary to acquire the data. Sweep VEPs (sVEP) offer the advantage of rapidly estimating visual acuity in amblyopic patients. In this retrospective study, the relationship between sVEP acuities measured pre-amblyopic therapy and Snellen acuities measured post-amblyopic therapy was determined.

**Methods** Seventeen patients with amblyopia were studied. Monocular sVEP and Snellen acuities were determined pre-amblyopic therapy and Snellen acuities were determined post-amblyopic therapy. An Infant 4010 computer system was used to produce the stimuli, record the VEPs, and extrapolate the acuity. The stimuli were horizontally oriented, sine wave gratings (11 spatial

frequencies from 2 to 24 cpd) with a contrast of 80%, counterphased at 7.5 Hz. Standard VEP recording techniques were employed. Therapy consisted of the full refractive correction and occlusion combined with active vision therapy.

**Results** The patients demonstrated a significant improvement in pre- to post-amblyopic therapy Snellen acuities ( $P < 0.00001$ ). The intraclass correlation coefficient ( $r_i$ ) between the pre-therapy sVEP acuities and the post-therapy Snellen acuities was 0.73. A paired t-test did not find a significant difference between the two sets of data ( $P = 0.94$ ). For the amblyopes in this study, the average difference ( $\pm$ SD) in the sVEP acuity estimate and the final Snellen visual acuity was  $+0.002 \pm 0.123$  logMAR acuity lines.

**Conclusion** The results indicate that pre-amblyopic therapy sVEP acuity can be a good predictor of post-amblyopic therapy Snellen acuity.

**Keywords** Visual evoked potential · Visual acuity · Amblyopia · Anisometropia · Strabismus

### Introduction

Amblyopic patients, as well as their doctors, often want to know their potential visual acuity prior to committing to amblyopia therapy. The potential visual acuity can be used by the doctor as an end point for amblyopia therapy and as an

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inducement for the patient to diligently perform the therapy. At present, there are no clinically acceptable tests that can predict the acuity of amblyopes after they have completed amblyopia therapy.

Amblyopia is a developmental disorder that generally results in decreased visual acuity and is associated with strabismus, anisometropia, or form deprivation. The initial site of the defect in amblyopia is the primary visual cortex [1–5]. The conditions associated with amblyopia must be present prior to the end of the critical period of neural development for amblyopia to develop [6]. The critical period refers to the time during development when the neural cells of the visual system can be modified by deprivation. The critical period ends at different times for different visual functions [7]. For example, monkeys raised with form deprivation have different critical periods for their absolute sensitivity to light (3 months of age) and for contrast sensitivity to high spatial frequencies (18 months of age) [7]. Furthermore, the critical period is shorter for cells early in the visual pathway (e.g., the LGN) than those further downstream (e.g., the cortex) [6]. Since the initial defect associated with amblyopia is located in the primary visual cortex and this is the earliest cortical area to mature, the best test of potential acuity in amblyopia should assess the function of the primary visual cortex.

The Snellen letter chart, a minimum resolvable acuity measurement, is the most common clinical method of acuity assessment [8]. Since this measurement utilizes complex symbols and requires a subjective response from the patient, it involves processing by the visual pathway through to the frontal cortex [9–11]. Little is known about the effects of amblyopia on the higher cortical centers, however, several of these areas do appear to have abnormal processing [12, 13]. The defects associated with amblyopia may be greater in the higher cortical centers because these areas mature later than the primary visual cortex which allows the amblyogenic factors that are present more time to alter neural function. Thus, Snellen acuity, which is a function of higher cortical processing, may not yield the best estimate of visual potential in amblyopia.

Grating acuity, assessed with simple repetitive patterns, is a minimum visible acuity measurement [8]. Psychophysical and anatomical studies suggest that grating acuity is processed by lower cortical visual centers, possibly the striate cortex [14, 15]. Since the initial locus of damage in amblyopes is the striate cortex, grating acuity measurements may more accurately reflect an amblyopic patient's capabilities.

A form of grating acuity, laser interferometry, has been used to predict amblyopes' post-therapy acuity [16]. Initially, Gstalder and Green demonstrated that in amblyopes, laser interferometry acuity is better than Snellen acuity [17]. Selenow et al. confirmed that prior to amblyopia treatment, the laser interferometry acuity was better than Snellen acuity [16]. They also demonstrated that the pre-therapy laser acuity was generally within 2 Snellen lines of the post-therapy Snellen acuity. A similar observation was made with white light interferometry [18]. However, interferometry has not become an accepted clinical test to determine post-therapy acuity. One reason may be that interferometry is a subjective test and the patient responses can be somewhat variable, especially in young children. An objective test which assesses the striate cortex, such as visual evoked potentials (VEPs), may overcome this objection [19–21].

Pattern VEPs (pVEP) have been used to identify amblyopes and monitor their acuity and progress during amblyopia therapy. The pVEP response has been shown to increase in amplitude during amblyopia therapy along with the improvement in visual acuity [19, 22, 23]. Recent reports have indicated that the pVEP can be used as a predictor of the outcome of amblyopia therapy [20]. Patients with moderate increases in the P100 latency before therapy had poorer therapy outcomes [20].

Acuities determined with the pVEP in normal subjects display a good correlation with acuities measured psychophysically, however, the procedure is time consuming [24–30]. Pattern VEPs have not been employed to predict post-amblyopic therapy acuity in amblyopes. Furthermore, because of the time required to measure acuity with pVEPs, it is not clinically feasible in all patients. Acuity measurements with the sweep

VEP (sVEP) can be made in a significantly less amount of time and can subsequently be used on patients with short attention spans like young children.

The correlation between sVEP acuity and psychophysical measures of acuity have been determined in normal subjects [31–35]. Norcia and Tyler demonstrated that sVEPs gave rapid, reliable estimates of acuity in infants [36]. In normal, adult subjects, the relationship between sVEP acuity and Snellen acuity has been examined by blurring the individual with spectacle lenses [33, 34, 37]. Katsumi et al. found that with a small amount of blur (visual acuities better than 20/40 or 6/12 and blur less than +1.00 D) the sVEP acuities were equal to or slightly poorer than the Snellen acuities [34]. With blur of about +1.50 D (acuities of about 20/70 or 6/21), the sVEP acuities were better than the Snellen acuities. Similar to Katsumi's observation, Ridder et al. found that when the acuities were good (about 6/6 or 30 cpd) in normal subjects, the sVEP acuity was equal to or poorer than the logMAR acuity [35, 38]. Patients with moderate losses in acuity due to pathology typically had sVEP acuities within one octave of their Snellen acuities [38].

Acuity estimates have been made in amblyopes with the sVEP technique [31, 32, 39–41]. Day et al. demonstrated that the acuity development in esotropes is significantly below age matched normals [39]. Cibis and Fitzgerald using the sVEP were able to show acuity losses in patients with amblyopia due to congenital ptosis [32]. None of these studies have used the sVEP technique to predict acuity after amblyopia treatment. The purpose of the present study is to demonstrate the relationship between sVEP acuities measured pre-amblyopic therapy and Snellen acuities measured post-amblyopic therapy.

## Methods

### Subjects

Seventeen patients (mean age in years  $\pm$  SD =  $8.4 \pm 4.15$ ; 7 male and 10 female) took part in this study. Patients were identified retrospectively from clinic files. All amblyopes, with no

previous treatment, that had a VEP and visual acuity measurement (Snellen) done following the baseline clinical amblyopia evaluation were included. None of the patients exhibited ocular or systemic pathology. Three of the patients also had the VEP measured at the conclusion of amblyopia therapy. Patients' characteristics are shown in Table 1. Only visual acuity of the poorer acuity eye is reported. Eleven of the patients were refractive amblyopes (anisometropic and isometropic) and six were strabismic amblyopes. All of the patients were compliant with therapy. Compliance was based on the percentage of office visits kept (>80%) and parental reports that the home therapy was being performed as directed. The Institutional Review Board approved the following procedures, which conformed to the Declaration of Helsinki for research involving human subjects.

Using the variance of the pre-amblyopic therapy sVEP and post-amblyopic therapy Snellen acuities, the power and sample size necessary to detect a  $\pm 0.1$  logMAR change in acuity was made. A sample size of 17 resulted in a power greater than 0.80 (power = 0.897, alpha = 0.05, assumed standard deviation = 0.12,  $N = 17$ ). Thus, the sample size of 17 was adequate to detect a difference of  $\pm 0.1$  logMAR between the pre-amblyopic therapy sVEP and the post-amblyopic therapy Snellen acuity.

### Amblyopia therapy

The amblyopia therapy was specific to each patient's diagnosis and is summarized in Table 1. In general, therapy for refractive isoametropic amblyopia involved full-time optical correction (spectacles or contact lenses), limited active vision therapy to improve accommodative function and frequent follow-up to monitor changes in visual acuity. Refractive anisometropic amblyopia therapy involved full-time optical correction (spectacles or contact lenses), part-time occlusion (2–5 h per day typically), monocular active vision therapy to improve oculomotor control and fixation, spatial perception, and accommodative function [42–45]. Binocular (anti-suppression) active vision therapy was used in cases where visual acuity was or improved to 20/60 or better

**Table 1** Patient characteristics

Subj	Age at onset of Tx (yr-mo)	Tx	Tx Length	Initial snellen VA (logMAR)	Final snellen VA (logMAR)	Vep VA (logMAR)	Refractive status	Fixation	Origin of amblyopia
1	7-7	SRx, PTO, AVT	3 mos	20/40 (0.30)	20/20 (0.00)	20/29 (0.16)	+1.75-0.50x180 +3.75-0.50x180	FF	NS HA
2	7-1	SRx, PTO, AVT	9 mos	20/70 (0.54)	20/22 (0.04)	20/24 (0.08)	+0.50-0.50x005 +4.25-0.50x180	FF	NS HA
3	6-4	SRx, PTO, AVT	9 mos	20/200 (1.00)	20/25 (0.10)	20/36 (0.26)	+0.50-0.75x102 +3.50-0.50x042	FF	CLET HA
4	12-5	CLR <sub>x</sub>	15 mos	20/40 (0.30)	20/20 (0.00)	20/25 (0.10)	+5.25-1.00x180 +5.25-1.00x180	FF	NS HI
5	7-0	SRx, PTO, AVT	11 mos	20/50 (0.40)	20/30 (0.18)	20/30 (0.18)	+4.50 DS +2.50 DS	FF	NS HA
6	4-7	CLR <sub>x</sub> , PTO, AVT	5 mos	20/160 (0.90)	20/40 (0.30)	20/30 (0.18)	+1.75 DS +6.00-0.75x016	FF	CLET HA
7	9-7	CLR <sub>x</sub>	20 mos	20/50 (0.40)	20/30 (0.18)	20/25 (0.10)	-7.00-1.00x030 -7.25-1.25x126	FF	NS MI
8	12-8	CLR <sub>x</sub> , PTO, AVT	6 mos	20/200 (1.00)	20/50 (0.40)	20/58 (0.46)	+1.00 DS +6.75 DS	FF	NS HA
9	8-3	SRx, PTO	8 mos	20/80 (0.60)	20/58 (0.46)	20/47 (0.37)	-3.00-2.00x180 -2.75-2.00x180	NA	CRET
10	21-6	CLR <sub>x</sub> , PTO	18 mos	20/100 (0.70)	20/60 (0.48)	20/49 (0.39)	-9.75-3.00x095 -9.25-2.25x082	FF	CRET MI
11	7-3	CLR <sub>x</sub> , FTO, AVT	7 mos	20/200 (1.00)	20/77 (0.59)	20/54 (0.43)	+1.50-0.25x090 +2.25-5.25x180	FF	CLXT AA
12	4-5	SRx, PTO, AVT	12 mos	20/400 (1.30)	20/80 (0.60)	20/58 (0.46)	-5.75-2.50x100 -0.50-0.37x055	FF	NS MA
13	5-8	SRx, FTO	13 mos	20/120 (0.78)	20/40 (0.30)	20/45 (0.35)	Plano +3.50 DS	EF	CLXT HA
14	10-3	CLR <sub>x</sub> , PTO, AVT	12 mos	20/100 (0.70)	20/50 (0.40)	20/35 (0.24)	+6.75-0.50x180 +0.50-0.50x180	FF	NS HA
15	5-7	CLR <sub>x</sub> , PTO, AVT	9 mos	20/200 (1.00)	20/40 (0.30)	Pre-Tx 20/45 (0.35) Post-Tx 20/60 (0.48)	+1.25 -11.50-1.25x130	FF	NS MA
16	5-6	SRx, PTO, AVT	7 mos	20/250 (1.09)	20/40 (0.30)	Pre-Tx 20/34 (0.23) Post-Tx 20/50 (0.40)	+0.75-0.50x180 +5.00-0.75x020	FF	NS HA
17	7-8	CLR <sub>x</sub> , PTO, AVT	20 mos	20/800 (1.60)	20/40 (0.30)	Pre-Tx 20/70 (0.54) Post-Tx 20/47 (0.37)	-7.50-0.75x045 -2.50-0.50x040	2-3Δ EF (central after treatment)	NS MA

SR<sub>x</sub>—spectacle Rx; CLR<sub>x</sub>—contact lens Rx; FTO—full-time occlusion; PTO—part-time occlusion; AVT—active vision therapy; FF—foveal fixation; EF—eccentric fixation; NA—not available; CLET—constant left esotropia; CLXT—constant left exotropia; NS—nonstrabismic; AA—astigmatic anisometropia; HA—hyperopic anisometropia; HI—hyperopic isometropia; MI—myopic isometropia; MA—myopic anisometropia; Pre-Tx—acuity before amblyopia therapy; Post-Tx—acuity after amblyopia therapy

[43, 46, 47]. Therapy for strabismic amblyopia involved full-time optical correction (spectacle or contact lenses), full-time occlusion (where normal binocular vision was the goal) or part-time occlusion (where the prognosis for normal binocular vision was poor), and active monocular and binocular vision therapy [46, 47]. The length of therapy was typically less than 12 months (Table 1). The average duration of therapy for the anisometric and strabismic amblyopes was  $11.3 \pm 5.41$  and  $10.0 \pm 4.73$  months, respectively. The length of therapy was not significantly different between the groups ( $P = 0.64$ ,  $t = 0.48$ ,  $df = 15$ ). Visual acuity was monitored periodically during treatment (every 1–4 weeks) and treatment was discontinued when the acuity was stable (less than  $\pm 1$  line of Snellen visual acuity change) over approximately a 2-month period of time.

### Stimulus

The stimulus was a horizontal-oriented, sine wave grating. The spatial frequencies presented were 2, 4, 6, 8, 10, 12, 13.4, 15, 17.2, 20, and 24 cpd when viewed at 1 meter. During the sweep, each spatial frequency was presented for 1 s in order from 2 to 24 cpd. Additionally, a 1-s adaptation stimulus was used so that the entire sweep took 12 s (11 spatial frequencies plus 1 s adaptation). Neural adaptation does not significantly alter the acuity obtained with the sVEP [35]. The test distance for the amblyopic eye was either 1 or  $\frac{1}{2}$  m. A  $\frac{1}{2}$  m viewing distance was used for patients with poor acuity ( $<20/200$ ) so that a greater number of spatial frequencies were visible to the patient. This also results in a better estimate of visual acuity [35]. The contrast was 80% and the temporal reversal rate (square wave) was 7.5 Hz. The screen luminance was  $100 \text{ cd/m}^2$ . The stimulus screen ( $19^\circ \text{ (H)} \times 14.5^\circ \text{ (V)}$ ) at 1 m) was viewed monocularly with the patient's best correction in place. Sweeps were repeated until the confidence intervals for the data were no longer decreasing (typically seven or more sweeps per patient).

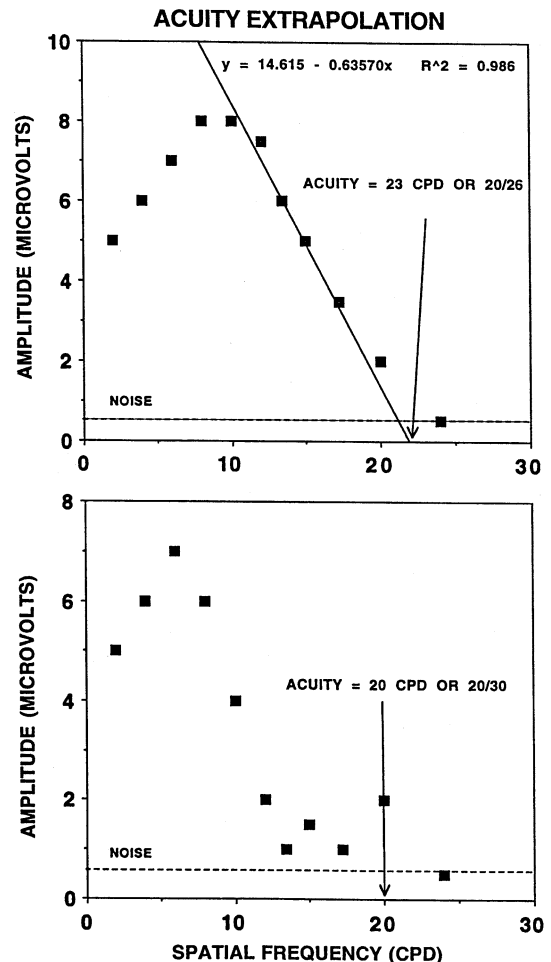
### Recording technique

Data were acquired with an Enfant 4010 system (Neuroscientific Corp.). The recording electrode

(Ag/AgCl) was placed 2 cm above theinion on the midline. The reference and ground electrodes were placed on the earlobes. The signal was amplified 10,000 $\times$ , bandpass filtered (0.5–100 Hz) and digitized at 300 Hz with 12 bits resolution. The active electrode impedance was maintained below 10 k $\Omega$ .

### Data analysis and acuity extrapolation

Figure 1 displays the sVEP data for two patients. The graph displays the response amplitude of the second harmonic (discrete Fourier transform) of the sVEP for all eleven spatial frequencies. The data were determined to be noise if either of the following criteria were met: 1) the 95% confidence



**Fig. 1** Representative data for 2 patients. The methods of acuity extrapolation are displayed

intervals for the sVEP amplitude data overlapped with zero or 2) the 95% confidence intervals for phase (not shown) were greater than  $90^\circ$ . For the majority of the data that were determined to be noise, both criteria were met. For the data in Fig. 1, these criteria were exceeded for the 24 cpd data. None of the data collected at the lower spatial frequencies were considered to be noise for these patients.

Acuities were determined by one of two methods that utilized the high spatial frequency data that were above noise (Fig. 1). This method was employed in previous studies and the results were not significantly different from noise levels and acuity estimates derived based on the Fourier transform of the data [35, 38]. With the first method (Fig. 1, upper graph), the linear fit to the response function included data points between the spatial frequency with the peak amplitude (i.e., in this case 10 cpd) and the response amplitude of the highest spatial frequency still significantly above noise (in this case 20 cpd). The linear fit was extrapolated to the  $X$ -axis (zero amplitude) for the resolution or visual acuity estimate (23 cpd or 20/26). This method was employed to obtain the acuity estimate for 9 of the 17 patients. The second method for determining acuity is displayed in the lower graph of Fig. 1. This graph displays data that can not be fit well by a linear function. The graph has two peaks (i.e. at 6 and 20 cpd) with a trough between the peaks. A linear function fit to the lower peak (i.e. the data between 6 and 13.4 cpd) would yield an acuity estimate lower than the highest spatial frequency above noise (i.e., 20 cpd). Clearly this estimate is lower than the acuity limit. Since there were no data points between 20 cpd and the noise level (i.e., 24 cpd) a linear fit could not be employed for this higher peak and the acuity was taken as 20 cpd. This second method was used to obtain the acuity estimates for 8 patients. If it was possible to fit the data by both of the above methods, the method that resulted in the highest acuity estimate was used in the analysis.

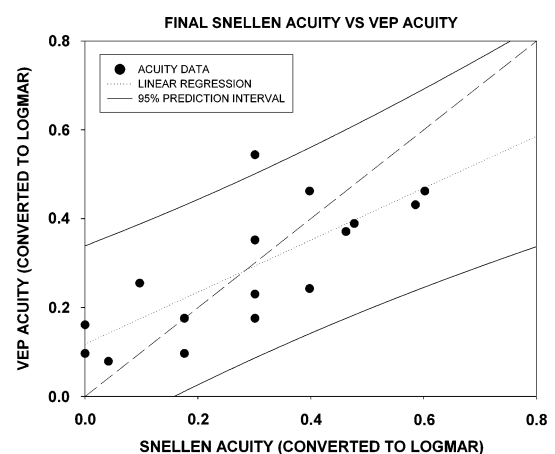
### Statistical analysis

Comparisons between groups were made with  $t$ -tests. Pearson and intraclass correlation

coefficients were used to determine relationships between data sets. The statistical tests were performed with the software package Minitab (Minitab, Inc.).

### Results

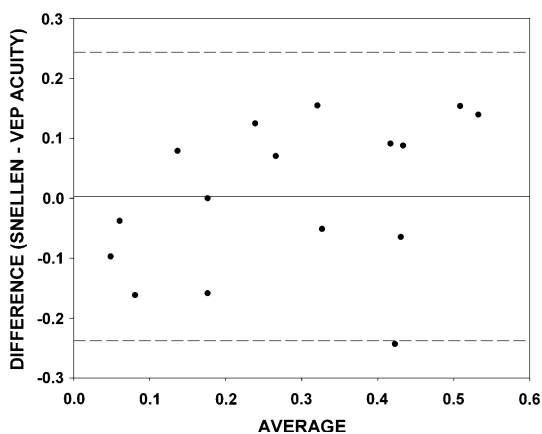
A paired  $t$ -test indicated that the initial Snellen visual acuity for all of the patients was different from their final Snellen visual acuity ( $P < 0.00001$ ,  $t = 6.95$ ,  $df = 16$ ). Thus, the therapy improved the acuity in the amblyopic patients by an average of  $5.1 \pm 3.03$  (SD) logMAR lines. The pre-amblyopic therapy sVEP acuity is plotted against the patient's post-amblyopic therapy Snellen visual acuity in Fig. 2. The acuities were converted to logMAR values for all analyses and plotting ( $\text{logMAR} = \text{Log}(\text{Snellen denominator}/20)$ ). This figure contains data from all 17 patients (the data for patients 13 and 15 overlap). The dashed line is the one-to-one line. The dotted line is the best-fit line to the data ( $y = (0.5847)X + 0.1179$ ). The correlation coefficient for this line is 0.76 (Pearson correlation,  $r$ ). The intraclass correlation coefficient ( $r_i$ ) for the data is 0.73. The intraclass correlation coefficient is a measure of how well the data fits the one-to-one line. The solid lines display the 95% prediction interval for the data. The prediction interval encompasses the



**Fig. 2** Pre-amblyopic therapy sVEP acuity plotted against the patient's post-amblyopic therapy Snellen visual acuity. The best-fit line to the data is displayed. The intraclass correlation coefficient ( $r_i$ ) is 0.73

one-to-one line. A paired t-test did not find a significant difference between the 2 sets of data ( $P = 0.94$ ,  $t = 0.08$ ,  $df = 16$ ). The mean of the difference (Snellen—VEP) in logMAR acuity was  $+0.002 \pm 0.123$  (mean of the differences  $\pm$  SD). The 5th and 95th percentiles for the differences were  $-2.4$  and  $+1.5$  logMAR acuity chart lines (calculated with the Tally function of Minitab). Thus, we would predict that 90% of the time, amblyopes post-therapy logMAR acuity would be within  $-2.4$  and  $+1.5$  logMAR acuity chart lines of the predicted sVEP acuity.

The relationship between the best fit and one-to-one lines for the amblyopes in Fig. 2 appears to be similar to that seen for normal patients and patients with decreased acuity due to an organic cause [34, 35, 38, 48]. A mean versus difference plot [49] was produced (Fig. 3) to determine if the present data displayed a systematic bias or a trend similar to previous reports. All the data points lie within  $\pm 1.96$  standard deviations (the horizontal dashed lines) of the mean. There is no clear indication of a systematic bias however there is a modest trend in the data. A linear fit to the data has a positive slope ( $Y = 0.29X - 0.082$ ). When the Snellen acuity is good (i.e., about 20/20 or 0 logMAR), the sVEP acuity is slightly poorer than 20/20. For moderately decreased Snellen acuities (i.e., about 20/40 or 0.3 logMAR), the sVEP acuity is similar. When the Snellen acuity is poor, the sVEP acuity is better than the Snellen acuity. The modest trend seen in this data agrees

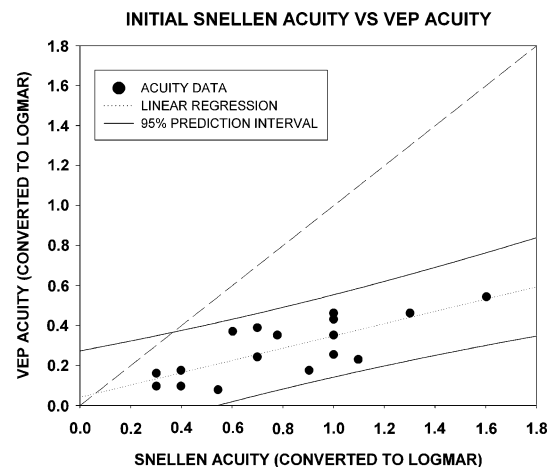


**Fig. 3** A plot of the mean acuity versus the difference in acuity for each patient. See the text for details

with that of previous reports for normal subjects [34, 35, 38, 48]. Thus, for amblyopes, the relationship between Snellen and sVEP acuity normalizes after amblyopia therapy.

Figure 4 displays the pre-amblyopic therapy sVEP acuity plotted against the patient's pre-amblyopic therapy Snellen visual acuity. Again, the dashed line is the one-to-one line and the dotted line is the best-fit line to the data ( $y = (0.3068)X + 0.0412$ ). The correlation coefficient for this line is 0.77 (Pearson correlation,  $r$ ). The intraclass correlation coefficient is  $-0.21$ . Overall, the 95% prediction interval does not encompass the one-to-one line suggesting that there is not a good correlation between the initial Snellen acuity and the sVEP acuity. The sVEP acuities are typically better than the pre-therapy Snellen acuities ( $P < 0.000001$ ,  $t = 7.92$ ,  $df = 16$ ). The average difference in logMAR acuity was  $0.51 \pm 0.268$  (mean  $\pm$  SD) or 5.1 logMAR acuity lines.

The etiology of amblyopia can play a significant role in the effectiveness of amblyopia therapy [44]. For this reason, the refractive amblyopes and the strabismic amblyopes were examined separately. Figure 5 displays the pre-amblyopic therapy sVEP acuity plotted against the post-amblyopic therapy Snellen visual acuity for all of the refractive amblyopes. The two sets of data



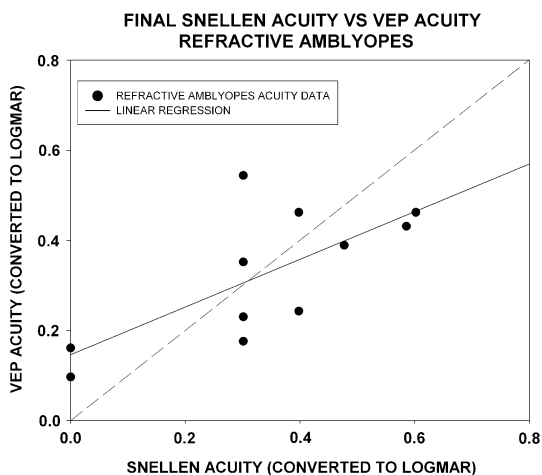
**Fig. 4** Pre-amblyopic therapy sVEP acuity plotted against the patient's pre-amblyopic therapy Snellen visual acuity. The best-fit line to the data is displayed. The intraclass correlation coefficient ( $r_i$ ) is  $-0.21$

were not significantly different ( $P = 0.81$ ,  $t = 0.25$ ,  $df = 10$ ). The intraclass correlation coefficient is 0.68. Figure 6 displays the pre-amblyopic therapy sVEP acuity plotted against the post-amblyopic therapy Snellen visual acuity for all of the strabismic amblyopes. The two sets of data were not significantly different ( $P = 0.75$ ,  $t = 0.34$ ,  $df = 5$ ). The intraclass correlation coefficient is 0.78. Thus, the etiology of the amblyopia did not have an effect on the predictability of the post-therapy vision.

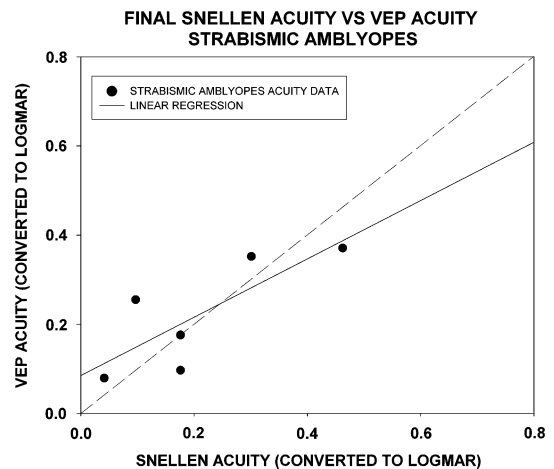
## Discussion

The pre-amblyopic therapy acuity estimate from the sVEP is a good estimate of the post-amblyopic therapy Snellen acuity ( $r_i = 0.73$ ). For the patients in this study, the sweep VEP acuity estimate was usually within 1 logMAR acuity chart line of the final visual acuity (mean of the differences  $\pm$  SD =  $+0.002 \pm 0.123$ ). The 90% predictive interval for the sVEP was  $-2.4$  to  $+1.5$  logMAR acuity chart lines. The intraclass correlation coefficient for the refractive amblyopes was not different from the strabismic amblyopes (0.68 vs. 0.78).

Selenow et al. reported that laser interferometry before amblyopia therapy was a good



**Fig. 5** Pre-amblyopic therapy sVEP acuity plotted against the post-amblyopic therapy Snellen visual acuity for the refractive amblyopes. The best-fit line to the data is displayed. The intraclass correlation coefficient ( $r_i$ ) is 0.68



**Fig. 6** Pre-amblyopic therapy sVEP acuity plotted against the post-amblyopic therapy Snellen visual acuity for the strabismic patients. The best-fit line to the data is displayed. The intraclass correlation coefficient ( $r_i$ ) is 0.78

predictor of acuity after amblyopia therapy [16]. To make a comparison with the results presented here, we took their published data and determined the intraclass correlation coefficient after their data was converted to logMAR units. The result was an intraclass correlation coefficient of 0.92. It is possible that their correlation coefficient was higher because they had a larger sample size (39 vs. 17), thus, the effect of outliers would be less on the correlation. However, the mean difference between the laser interferometry acuity and post-therapy Snellen acuity was similar to the results from this study (mean  $+0.05 \pm 0.118$  vs.  $+0.002 \pm 0.123$ ) and the two data sets were not significantly different (2 sample  $t$ -test,  $P = 0.22$ ,  $t = 1.25$ ,  $df = 31$ ). Furthermore, the range of the 90% predictive interval was the same for the Selenow et al. data ( $-1.7$  to  $+2.2$  logMAR acuity chart lines) and the sVEP data ( $-2.4$  to  $+1.5$  logMAR acuity chart lines).

Selenow et al. proposed that laser interferometry could predict potential acuity in amblyopes because 1) the laser bypassed the optics of the eye which removed focusing problems, 2) the pattern was spatially redundant which discounted eye position errors, and 3) determining the orientation of a grating is easier than identifying complex letter forms [16]. Similar explanations can be used to explain why the sVEP acuity is a good

predictor of post-therapy Snellen acuity. First, the pattern that was employed in this study was of high contrast and spatially redundant (i.e., a horizontal-oriented, sine-wave grating). Thus, moderate amounts of eccentric fixation would not affect the VEP measurement. Additionally, since many amblyopes have unsteady central fixation with movement in the horizontal direction, the grating orientation may be critical to obtaining the best acuity estimate in these patients [45]. Amblyopes also have greater neural noise in the visual system than normal subjects [50, 51]. The repetitive pattern of a sine-wave grating may optimize the signal/noise ratio and result in a better estimate of acuity than that obtained with Snellen letters.

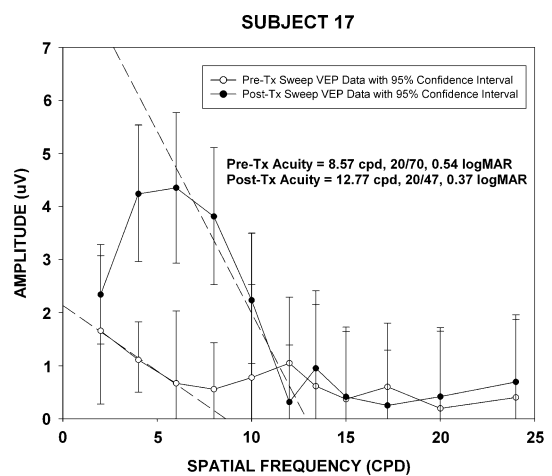
Second, the patient's best distance correction was employed during the test procedure. Since the test distance was either  $\frac{1}{2}$  or 1 m, the maximum amount of accommodation necessary was no more than 2 diopters. Thus, the impact of accommodative problems associated with amblyopia should be minimal [52].

There are other reasons why the sVEP acuity estimate may be a better predictor of post-therapy acuity than interferometry or Snellen acuity. First, the VEP does not require a response from the subject. Thus, the task is easier than laser interferometry or letter identification for the patient. This may result in better performance for young children. Second, the initial site of the defect in amblyopia is the striate cortex [1–5]. Using source localization techniques, the VEP has been shown to originate in the striate and extrastriate cortex in primates [21, 53–58]. Laser interferometry and Snellen acuity, since they require a subjective response from the patient, involves processing by the frontal cortex [9–11]. Thus, the VEP is an excellent tool to assess the effects of amblyopia on the visual cortex which could make it a better tool to assess post-amblyopic therapy acuity than laser interferometry or Snellen acuity.

The results do not suggest that the etiology of amblyopia affects the predictability of the sVEP acuity estimate. Our results are in agreement with recent amblyopia treatment results showing no difference in the treatment effects based on etiology [59, 60].

Pattern VEP results with amblyopes suggested that the amplitude of the response increased throughout the course of therapy [19, 22, 23]. This possibility was assessed in three patients (# 15, 16, 17) using the sVEP. The sVEP was measured before and at the termination of amblyopia therapy. Figure 7 displays the results for patient 17. The pre- and post-therapy sVEP results are shown (open and filled symbols, respectively). The results demonstrate that the amplitudes of the responses at 4, 6, and 8 cpd have increased after amblyopia therapy. However, the acuities have not changed substantially (0.54 vs. 0.37 logMAR) because the slopes of the lines that were fit to the data changed. The pre-therapy slope is lower than the post-therapy slope. The results of the other 2 patients were similar except that their acuity estimates decreased after therapy (see Table 1). Thus, the sVEP acuity determined before therapy is similar to that obtained after ( $N = 3$ , Pre-Therapy sVEP acuity =  $0.37 \pm 0.156$  logMAR and Post-Therapy sVEP acuity =  $0.42 \pm 0.057$  logMAR, paired  $t$ -test  $P = 0.73$ ,  $t = 0.40$ ,  $df = 2$ ).

Future studies will need to determine if there is an age dependent predictive effect for the sVEP. As the visual system matures, the sVEP acuity estimate for an untreated amblyope may decline. For example, a 5-year-old patient might yield a better sVEP acuity estimate than a 30-year-old



**Fig. 7** Pre- and post-amblyopic therapy sVEP data for subject 17. The dashed lines are the fits to the data to determine the acuity. See text for further details

patient with the same amblyopic etiology. However, recent studies have suggested that the improvement in post-therapy acuity may not be correlated with age, at least in anisometric amblyopes [61]. Our patient population is too small to make any definitive statements concerning the effect of age.

In conclusion, the pre-amblyopic therapy estimate of acuity with the sVEP is a good predictor of the post-amblyopic therapy Snellen acuity. The estimates of post-therapy acuity with the sVEP are as good as those obtained with laser interferometry (i.e., typically within 1 logMAR acuity chart line of the post-therapy acuity). The pre-therapy sVEP acuity estimate may be a good predictor of post-therapy acuity because it assesses the specific location affected by amblyopia (i.e., the visual cortex) and it uses a stimulus that maximizes the signal/noise ratio (i.e., a sine-wave grating).

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