Disparity vergence responses before versus after repetitive vergence therapy in binocularly normal controls

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This study sought to determine whether significant changes would be observed between vergence eye movements before and after 12 hr of repetitive vergence therapy (1 hr per day on different days) in subjects with normal binocular vision compared to controls. Disparity vergence responses from 23 subjects were studied. An assessment protocol that minimized the influence of the near dissociated phoria on the disparity vergence system was designed. The following parameters were quantified for the responses: latency, time to peak velocity, settling time, peak velocity, and accuracy (difference between the response and stimulus amplitudes). The following outcomes were observed when comparing the results after vergence therapy to the baseline measurements: (a) near point of convergence and near dissociated phoria did not significantly change ($p > 0.15$); (b) latency, time to peak velocity, and settling time significantly decreased ($p \leq 0.01$); and (c) accuracy significantly improved ($p < 0.01$). Results support that vergence peak velocity is dependent on the subject's near dissociated phoria. The accuracy and temporal properties of vergence eye movement responses from subjects with normal binocular vision can be improved after vergence therapy. These methods can be utilized within future studies to quantitatively assess vergence therapy techniques for patients with binocular dysfunction.

Introduction

Symmetrical vergence eye movements are rarely performed in our daily activities. However, symmetrical vergence stimuli (visual targets presented on the midsagittal plane) are the core of many vision therapy protocols (also called orthoptics, vergence therapy, or oculomotor rehabilitation). Randomized clinical trials have demonstrated that office-based vergence and accommodative therapy (OBVAT) with home reinforcement leads to a sustained reduction in vision symptoms and improved clinical findings for those with the binocular dysfunction called convergence insufficiency (CI; Convergence Insufficiency Treatment Trial [CITT], 2008; Scheiman, Cotter, et al., 2005; Scheiman, Mitchell, Cotter, Cooper, et al., 2005; Scheiman, Mitchell, Cotter, Kulp, et al., 2005). The reduction of visual symptoms after therapy may lead to an improvement in activities of daily living, such as reading and computer-, tablet-, and smartphone-related activities.

Because these randomized clinical trials were investigating vergence therapy for patients with binocular vision disorders, they did not include subjects with normal binocular vision. There are limited available data about the effect of repetitive vergence therapy with binocularly normal subjects (van Leeuwen, Westen, van der Steen, de Faber, & Collewijn, 1999). However, this topical area is important because our society is becoming more dependent on small, handheld devices, such as smartphones and tablets (Lodin, Forsman, & Richter, 2012). It is not surprising that literature is emerging from eye care professionals and laboratory studies supporting a relationship between sustained near vision (i.e., computer use) and an increase in visual symptoms and discomfort even for those with normal

binocular vision (Bababekova, Rosenfield, Hue, & Huang, 2011; Lodin et al., 2012; Rosenfield, 2011). It is reasonable to hypothesize that visual symptoms related to near sustained visual activities will become more common even in people with normal binocular vision because of the increasing near visual demands of our society. We speculate that optimizing vergence function in people with normal binocular vision may allow these individuals to engage in sustained near activity with less likelihood of visual symptoms. Hence, a study that investigates the effect of repetitive vergence eye movement therapy on the temporal and accuracy parameters of the vergence system in subjects without binocular dysfunctions is timely.

There are a number of challenges when designing a study to evaluate the effect of repetitive vergence eye movement therapy. The first challenge is the complexity of the disparity vergence system, which includes both a fast fusional phasic system (FFPS) and a slow fusional tonic system (SFTS). When a vergence disparity stimulus is presented, the SFTS adjusts to the new visual stimulus via adaptation (C. Schor, 1980, 1988; C. Schor & Horner, 1989; C. M. Schor, 1979, 2009). The dissociated heterophoria (or simply phoria) represents the eye position when the two eyes are dissociated (Han, Guo, Granger-Donetti, Vicci, & Alvarez, 2010; Rosenfield, 1997). The occluded eye may maintain its position; rotate nasally, temporally, superiorly, or inferiorly; or a have combination of a horizontal and vertical movement. The eye could also experience movement around the *z*-axis. These positions are termed orthophoria, esophoria, exophoria, hyperphoria, hypophoria, excyclophoria, and incyclophoria, respectively. The SFTS can be quantified as a person's phoria level. A person's phoria level may change as a result of the visual demand (via sustained vision, prisms, or lenses), the duration of the visual task, or the amount of time that the subject is visually dissociated (Kim, Granger-Donetti, Vicci, & Alvarez, 2010; Lee, Chen, & Alvarez, 2008; Rosenfield, 1997; Ying & Zee, 2006). When fusion is interrupted during dissociation, changes in the SFTS vergence levels (adaptation) can be measured as changes in the angle of the phoria. A subject's phoria is commonly used as part of the diagnoses for binocular dysfunctions. In addition, patients with CI have been shown to have a reduced rate and magnitude of phoria adaptation compared to controls (Brautaset & Jennings, 2005; R. North & Henson, 1981; R. V. North & Henson, 1992). The importance of improved vergence adaptation appears, at least in part, to arise from a reduction in excessive convergence accommodation in patients with CI (Sreenivasan & Bobier, 2014) in whom phoria adaptation is improved after vision therapy (Sreenivasan & Bobier, 2015). Hence, to study disparity vergence, you must consider both the FFPS and the SFTS.

A second challenge of assessing the effect of repetitive vergence therapy on FFPS, SFTS, or both systems of disparity vergence involves the interaction between the FFPS and SFTS. Randomized clinical trials on children with CI support a sustained reduction of visual symptoms for at least up to 1 year post successful treatment of OBVAT (Rouse et al., 2009). Such sustained improvement suggests a form of long-term adaptation to the vergence system. Several independent researchers have suggested that orthoptics may reduce visual symptoms in those with binocular dysfunction by increasing the rate and magnitude of phoria adaptation (the SFTS; R. North & Henson, 1981; R. V. North & Henson, 1992; C. M. Schor, 2009; Sreenivasan & Bobier, 2014, 2015). Our laboratory and other independent groups have shown that sustained vision or the current state of the near dissociated phoria varies with the peak velocity of the FFPS (Alvarez et al., 2009; Jaschinski, Svede, & Jainta, 2008; Kim & Alvarez, 2012a; Kim et al., 2010; Kim, Vicci, Granger-Donetti, & Alvarez, 2011; Kim, Vicci, Han, & Alvarez, 2011; Patel, Jiang, White, & Ogmen, 1999). It is currently unknown how repetitive vergence therapy modifies the interaction between the FFPS and SFTS.

This present study concentrates on quantifying the modification to the FFPS from vergence therapy. Hence, because the SFTS adapts depending on visual demand, which modifies the FFPS, then one should take into account the SFTS when studying the FFPS. Our experimental design attempts to maintain the SFTS so that this study can concentrate on analyzing the FFPS. To do so, first, the disparity steps were kept small (2° step changes). Second, the experiment was individualized so that each subject's phoria level became the starting point around which the disparity steps were presented. Third, the amount of required sustained convergence from the subject's phoria level was equal to the amount of required sustained divergence from the subject's phoria level.

The therapy procedure used within this study was designed based on two current theories of how vision therapy may alter the visual system in subjects with CI leading to a sustained reduction in visual symptoms. The first theory is CI patients have a reduced ability to adapt to near space when they are initially looking in the distance compared to binocularly normal controls (R. North & Henson, 1981; R. V. North & Henson, 1992; C. Schor, 1988; C. Schor & Horner, 1989; C. M. Schor, 2009; Sreenivasan & Bobier, 2014, 2015). The second theory is CI patients have inadequate disparity vergence to control the phoria compared to binocularly normal controls, which forces them to use excessive neuromuscular innervation to control the deviation and diplopia (Cooper & Jamal, 2012; Scheiman, Gwiazda, & Li, 2011; Scheiman & Wick, 2008). The literature supports the idea that these two theories are related

because empirical evidence shows that positive fusional vergence ranges used in clinical testing are strongly correlated to vergence adaptation in binocularly normal controls (Scheiman & Wick, 2008; Thiagarajan, Lakshminarayanan, & Bobier, 2010) and patients with CI (Sreenivasan & Bobier, 2015).

This study was designed to empirically study the following question: Does repetitive vergence therapy reduce temporal measurements (i.e., response latency, time to peak velocity, and settling time) and improve accuracy performance (analysis of the response amplitude and peak velocity) of the FFPS in those with asymptomatic normal binocular vision? In order to answer this question, an experimental assessment protocol was designed that minimized the influence of the SFTS on the FFPS. Improvements observed within the vergence responses are hypothesized to be the following: (a) initiating the response earlier (quantified via a reduction in latency and time to peak velocity), (b) acquiring a new target earlier (quantified via a reduction in settling time), and (c) fusing a target with improved accuracy (quantified as a reduction of the difference between the stimulus and response amplitude). These results are hypothesized because repetitive vergence therapy has been shown to improve these vergence parameters in patients with binocular dysfunctions (Alkan, Biswal, & Alvarez, 2011; Alkan, Biswal, Taylor, & Alvarez, 2011; Alvarez, 2015; Alvarez, Jaswal, Gohel, & Biswal, 2014; Alvarez & Kim, 2013; Alvarez et al., 2010; Bucci, Kapoula, Bui-Quoc, Bouet, & Wiener-Vacher, 2011; Jainta, Bucci, Wiener-Vacher, & Kapoula, 2011; Jaswal, Gohel, Biswal, & Alvarez, 2014).

Methods

An experimental procedure was designed to serve as an assessment protocol for the vergence system of asymptomatic, binocularly normal subjects. The key element of the design is that all visual stimuli presented were centered about the subject's near dissociated phoria level. A haploscope with eye movement recording instrumentation was utilized for both the assessment protocol and vergence therapy regimen to stimulate disparity vergence and minimize proximal and accommodative vergence visual cues. The subject criteria, experimental setup, protocols, data, and statistical analyses are described below.

Subjects and inclusion/exclusion criteria

Subjects signed written informed consent approved by the New Jersey Institute of Technology Institution

Review Board in accordance with the Declaration of Helsinki. There were two groups of binocularly normal subjects. The first group participated in vergence therapy, and the second group (controls) did not.

To be eligible for the study, the subjects were required to have normal binocular vision defined as (a) best corrected visual acuity in each eye of 20/20, (b) stereopsis better than 70 arcsec, (c) near point of convergence less than or equal to 6 cm, (d) a near dissociated phoria between 4 esophoria to 6 exophoria, and (e) no history of neurological or ophthalmic disease or dysfunction. All subjects (those who participated in vergence therapy and controls) wore appropriate refractive correction during all assessments and vergence therapy (for those who participated in therapy) sessions. Wearing spectacles did not substantially impact the quality of the eye movement recordings because the eye-tracking cameras were placed below the line of sight under the partially reflective mirrors of the haploscope as shown in Figure 1.

The near dissociated phoria was subjectively measured using a Maddox rod and the Bernell Muscle Imbalance Measure (MIM) card (Bernell Corp., South Bend, IN). The MIM has a resolution of 1Δ and a range of 28Δ exophoria to 28Δ esophoria. The phoria was measured with the left eye fixating on a penlight shown through the MIM card set 40 cm away along the subject's midline. The visual target equates to an accommodative demand of 2.5 D. The "flashed" Maddox rod procedure used in this study occluded the subject's right eye for 15 s followed by rapid and brief uncover/cover to assess the location of the red vertical line on the MIM card calibrated grid. Typically, three or four flashes were presented, and the flashes were repeated until the subject could confidently report the number at which the red vertical line appeared to be located observed within his or her peripheral vision. Both local and global stereopsis were assessed using the Randot Stereotest (Bernell). Finally, the near point of convergence (NPC) was evaluated using the Astron International (ACR/21) Accommodative Rule (Gulden Ophthalmics, Elkins Park, PA) with a printed Gulden fixation target consisting of a single column of 20/30 letters at 40 cm. We followed the testing protocol established in the CITT study (CITT, 2008).

Experimental setup

Instrumentation

The experimental setup can be seen in Figure 1A. For this study, the ISCAN RK-826PCI binocular tracking system (Burlington, MA) instrumentation was used to noninvasively record horizontal eye movements using the pupil as a natural anatomical marker. This device can also detect vertical movements of the pupil and the pupil diameter. This system utilizes an infrared
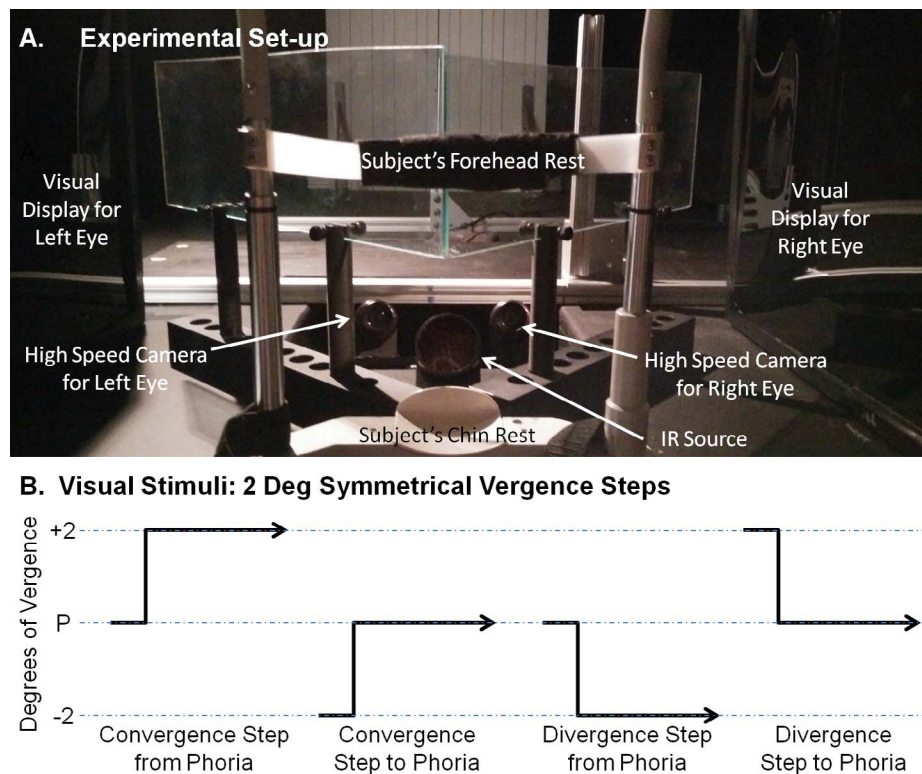
Figure 1. Experimental setup of haploscope with components labeled (A) and each of the four types of visual stimulus steps (B). "P" denotes the near dissociated phoria level of the subject as assessed using the flashed Maddox rod technique.

emitter (950 nm) directed toward the eyes and two cameras to capture each individual eye movement. The system has a power limit of 1.2 mW/cm^2, which is considerably lower than the ANSI Z136 specification safety limit of 10 mW/cm^2. Two high-speed infrared cameras (one for each eye) were used. Each camera sampled data at 240 frames per second (fps) to quantify the reflection of infrared light, which allowed for the determination of the pupil centroid location utilizing ISCAN's software. The manufacturer reports an average accuracy of 0.3° over a ±20° horizontal and vertical range.

VisualEyes software, stimuli presentation, and data collection

A custom LabVIEW™ (National Instruments, Austin, TX) program called VisualEyes controlled the stimuli presentation and data collection from the integrated instrumentation. This software was designed to independently generate visual stimuli to the left and right eyes with the use of two Dell computer monitors (Dell Model: P2211Ht) and partially reflecting mirrors (Guo, Kim, & Alvarez, 2011). As seen in Figure 1A, our VisualEyes software produces a visual stimulus in each visual display that is viewed dichoptically through 50% partially reflective mirrors. Image alignment can be varied to induce retinal disparities along the

subject's midline (the midsagittal plane). The high-speed cameras and infrared source are located behind and below the partially reflective mirrors (see Figure 1A) to ensure that the partially reflective mirrors do not reduce the eye-movement position signal quality. A 12-bit digital acquisition card (National Instruments 604 E series) digitized the eye-movement data recorded from each eye using the ISCAN instrumentation with a sampling frequency greater than the cameras' acquisition speed of 240 fps. This sampling rate is well above the Nyquist sampling criterion for the dynamic measure of saccades (Zuber, Semmlow, & Stark, 1968) and hence also vergence eye movements.

Experimental procedure

Assessment procedure

In order to determine whether changes occur to the disparity vergence system, an assessment procedure was designed that was dependent on each subject's near dissociated phoria level. Measurements were attained at baseline for all subjects and then after either the repetitive vergence therapy (for the therapy group) or after 2–3 weeks (for the control group; see Figure 2). The assessment procedure differed from the vergence therapy protocol to reduce the influence of procedural learning, which is the modification of a system from

Main Effect = GROUP

| Control Group N=11 | Vergence Therapy Group N=12 |

Baseline Assessment (Test and Retest)

Main Effect = TIME

2-3 Week Break

Vergence Therapy

1st, 3rd, 5th … Day of Therapy	2nd, 4th ,6th … Day of Therapy
Vergence Steps 'Near Range'	Ramp Stimuli at 1°/s
Vergence Steps 'Far Range'	Ramps Stimuli at 4 °/s
Ramp Stimuli at 1°/s	Vergence Steps 'Near Range'
Ramps Stimuli at 4 °/s	Vergence Steps 'Far Range'
Vergence Steps 'Near Range'	Ramp Stimuli at 2°/s
Vergence Steps 'Far Range'	Ramps Stimuli at 8 °/s
Ramp Stimuli at 2°/s	Vergence Steps 'Near Range'
Ramps Stimuli at 8 °/s	Vergence Steps 'Far Range'

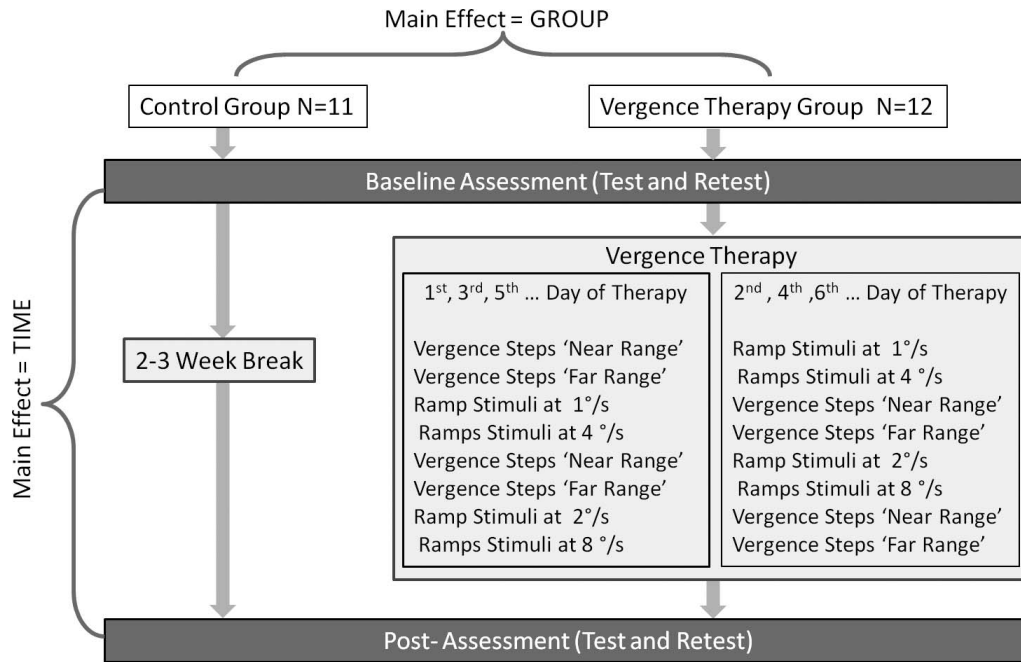**Post- Assessment (Test and Retest)**

Figure 2. Experimental design showing the two main effects of group (control subjects who did not participate in therapy and the subjects who did participate in vergence therapy) and time (baseline and postassessment). Both assessments had test and retest sessions to assess reliability.

performing a task multiple times (Gibson, 1969; Jacoby & Dallas, 1981; Shiffrin & Schneider, 1977). Prior research has shown that phoria adaptation and the subject's current phoria position affect vergence peak velocity (Lee et al., 2009; Kim et al., 2010; Kim et al., 2011a, b; Kim et al., 2012a). Phoria can adapt or change based upon sustained vision (Han et al., 2010). Hence, we kept the binocular disparity step changes to 2°, which equates to about 3.6Δ, to minimize any potential changes to the phoria level. The movements were counterbalanced around each subject's phoria level so that the subjects had equal amounts of sustained vision 2° more convergent from their phoria and 2° more divergent from their phoria. Balancing the visual stimuli around a subject's phoria level reduces the influence of phoria adaptation. In addition, it has been shown that near work, which stimulates sustained fixation close to a subject, induces an esophoric shift in the baseline phoria (Ehrlich, 1987). Hence, our vergence assessment was performed during the morning before any visually demanding activities.

The near dissociated phoria became the pedestal or initial vergence angle for each individual subject. Subjects with very large near exophoria or esophoria were excluded because the visual stimuli would be beyond physiological fusional limits. The near dissociated phoria within this experiment was measured at 40 cm, which is the same distance the visual stimuli (shown on computer screens) were placed within the haploscope. This equates to a 2.5 D accommodative demand. Assuming an interpupillary distance of 6 cm and that

the visual targets are located 40 cm away from the subject's midline, then this would equate to a binocular vergence angle of 8.44° (4.22° per eye). Each subject's interpupillary distance was measured to calculate the correct vergence angles. The initial vergence angle for each eye can be calculated with the following equation in which the angle is denoted in degrees:

$$\text{Initial vergence angle of each eye} = 4.22°$$
$$+\arctan(\text{phoria level in diopters}\Delta/100) \qquad (1)$$

For example, if a subject had a 2Δ exophoria at near, then the initial vergence angle for one eye would be 2Δ divergent from 4.22° or 4.22° − 1.13° = 3.09°. The binocular vergence angle would be 6.18°. The subject would then be shown visual stimuli either 2° more convergent or divergent from the initial vergence angle along the subject's midline (see Figure 1B).

During the assessment, the subject was first dark-adapted for 5 min to uncouple accommodation and vergence and relax both systems (Wolf et al., 1990; Kotulak & Schor, 1986). Then, the subject was given a randomized sequence of four types of 2° symmetrical vergence step movements presented on a haploscope (Figure 1A) to keep accommodative cues constant (Kotulak & Schor, 1986). These movements were convergence steps from the phoria, convergence steps to the phoria, divergence steps from the phoria, and divergence steps to the phoria as visually displayed in Figure 1B. The visual stimulus for the assessment sessions was a line with a height of 6° and width of 0.1°

with a crosshair at the middle. A random delay of 0.5 to 2.0 s before each movement reduced anticipatory cues, which are known to alter the temporal properties and peak velocities of vergence responses (Alvarez et al., 2002; Alvarez et al., 2010; Kumar et al., 2002). Twenty observations of each stimulus type were recorded. There were 80 step responses recorded during each session. Each subject performed the assessment procedure twice on different days (test and retest) to quantify repeatability both at baseline and postassessment measurements (see Figure 2). Hence, the subject participated in four 1-hr assessment sessions (two sessions before and two sessions after vergence therapy or after a 2- to 3-week break for control subjects).

Repetitive vergence therapy procedure

After the baseline assessments, 12 subjects participated in 12 1-hr vergence therapy sessions in the haploscope performed on different days. The first, third, fifth, and so forth were considered "odd" therapy days. Conversely, the second, fourth, sixth, and so forth were considered "even" therapy days. Typically, two therapy sessions were conducted per week, and the therapy took place over approximately a 6-week period.

The therapy consisted of a random step sequence composed of several symmetrical vergence eye-movement stimuli alternating between vergence angular demands. Each session consisted of two 5-min trials of a random step sequence at far (1° to 5°), two 5-min trials of a random step sequence at near (20° to 16°), and four 5-min trials of ramps that ranged from 1° to 20°. The ramp stimulation consisted of four different ramp rates whereby the ramp would start at 1° and become more convergent to 20° and then become divergent to 1° at a rate of 1°/s, 2°/s, 4°/s, or 8°/s. The visual stimulus, a difference-of-Gaussian target, was used because it minimizes accommodative stimulation (Kotulak & Schor, 1986). The stimulus was 2° wide by 6° in height. The random step sequence trial randomizes 2° or 4° symmetrical vergence steps within the "far" or "near" range. The "far" range was defined as 1° to 5° of vergence angular position, and the "near" range was defined as 16° to 20° of binocular eye rotation. As with the assessment procedure, a random temporal delay preceded each step to reduce anticipatory cues. The sequence of the trials for a session was changed depending on whether the therapy day number was an odd day (first, third, fifth, etc. therapy day) or even day (second, fourth, sixth, etc. therapy day) to counterbalance the near and far visual stimulation presentation order to further reduce procedural learning.

The overall experimental design is shown in Figure 2. The first main effect of the study was group (those who participated in vergence therapy and controls who did not). For the group who participated in vergence therapy, during the odd days, the session sequence was near random step sequence, far random step sequence, ramps at 1°/s, ramps at 4°/s, near random step sequence, far random step sequence, ramps at 2°/s, and ramps at 8°/s. The even days were counterbalanced by switching the order of the near and far random step and ramp (1°/s and 4°/s vs. 2°/s and 8°/s) sequence. For the control group who did not participate in vergence therapy, a break of 2–3 weeks was given between the baseline and postassessment time points. The other main effect was time; the first time point was at baseline and the second time point was postassessment.

Individual-level data analysis

Data processing

Data were imported and analyzed using a custom MATLAB program. The vergence response for each movement was calculated by subtracting the right eye data from the left eye data. Data were calibrated individually for the left and right eyes. Calibration was performed monocularly to reduce the potential of fixation disparity influencing the calibration measurements, which could potentially occur if a subject had a large exo or eso fixation disparity. A calibration point was the average voltage value recorded when a subject maintained sustained fixation for 500 ms on a visual target that was a measured distance from the subject. A calibration set was defined as two calibration points recorded for the right eye and two calibration points for the left eye. The gain of the calibration set is the conversion constant to convert from voltage values to a degree of ocular rotation.

Data were inspected individually, and responses that contained saccades within the transient were omitted because saccades have been shown to increase the peak velocity of vergence (Alvarez & Kim, 2013; Chen, Lee, Chen, Semmlow, & Alvarez, 2010; Kim & Alvarez, 2012b; Semmlow, Chen, Granger-Donetti, & Alvarez, 2009; Semmlow, Chen, Pedrono, & Alvarez, 2008; Zee, Fitzgibbon, & Optican, 1992). Data were low-pass filtered with a fourth-order Butterworth filter with a cutoff frequency at 50 Hz. Blinks were easily identified because the signal saturated at the upper or lower bound when the eye image was lost due to eye closure. Blinks occurring within the steady state were removed from the response by interpolating the eye movement response before and after the blink. If a blink occurred during the transient portion of the response, then it was omitted from the analysis. Outliers were defined as any responses that were more than two standard deviations from the average and were omitted from further analysis. The velocity response was calculated using a two-point central difference algorithm (Bahill, Kallman, & Lieberman, 1982).
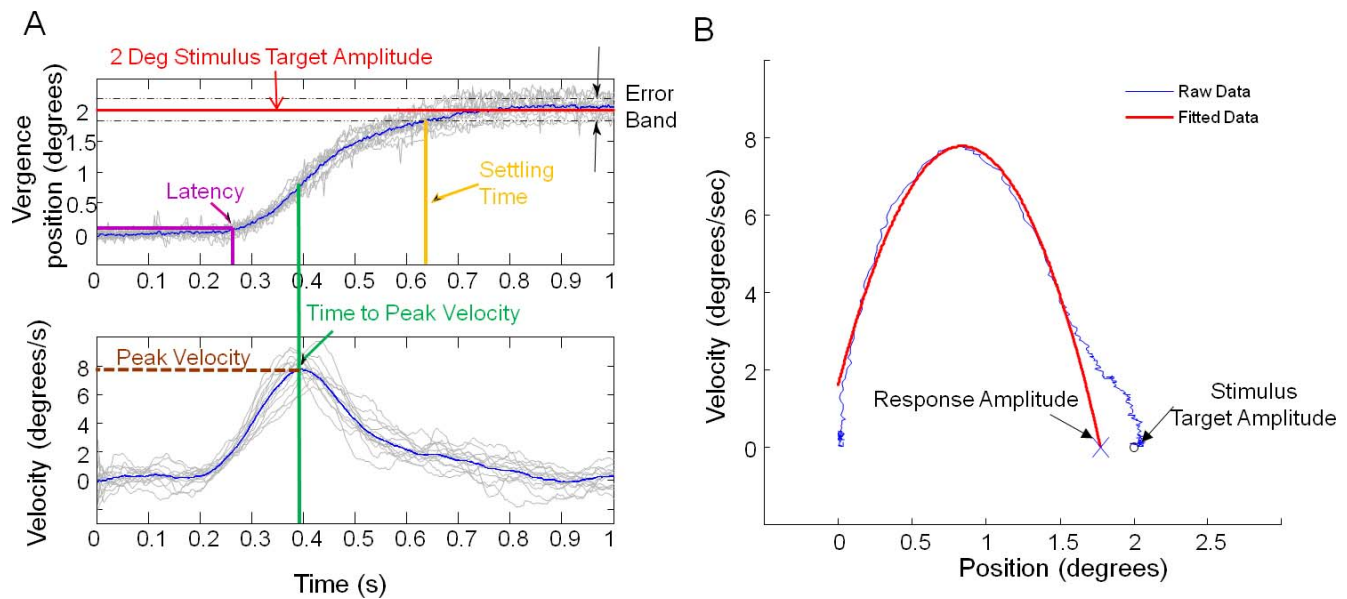
Figure 3. (A) Data analysis graphs of convergence position and velocity as a function of time traces. (B) Phase plane plot (i.e., velocity as a function of position).

Response analysis

The temporal data analysis (i.e., latency, time to peak velocity, and settling time) and dynamic data analysis (i.e., peak velocity and accuracy) were conducted for all vergence step movements across all subjects during the baseline and postassessment sessions. There were four types of eye movements as shown in Figure 1B analyzed for all 23 subjects.

Eye-movement ensembles are shown in Figure 3 to describe the response analysis. Figure 3A shows an ensemble of several convergence position traces (measured in degrees) as a function of time (measured in seconds) on the upper plot and the corresponding ensemble of velocity traces (measured in degrees per second) as a function of time in the lower plot. Each gray line is an individual convergence response (convergence is denoted as positive). The thicker blue line represents the average convergence response for this ensemble group of data. Latency is defined as the time at which the average positional data deviates 5% from the stimulus amplitude. Hence, for our study, this threshold is at 0.1° away from the initial response position. An example of the average response latency is denoted by the purple arrow and lines in Figure 3A. Time to peak velocity is defined as the time when the movement reaches its peak velocity within the transient portion of the response; the brown dashed line in the lower plot depicts the peak velocity, and the green line depicts the time when peak velocity occurs. The settling time was defined as the time when the response was within the 5% error band (black dashed lines in Figure 3A) of the stimulus target amplitude (red line in Figure 3A). For our 2° stimulus, it would be the time when the response

was sustained within the band from 1.9° to 2.1° as depicted by the yellow line and arrow in Figure 3A.

The initial transient response amplitude for each movement was measured using techniques reported from prior literature (Alvarez, Semmlow, & Yuan, 1998; Lee et al., 2008). The phase plane is a plot of the response velocity as a function of position and highlights the dynamics of the response. The response amplitude is the position in degrees at which the velocity returns to about 0°/s in the phase plane plot. The FFPS is described using the dual mode theory of vergence, which is composed of two components, the fusion-initiating component (FIC) and the fusion-sustaining component (FSC; Alvarez, Semmlow, & Pedrono, 2007; Lee, Semmlow, & Alvarez, 2012; Semmlow, Alvarez, & Pedrono, 2007). We assessed the response amplitude of the FIC. The FIC is described as a preprogrammed system that brings the eyes to the new visual target as quickly as possible. A second-order polynomial equation was fit (red line in Figure 3B) to the raw data (blue line in Figure 3B) within the phase plane plot for the time interval defined as when the response is between 10% and 90% of the steady-state thresholds. During this interval, the FIC of the FFPS is dominant (Alvarez, Semmlow, Yuan, & Munoz, 1999). The positive root of the fitted curve (shown as "X" in Figure 3B) is quantified as the response amplitude of the FIC. Using the root of the fitted curve reduces operator bias and has been used in other research (Alvarez, Semmlow, Ciuffreda, Gayed, & Granger-Donetti, 2007; Alvarez, Semmlow, & Pedrono, 2007; Alvarez et al., 1998; Alvarez et al., 1999; Alvarez, Semmlow, Yuan, & Munoz, 2000; Gayed & Alvarez, 2006; Lee et al., 2008). The response amplitude to

target ratio was calculated for each movement. This ratio assesses how well the FIC of the FFPS generated a response to the intended stimulus target. For example, if the FIC moves the eyes to exactly the visual stimulus, then the ratio would be one. Responses that overshoot the visual target would have ratios greater than one, and responses that undershoot the visual target would have ratios less than one. Accuracy was defined as the absolute value of the difference between the stimulus amplitude (2° for this study) and the response amplitude of the FIC. Accuracy was used to assess the absolute error between the response amplitude and the stimulus target when comparing the responses from the baseline and postassessment sessions.

Data reliability testing

Intraclass correlation coefficients (ICCs) of five measures (latency, time to peak velocity, settling time, peak velocity, and accuracy) were calculated in the whole study sample from two sets of measurements at the baseline time point and at the postassessment time point, respectively. An ICC estimates the ratio of variances:

$$ICC = \frac{Var(subjects)}{Var(subjects) + Var(error)} \quad (2)$$

where *subjects* is defined as the between-subjects differences. And *error* is defined as the within-subject differences of the measurements acquired at the two different time points (Shrout & Fleiss, 1979).

In addition, a two-tailed, paired t test was conducted to compare the NPC and near dissociated phoria from the initial baseline and the postassessment measurements. Statistical significance was defined as $p < 0.05$. The data within this study passed the Levene's test of equality because significance was 0.074, and thus variance was equal across groups. All the statistical calculations for reliability testing were performed using SPSS (IBM Corp, Armonk, NY).

Statistical analyses for group comparisons

The model of a 2×2 repeated-measures ANOVA was utilized to assess the between-groups differences and group versus time interactions in the five measures (latency, time to peak velocity, settling time, peak velocity, and accuracy). The group types were the following: (a) subjects who participated in vergence therapy and (b) controls who did not participate in vergence therapy. The timing types were the following: (a) the baseline initial assessment measurements and (b) the postassessment measurements. Statistical significance

was defined as $p < 0.05$ by controlling the false discovery rate. Last, a linear regression analysis was conducted on the settling time as a function of accuracy measurements. The Pearson correlation coefficient was calculated.

Results

The first group who participated in vergence therapy had seven males and five females with an average age of 22.3 years $\pm$ 2.8 (range 18 to 28). The second group composed of controls had six males and five females with an average age of 25.1 years $\pm$ 4.2 (range 19 to 33). The age and gender were not significantly different between groups. For the group who participated in vergence therapy, six of the 12 subjects were myopic. For the control group, seven of the 11 subjects were myopic. No subjects were hyperopic, and all myopes had a prescription between -1 D and -2 D.

The NPC and near dissociated phoria measurements from each subject at baseline and postassessment are summarized in Table 1. A two-tailed paired t test ($\alpha = 0.05$) determined that these two populations were not significantly different from each other ($p > 0.1$) at baseline for NPC or near dissociated phoria. A two-tailed paired t test ($\alpha = 0.05$) determined that the near dissociated heterophoria also did not significantly change after being compared to before vergence therapy ($p > 0.1$) for the group who participated in therapy. For the control group, the NPC and near dissociated heterophoria also did not significantly change between baseline and postassessment ($p > 0.06$).

The ICCs of the following measurements demonstrated high reliability within this study: latency, time to peak velocity, settling time, peak velocity, and accuracy. As shown in Table 2, all the ICCs are equal to or greater than 0.7.

The group-level statistical analyses in the measurements of latency, time to peak velocity, settling time, and accuracy showed significant between-groups differences in the main factors and different group-by-time interaction patterns in the two groups. Significant main effects of the group and time included the following: latency, $F(1, 21) = 7.15$, $p < 0.01$; time to peak velocity, $F(1, 21) = 8.86$, $p < 0.01$; settling time, $F(1, 21) = 17.23$, $p < 0.001$; and accuracy, $F(1, 21) = 5.37$, $p < 0.03$. For both groups (those who participated in vergence therapy and those who were controls), these four parameters significantly decreased as showed in Figure 4. A group-by-time interaction effect was observed for the measures of settling time and accuracy means. Although both groups significantly improved, the group who participated in vergence therapy improved more compared to the

Subjects who participated in vergence therapy

	NPC (cm)		Near dissociated phoria (Δ)	
Subject	Baseline	After vergence therapy	Baseline	After vergence therapy
1	6	2	4 Exophore	4 Exophore
2	3	4	Orthophore	Orthophore
3	6	5	2 Exophore	Orthophore
4	3	4	2 Exophore	2 Exophore
5	6	4	6 Exophore	8 Exophore
6	3	3	2 Exophore	Orthophore
7	6	7	6 Exophore	6 Exophore
8	6	4	4 Exophore	2 Exophore
9	2	2	Orthophore	Orthophore
10	3	3	Orthophore	Orthophore
11	4	3	2 Exophore	4 Exophore
12	6	5	2 Exophore	3 Exophore
Average	4.5 ± 1.6	3.8 ± 1.4	2.5 Exophore ± 2.1	2.4 Exophore ± 2.7

Control subjects who did not participate in vergence therapy

	NPC (cm)		Near dissociated phoria (Δ)	
Subject	Baseline	After break	Baseline	After break
13	3	3	2 Exophore	2 Exophore
14	3.5	4	2 Exophore	4 Exophore
15	6	7	Orthophore	Orthophore
16	2.5	3.5	2 Esophore	2 Esophore
17	2.5	2.5	2 Esophore	4 Esophore
18	3	3	2 Exophore	Orthophore
19	4	5	2 Exophore	Orthophore
20	4	5.5	6 Exophore	5 Exophore
21	5	4	2 Exophore	3 Exophore
22	3	5	6 Exophore	4 Exophore
23	5	5	2 Exophore	4 Exophore
Average	3.7 ± 1.1	4.3 ± 1.3	1.8 Exophore ± 2.6	1.5 Exophore ± 2.9

Table 1. NPC and near dissociated phoria measurements for subjects who participated in vergence therapy (subjects 1 to 12) and for controls (subjects 13 to 23) who did not participate in vergence therapy.

Variable	2 sets of measurements at baseline assessment	2 sets of measurements at postassessment
Latency	0.80	0.75
Time to peak velocity	0.70	0.85
Settling time	0.82	0.81
Peak velocity	0.90	0.90
Accuracy defined as response amplitude error	0.85	0.85

Table 2. Reliability assessment using intraclass correlation coefficient.

control group as observed by an increase in the slopes shown in Figure 4.

Figure 5 plots the average position and velocity of responses before (blue lines) and after (red lines) vergence therapy. This figure is used to explain why faster velocity is not optimum for group-level analysis. Figure 5A does not show substantial changes in peak velocity, and Figure 5B shows a reduction in peak velocity (17°/s to 14.5°/s). Conversely, Figure 5C and D shows that velocity increases after vergence therapy. Figure 5D shows a small change whereas Figure 5C shows a substantial increase in peak velocity (3°/s to 6°/s). In control theory, an ideal response is a critically damped response, which is a movement that changes from one initial vergence angle to the next intended vergence angle using the shortest amount of time without oscillation. In other words, the peak velocity
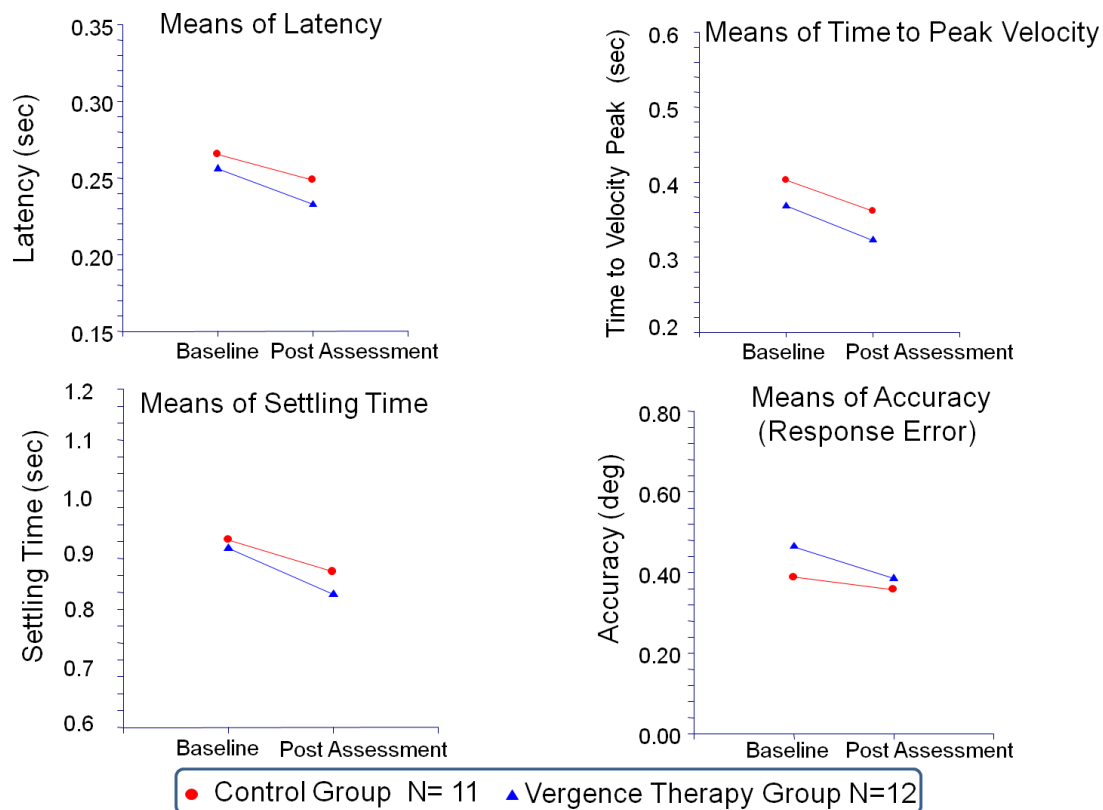
Figure 4. Group-level analysis of 12 subjects who participated in vergence therapy (blue triangles) and the 11 subjects who were controls and did not participate in vergence therapy (red circles). The means of the latency, time to peak velocity, settling time, and accuracy are plotted.

generated is optimized to drive the eyes to the next position as quickly as possible without substantial error. Figure 5A responses are closer to a critically damped system compared to Figure 5B, C, or D. Figure 5 qualitatively shows how a group-level analysis of strictly vergence peak velocity would mask changes potentially evoked from vergence therapy because, between subjects, the types of responses (hypermetric compared to hypometric) will confound any group-level analysis.

Because peak velocity cannot assess group-level differences due to an averaging or masking effect, Figure 6 shows why measuring for accuracy is more appropriate. Figure 6A plots position as a function of time for the following types of responses: overdamped, approximately critically damped, and underdamped responses using some of the data from Figure 5. Figure 6B contains the same responses as Figure 6A drawn within the phase plane. The phase plane is a plot of vergence response velocity as a function of vergence position. Figure 6B shows that, although all responses attain the given visual stimulus of a 2° symmetrical vergence step, the underdamped response overshoots the target, reaching an amplitude of about 2.6°. The overdamped response has the slowest peak velocity as the response amplitude is about 1.4°. Figure 6A shows the overdamped response has a long settling time of

more than 1.5 s. Figure 6 allows direct comparison between overdamped and underdamped responses. The response amplitude allows a group-level analysis of the accuracy of the data within this study. Figure 6 shows the response amplitude can vary from 1.4° for overdamped responses to 2.6° for underdamped responses even though the ideal response would generate a 2° response amplitude. The accuracy for the underdamped and overdamped responses in Figure 6 is a position error of 0.6° larger (underdamped) or 0.4° smaller (overdamped responses) than the stimulus amplitude.

Figure 7A shows a histogram that compares the response amplitude to visual stimulus ratios of all the movements across the 12 subjects who participated in vergence therapy before (blue) and after (red) vergence therapy. Figure 7B is for the 11 subjects who had baseline assessments (blue), had a break of between 2 and 3 weeks, and then postassessment measurements (red) without any therapy. The visual stimulus was consistently 2° throughout the study. If the response amplitude was ideal (2°), then the ratio would be one. If the response amplitude was due to an overshoot (underdamped response), then the ratio was greater than one. If a response amplitude was from a response with an undershoot (overdamped response), then the ratio was less than one. Before vergence therapy, the
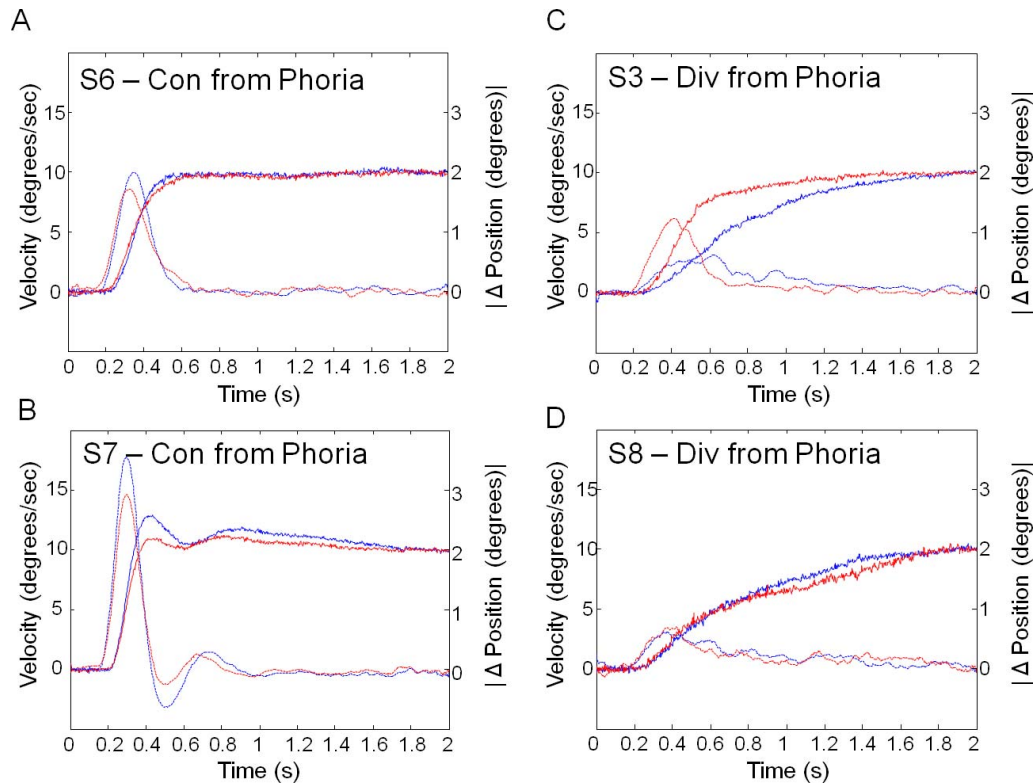
Figure 5. Average position (solid) and velocity (dotted) vergence eye movement responses before (blue) and after (red) vergence therapy that depicts different responses to the vergence therapy. (A) Average response that was approximately critically damped and did not substantially change after vergence therapy. (B) Average response that was underdamped before vergence therapy and became, on average, more critically damped after vergence therapy. (C) Average response that was overdamped before vergence therapy and then, on average, became more critically damped after vergence therapy. (D) Average response that was overdamped and did not exhibit substantial change after vergence therapy.

response to target ratio average with standard deviation was 0.95 ± 0.24, which became 0.96 ± 0.17 after vergence therapy. For the control group, the ratio was 0.84 ± 0.25 at baseline and 0.91 ± 0.24 during postassessment. Precision of a system is the repeatability of a response acquiring the same target location consistently. After vergence therapy, the precision of the responses improved as shown by the decrease of the standard deviation of the response amplitude to stimulus ratios for the subjects who participated in vergence therapy (Figure 7A). Conversely, the precision for the subjects who served as controls did not substantially change (Figure 7B).

A linear regression analysis was conducted to determine whether a positive correlation existed between the settling time and accuracy (error between response amplitude and visual stimulus). Figure 8 plots the linear regression analysis of all the averages for each of the four movement types for the 23 subjects studied. The Pearson correlation coefficient (r) was 0.65 and showed that the settling time was statistically correlated with the accuracy or error ($p < 0.001$). The linear trend line was plotted as a solid line and showed

that the settling time was equal to 0.43 times the response amplitude error (RA_{Error}) plus 0.71.

The last analysis assessed the peak velocities of all eye movements. Figure 9 plots the average with plus and minus one standard deviation of the following types of eye movements: convergence from phoria (blue), convergence to phoria (green), divergence from phoria (red), and divergence to phoria (purple) for all 23 subjects studied within the baseline and postassessment measurements. The schematic of the visual stimuli is shown in Figure 1B.

Discussion

Significant reduction in temporal parameters after vergence therapy compared to baseline measurements

The dependent parameters (latency, time to peak velocity, settling time, peak velocity, and accuracy) had high ICCs. Hence, these measurements were repeatable
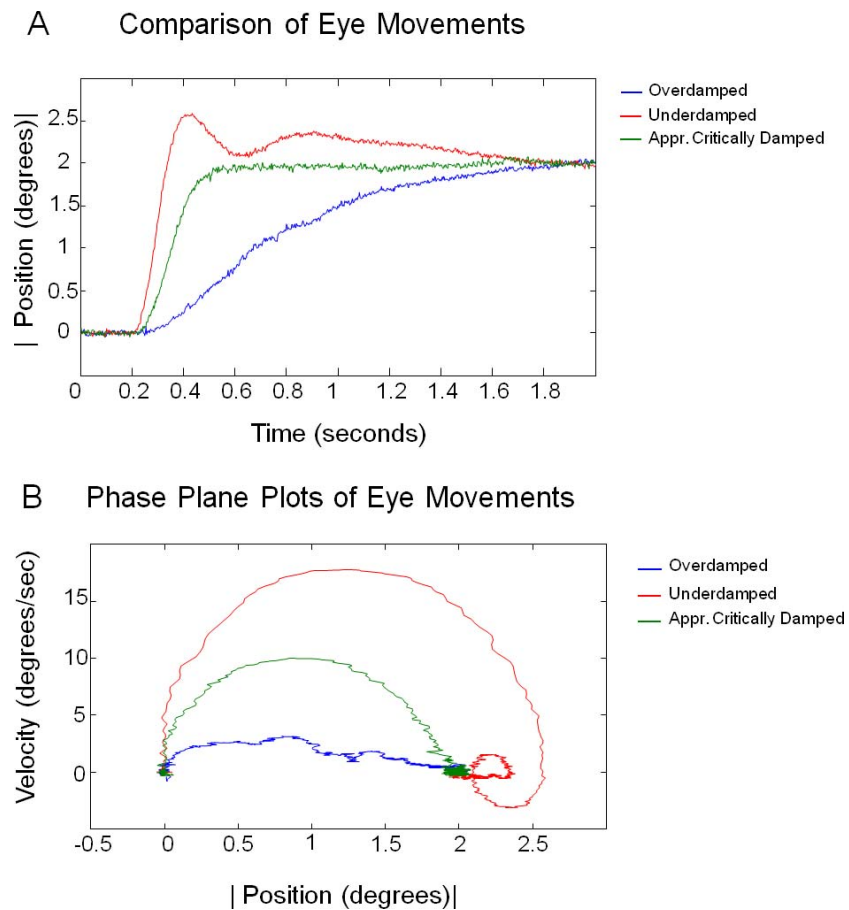
Figure 6. Typical average vergence eye movements that show an underdamped (red), an overdamped (blue), and an approximately critically damped (green) vergence response. (A) Position (degrees) as a function of time (seconds) data. (B) Velocity (degrees per second) as a function of position (degrees) also called the phase plane.
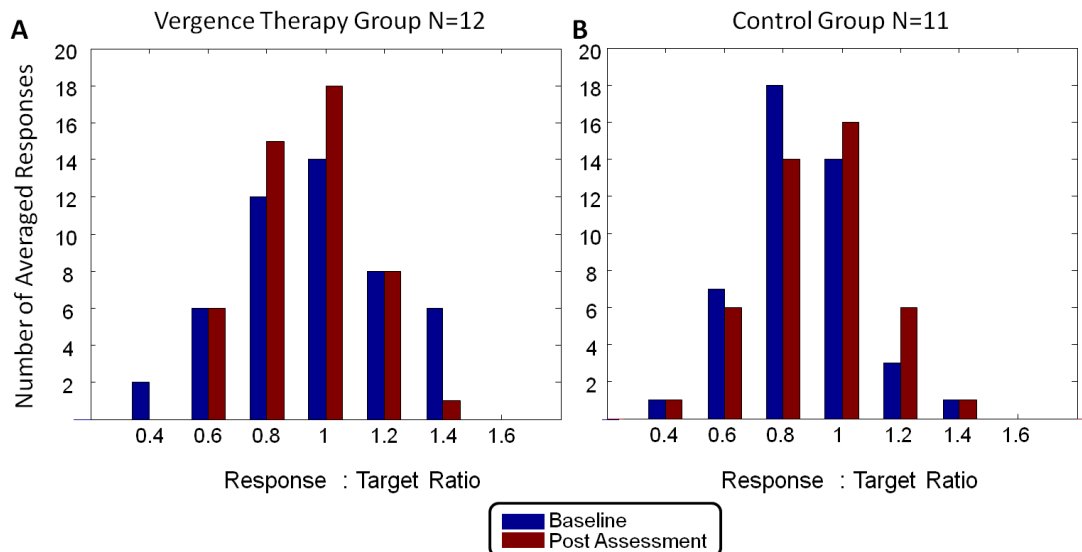

Figure 7. Group-level analysis of the response to stimulus target amplitude ratio for the 12 subjects who participated in vergence therapy (A) and the 11 control subjects who did not participate in vergence therapy (B). Histograms represent the average of the four types of the vergence eye movements measured at baseline (blue) and during postassessment (red). An ideal ratio is when the response amplitude equals the visual stimulus or a ratio equal to one.
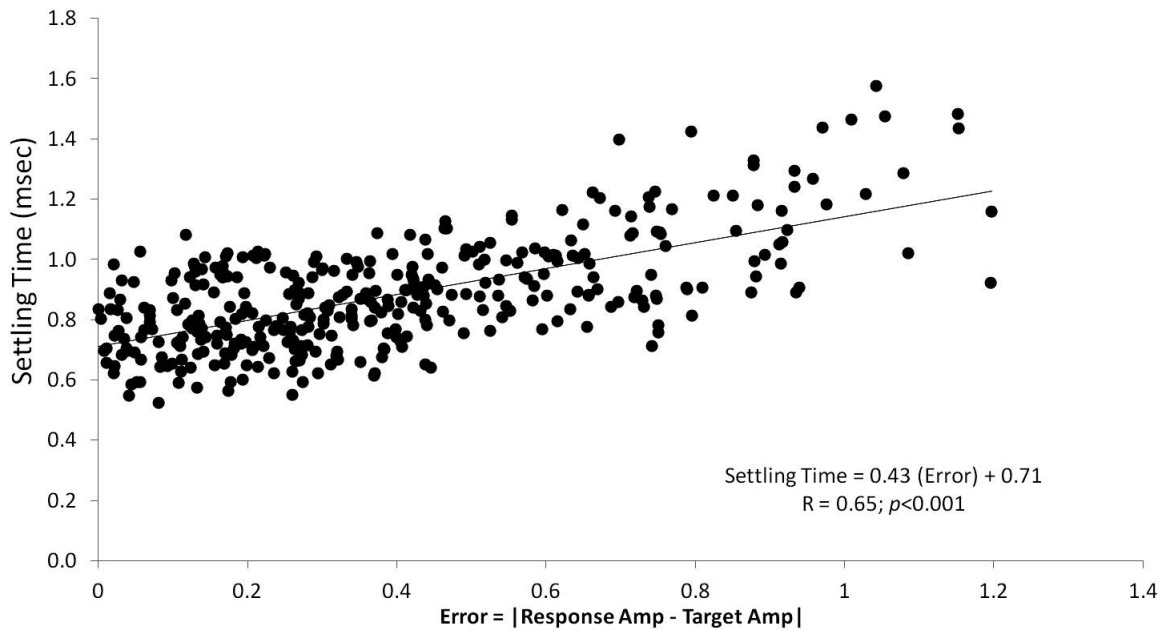
Figure 8. Linear regression analysis of settling time as a function of accuracy defined as the error between the response amplitude and stimulus amplitude.

and reliable. Significant differences were observed when comparing the temporal data at baseline to postassessment for both subjects who participated in vergence therapy and controls. There was a group versus time interaction with settling time, and the settling time improved more in subjects who participated in vergence therapy.

Improvement in accuracy and the underlying neural control of disparity vergence eye movements

The error between the visual stimulus and response amplitude was significantly reduced post vergence
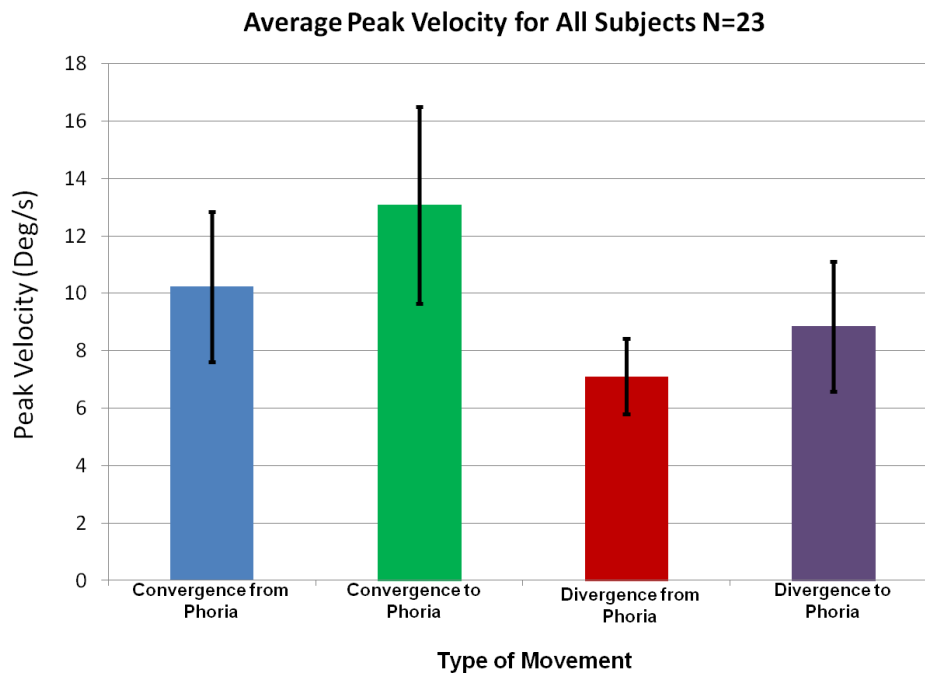

Figure 9. Average plus and minus one standard deviation of peak velocities (degrees per second) for the following types of eye movements: convergence from phoria (blue), convergence to phoria (green), divergence from phoria (red), and divergence to phoria (purple).

therapy for both groups. More importantly, there was a group–time interaction with which those who participated in vergence therapy improved more compared to the control subjects who did not participate in vergence therapy. These data support the concept that procedural learning was observed. Procedural learning is described as the improvement in doing a repetitive task (Gibson, 1969; Jacoby & Dallas, 1981; Shiffrin & Schneider, 1977). Our own laboratory in a prior study used the same visual stimuli for the vergence assessment and vergence therapy and showed a significant improvement in the peak velocity and accuracy of vergence responses from CI patients; however, we did not investigate vergence in subjects with binocularly normal vision within our past study (Alvarez et al., 2010). It is highly probable that within our own laboratory's past experiments some of the improvements we observed were due to procedural learning. Based upon the accuracy improvements from this current study, our data support the idea that the assessment procedures should be different compared to the vergence therapy protocol. This is important to reduce confounding variables and to assess the impact the vergence therapy is having on the accuracy of the movements as opposed to simply improving a very specific set of visual stimuli.

Next, we want to discuss our results in the context of how an improvement in accuracy translates to changes within the underlying neural control of disparity vergence eye movements. The improvement in accuracy could be attributed to modifications within the FFPS (C. Schor, 1980, 1988; C. Schor & Horner, 1989; C. M. Schor, 1979, 2009). The FFPS can be described using the dual mode theory. The dual mode theory describes the FFPS using two components, the FIC and the FSC (Hung, Semmlow, & Ciuffreda, 1986; Semmlow, Hung, Horng, & Ciuffreda, 1993). The FIC brings the eyes close to their desired visual target and is described as a preprogrammed, open-loop, feed-forward control system (Alvarez, Semmlow, & Pedrono, 2007; Alvarez et al., 1998; Alvarez et al., 2000; Horng, Semmlow, Hung, & Ciuffreda, 1998b; Lee et al., 2012; Semmlow et al., 2007; Semmlow, Yuan, & Alvarez, 1998). The FSC is responsible for the high accuracy of the vergence system and is described as a feedback control system. Past research supports that the FIC can be modeled as a pulse (Yuan, Semmlow, Alvarez, & Munoz, 1999). Vergence therapy can potentially be modifying the pulse height and/or width characteristics to become more optimal, leading to a reduction in error/improvement in accuracy (Alvarez et al., 2009; Alvarez et al., 1999; Castillo et al., 2006; Yuan et al., 1999; Yuan, Semmlow, & Muller-Munoz, 2001). When comparing the baseline and postassessment data, the accuracy significantly improved, meaning the error was reduced. We interpret these results to suggest that the

FIC pulse, which corresponds to the response amplitude, was significantly optimized. Future research is needed to determine whether similar neural control changes within the pulse are occurring within patients with binocular dysfunctions.

Vergence peak velocity is dependent on subject's near dissociated phoria

Controversy exists in the literature regarding the comparison of convergence and divergence peak velocity. Many investigations report that convergence is faster than divergence (Horng, Semmlow, Hung, & Ciuffreda, 1998a; Hung, Ciuffreda, Semmlow, & Horng, 1994; Zee et al., 1992), and others report that convergence and divergence have approximately the same peak velocity (Collewijn, Erkelens, & Steinman, 1995). Our laboratory reported that the peak velocity of divergence is dependent on the initial vergence angle (Alvarez, Semmlow, & Pedrono, 2005). However, more recent research from our laboratory shows that the peak velocity of vergence is also dependent on the person's near dissociated phoria level (Kim, Granger-Donetti, Vicci, & Alvarez, 2010; Kim & Alvarez, 2012a).

Our research supports the concept that esophoric subjects have a natural tendency to rotate the eyes inward, which would facilitate the maximum speed of convergence but impede the speed of divergence movements. Exophoric subjects have a predisposed tendency to rotate the eyes outward, which would facilitate the maximum speed of divergence while impeding the speed of convergence responses. Specifically, our previous research supports the idea that the ratio of convergence to divergence peak velocity is significantly correlated with the near dissociated phoria (Kim et al., 2010). In addition, when the phoria is adapted, which is dependent on the amount of near visual tasks prior to the experiment, the change in the ratio of convergence to divergence peak velocity is significantly correlated to the change in the near dissociated phoria (Kim & Alvarez, 2012a). Our papers and other independent researchers support that the peak velocity of vergence is dependent on a subject's current near dissociated phoria level (Kim & Alvarez, 2012a; Kim et al., 2010; Satgunam, Gowrisankaran, & Fogt, 2009).

One objective of this study was to minimize the impact of the near dissociated phoria from the SFTS on the peak velocity of the FFPS of vergence. To test whether we could reduce phoria's influence on vergence peak velocity, we designed our experiment with the following attributes. First, we minimized the amount of change in disparity ($2°$ symmetrical vergence step stimuli or about 3.5Δ). Second, the visual stimuli

throughout the experiment were centered at the individual subject's near dissociated phoria level (this became the stimulus pedestal position). Third, the amount of visual fixation more convergent from the subject's near dissociated phoria was equal to the amount of visual fixation more divergent from the subject phoria. We hypothesized that by using these three methods in our experimental assessment design, the impact of phoria on the vergence peak velocity would be insignificant. Our data did not support this hypothesis.

Our results show that peak velocity did significantly vary dependent on stimulus type (convergence to phoria [CTP], convergence from phoria [CFP], divergence to phoria [DTP], and divergence from phoria [DFP] shown schematically in Figure 1B) and that the phoria is acting as a spring. For example, when a subject is converging to the phoria, then the phoria level facilitates the movement, thus increasing the convergence peak velocity. In contrast, when the subject is diverging away from the phoria, the phoria level is impeding the movement and thus reducing the peak velocity (see Figure 8). This means that any assessment protocol that quantifies peak velocity of vergence must take into account that subject's near dissociated phoria level. For example, one study reports that repetitive eye movements reduce vergence peak velocity and speculate that it is due to fatigue (Yuan & Semmlow, 2000). On the contrary, another study reports that after repetitive vergence movements peak velocity increases and speculates that the increase is due to repetition or improvement of vergence responses (Jainta et al., 2011). Although these articles seem to contradict each other in their results, another interpretation of both of these reports is that potentially the phoria is becoming adapted. Hence, the vergence peak velocity is also changing. In some subjects, the phoria would reduce vergence velocity, and in others it would increase it. Phoria adaptation is dependent on where the visual stimuli are located with respect to the subject's midline as well as each individual's near dissociated phoria level. This cannot be determined because phoria was not reported in either study. Our data support the idea that any vergence study must take into account each subject's near dissociated phoria when assessing vergence peak velocity.

Conclusions

The main effects of this study demonstrate that even in subjects with normal binocular vision, temporal and accuracy measurements are significantly improved (reduced latency, time to peak velocity, and settling time with improved accuracy described as less error in response amplitude) postassessment compared to baseline measurements. The group versus time interaction supports that the settling time and accuracy changes were greater in the postassessment measurements of subjects who participated in vergence therapy compared to the control group who did not. This study suggests that any future investigations that assess vergence peak velocity should measure each person's near dissociated phoria and report the initial vergence angle. The analysis and eye-movement stimuli presented here can be used in future studies to assess commonly used vision therapy techniques, such as but not limited to the CITT OBVAT.

Keywords: convergence, divergence, near dissociated phoria, repetitive vergence therapy, peak vergence velocity, accuracy, vision therapy

References

Alkan, Y., Biswal, B. B., & Alvarez, T. L. (2011). Differentiation between vergence and saccadic functional activity within the human frontal eye fields and midbrain revealed through fMRI. *PLoS One, 6*(11), e25866.

Alkan, Y., Biswal, B. B., Taylor, P. A., & Alvarez, T. L. (2011). Segregation of frontoparietal and cerebellar components within saccade and vergence networks using hierarchical independent component analysis of fMRI. *Visual Neuroscience, 28*(3), 247–261.

Alvarez, T. L. (2015). A pilot study of disparity vergence and near dissociated phoria in convergence insufficiency patients before vs. after vergence therapy. *Frontiers in Human Neuroscience, 9*, 419.

Alvarez, T. L., Han, S., Kania, C., Kim, E., Tsang, O.,

Semmlow, J. L., . . . Pedrono, C. (2009). Adaptation to progressive lenses by presbyopes. *Neural Engineering '09, 4th International IEEE/EMBS Conference*, Antalya Turkey.

Alvarez, T. L., Jaswal, R., Gohel, S., & Biswal, B. B. (2014). Functional activity within the frontal eye fields, posterior parietal cortex, and cerebellar vermis significantly correlates to symmetrical vergence peak velocity: An ROI-based, fMRI study of vergence training. *Frontiers in Integrative Neuroscience, 8*, 50.

Alvarez, T. L., & Kim, E. H. (2013). Analysis of saccades and peak velocity to symmetrical convergence stimuli: Binocularly normal controls compared to convergence insufficiency patients. *Investigative Ophthalmology & Visual Science, 54*(6), 4122–4135. [PubMed] [Article]

Alvarez, T. L., Semmlow, J. L., Ciuffreda, K. J., Gayed, B., & Granger-Donetti, B. (2007). Vergence transient component: An index to oculomotor learning modification (pp. 4850–4853). *Conference Proceedings IEEE Engineering in Medicine and Biology Society*, August 22–26, 2007, Lyon, France.

Alvarez, T. L., Semmlow, J. L., & Pedrono, C. (2005). Divergence eye movements are dependent on initial stimulus position. *Vision Research, 45*(14), 1847–1855.

Alvarez, T. L., Semmlow, J. L., & Pedrono, C. (2007). Dynamic assessment of disparity vergence ramps. *Computers in Biology and Medicine, 37*(7), 903–909.

Alvarez, T. L., Semmlow, J. L., & Yuan, W. (1998). Closely spaced, fast dynamic movements in disparity vergence. *Journal of Neurophysiology, 79*(1), 37–44.

Alvarez, T. L., Semmlow, J. L., Yuan, W., & Munoz, P. (1999). Dynamic details of disparity convergence eye movements. *Annals of Biomedical Engineering, 27*(3), 380–390.

Alvarez, T. L., Semmlow, J. L., Yuan, W., & Munoz, P. (2000). Disparity vergence double responses processed by internal error. *Vision Research, 40*(3), 341–347.

Alvarez, T. L., Semmlow, J. L., Yuan, W., & Munoz, P. (2002). Comparison of disparity vergence system responses to predictable and non-predictable stimulations. *Psychology of Cognition, 21*(2–3), 243–261.

Alvarez, T. L., Vicci, V. R., Alkan, Y., Kim, E. H., Gohel, S., Barrett, A. M., . . . Biswal, B. B. (2010). Vision therapy in adults with convergence insufficiency: Clinical and functional magnetic resonance imaging measures. *Optometry and Vision Science, 87*(12), E985–E1002.

Bababekova, Y., Rosenfield, M., Hue, J. E., & Huang, R. R. (2011). Font size and viewing distance of handheld smart phones. *Optometry and Vision Science, 88*(7), 795–797.

Bahill, A. T., Kallman, J. S., & Lieberman, J. E. (1982). Frequency limitations of the two-point central difference differentiation algorithm. *Biological Cybernetics, 45*(1), 1–4.

Brautaset, R. L., & Jennings, J. A. (2005). Distance vergence adaptation is abnormal in subjects with convergence insufficiency. *Ophthalmic and Physiological Optics, 25*(3), 211–214.

Bucci, M. P., Kapoula, Z., Bui-Quoc, E., Bouet, A., & Wiener-Vacher, S. (2011). Saccades and vergence performance in a population of children with vertigo and clinically assessed abnormal vergence capabilities. *PLoS One, 6*(8), e23125.

Castillo, C. A., Gayed, B., Pedrono, C., Ciuffreda, K. J., Semmlow, J. L., & Alvarez, T. L. (2006). The transient component of disparity vergence may be an indication of progressive lens acceptability. *Conference Proceedings IEEE Engineering in Medicine and Biology Society, 1*, 5687–5690.

Chen, Y.-F., Lee, Y. Y., Chen, T., Semmlow, J. L., & Alvarez, T. L. (2010). Behaviors, models and clinical applications of vergence eye movements. *Journal of Medical and Biological Engineering, 3*(1), 1–15.

Collewijn, H., Erkelens, C. J., & Steinman, R. M. (1995). Voluntary binocular gaze-shifts in the plane of regard: Dynamics of version and vergence. *Vision Research, 35*(23–24), 3335–3358.

Convergence Insufficiency Treatment Trial (CITT) Study Group. (2008). The convergence insufficiency treatment trial: design, methods, and baseline data. *Ophthalmic Epidemiology, 15*(1), 24–36, doi: 10.1080/09286580701772037.

Cooper, J., & Jamal, N. (2012). Convergence insufficiency–A major review. *Optometry, 83*(4), 137–158.

Ehrlich, D. L. (1987). Near vision stress: vergence adaptation and accommodative fatigue. *Ophthalmic and Physiological Optics, 7*(4), 353–357.

Gayed, B. A., & Alvarez, T. L. (2006). Quantitative assessment of divergence eye movements to ramp stimuli. *Conference Proceedings IEEE Engineering in Medicine and Biology Society, 1*, 3954–3957.

Gibson, E. J. (1969). *Principles of perceptual learning and development*. New York: Appleton-Century-Crofts.

Guo, Y., Kim, E., & Alvarez, T. (2011). VisualEyes: A modular software system for oculomotor experi-

mentation. *Journal of Visualized Experiments, 25*(49), 2530.

Han, S. J., Guo, Y., Granger-Donetti, B., Vicci, V. R., & Alvarez, T. L. (2010). Quantification of heterophoria and phoria adaptation using an automated objective system compared to clinical methods. *Ophthalmic and Physiological Optics, 30*(1), 95–107.

Horng, J. L., Semmlow, J. L., Hung, G. K., & Ciuffreda, K. J. (1998a). Dynamic asymmetries in disparity convergence eye movements. *Vision Research, 38*(18), 2761–2768.

Horng, J. L., Semmlow, J. L., Hung, G. K., & Ciuffreda, K. J. (1998b). Initial component control in disparity vergence: A model-based study. *IEEE Transactions on Biomedical Engineering, 45*(2), 249–257.

Hung, G. K., Ciuffreda, K. J., Semmlow, J. L., & Horng, J. L. (1994). Vergence eye movements under natural viewing conditions. *Investigative Ophthalmology & Visual Science, 35*(9), 3486–3492. [PubMed] [Article]

Hung, G. K., Semmlow, J. L., & Ciuffreda, K. J. (1986). A dual-mode dynamic model of the vergence eye movement system. *IEEE Transactions on Biomedical Engineering, 33*(11), 1021–1028.

Jacoby, L. L., & Dallas, M. (1981). On the relationship between autobiographical memory and perceptual learning. *Journal of Experimental Psychology, 110*(3), 306–340.

Jainta, S., Bucci, M. P., Wiener-Vacher, S., & Kapoula, Z. (2011). Changes in vergence dynamics due to repetition. *Vision Research, 51*(16), 1845–1852.

Jaschinski, W., Svede, A., & Jainta, S. (2008). Relation between fixation disparity and the asymmetry between convergent and divergent disparity step responses. *Vision Research, 48*(2), 253–263.

Jaswal, R., Gohel, S., Biswal, B. B., & Alvarez, T. L. (2014). Task-modulated coactivation of vergence neural substrates. *Brain Connect, 4*(8), 595–607.

Kim, E. H., & Alvarez, T. L. (2012a). The changes in phoria and convergence to divergence peak velocity ratio are correlated. *Current Eye Research, 37*(11), 1054–1065.

Kim, E. H., & Alvarez, T. L. (2012b). The frequency of horizontal saccades in near and far symmetrical disparity vergence. *Vision Research, 63*, 9–19.

Kim, E. H., Granger-Donetti, B., Vicci, V. R., & Alvarez, T. L. (2010). The relationship between phoria and the ratio of convergence peak velocity to divergence peak velocity. *Investigative Ophthalmology & Visual Science, 51*(8), 4017–4027. [PubMed] [Article]

Kim, E. H., Vicci, V. R., Granger-Donetti, B., & Alvarez, T. L. (2011). Short-term adaptations of the dynamic disparity vergence and phoria systems. *Experimental Brain Research, 212*(2), 267–278.

Kim, E. H., Vicci, V. R., Han, S. J., & Alvarez, T. L. (2011). Sustained fixation induced changes in phoria and convergence peak velocity. *PLoS One, 6*(6), e20883.

Kotulak, J. C., & Schor, C. M. (1986). The dissociability of accommodation from vergence in the dark. *Investigative Ophthalmology & Visual Science, 27*(4), 544–551. [PubMed] [Article]

Kumar, A. N., Han, Y., Garbutt, S., & Leigh, R. J. (2002). Properties of anticipatory vergence responses. *Investigative Ophthalmology & Visual Science, 43*(8), 2626–2632. [PubMed] [Article]

Lee, Y. Y., Chen, T., & Alvarez, T. L. (2008). Quantitative assessment of divergence eye movements. *Journal of Vision, 8*(12):5, 1–13, doi:10.1167/8.12.5. [PubMed] [Article]

Lee, Y. Y., Granger-Donetti, B., Chang, C., & Alvarez, T. L. (2009). Sustained convergence induced changes in phoria and divergence dynamics. *Vision Research, 49*(24), 2960–2972.

Lee, Y. Y., Semmlow, J. L., & Alvarez, T. L. (2012). Assessment of dual-mode and switched channel models with experimental vergence responses. *Journal of Eye Movement Research, 5*(2), 1–14.

Lodin, C., Forsman, M., & Richter, H. (2012). Eye- and neck/shoulder-discomfort during visually demanding experimental near work. *Work, 41*(Suppl. 1), 3388–3392.

North, R., & Henson, D. B. (1981). Adaptation to prism-induced heterophoria in subjects with abnormal binocular vision or asthenopia. *American Journal of Optometry and Physiological Optics, 58*(9), 746–752.

North, R. V., & Henson, D. B. (1992). The effect of orthoptic treatment upon the vergence adaptation mechanism. *Optometry and Vision Science, 69*(4), 294–299.

Patel, S. S., Jiang, B. C., White, J. M., & Ogmen, H. (1999). Nonlinear alteration of transient vergence dynamics after sustained convergence. *Optometry and Vision Science, 76*(9), 656–663.

Rosenfield, M. (1997). Tonic vergence and vergence adaptation. *Optometry and Vision Science, 74*(5), 303–328.

Rosenfield, M. (2011). Computer vision syndrome: A review of ocular causes and potential treatments. *Ophthalmic and Physiological Optics, 31*(5), 502–515.

Rouse, M., Borsting, E., Mitchell, G. L., Cotter, S. A., Kulp, M., Scheiman, M., . . . Convergence Insufficiency Treatment Trial (CITT) Investigator Group. (2009). Validity of the convergence insufficiency symptom survey: a confirmatory study. *Optometry and Vision Science, 86*(4), 357–363, doi: 10.1097/OPX.0b013e3181989252.

Satgunam, P., Gowrisankaran, S., & Fogt, N. (2009). The influence of vergence adaptation on open-loop vergence dynamics. *Vision Research, 49*(14), 1795–1804.

Scheiman, M., Cotter, S., Rouse, M., Mitchell, G. L., Kulp, M., Cooper, J., . . . Convergence Insufficiency Treatment Trial Study Group. (2005). Randomised clinical trial of the effectiveness of base-in prism reading glasses versus placebo reading glasses for symptomatic convergence insufficiency in children. *British Journal of Ophthalmology, 89*(10), 1318–1323.

Scheiman, M., Gwiazda, J., & Li, T. (2011). Non-surgical interventions for convergence insufficiency. *Cochrane Database of Systemic Reviews, 3,* CD006768.

Scheiman, M., Mitchell, G. L., Cotter, S., Cooper, J., Kulp, M., Rouse, M., . . . Convergence Insufficiency Treatment Trial Study Group. (2005). A randomized clinical trial of treatments for convergence insufficiency in children. *Archives of Ophthalmology, 123*(1), 14–24.

Scheiman, M., Mitchell, G. L., Cotter, S., Kulp, M. T., Cooper, J., Rouse, M., . . . Wensveen, J. (2005). A randomized clinical trial of vision therapy/orthoptics versus pencil pushups for the treatment of convergence insufficiency in young adults. *Optometry and Vision Science, 82*(7), 583–595.

Scheiman, M., & Wick, B. (2008). *Binocular vision heterophoric, accommodative and eye movement disorders* (3rd ed.). Philadelphia, PA: Lippincott, Williams, & Wilkins.

Schor, C. (1980). Fixation of disparity: A steady state error of disparity-induced vergence. *American Journal of Optometry and Physiological Optics, 57*(9), 618–631.

Schor, C. (1988). Influence of accommodative and vergence adaptation on binocular motor disorders. *American Journal of Optometry and Physiological Optics, 65*(6), 464–475.

Schor, C., & Horner, D. (1989). Adaptive disorders of accommodation and vergence in binocular dysfunction. *Ophthalmic and Physiological Optics, 9*(3), 264–268.

Schor, C. M. (1979). The relationship between fusional vergence eye movements and fixation disparity. *Vision Research, 19*(12), 1359–1367.

Schor, C. M. (2009). Neuromuscular plasticity and rehabilitation of the ocular near response. *Optometry and Vision Science, 86*(7), E788–E802.

Semmlow, J. L., Alvarez, T. L., & Pedrono, C. (2007). Dry dissection of disparity divergence eye movements using independent component analysis. *Computers in Biology and Medicine, 37*(7), 910–918.

Semmlow, J. L., Chen, Y.-F., Granger-Donetti, B., & Alvarez, T. L. (2009). Correction of saccade-induced midline errors in responses to pure disparity vergence stimuli. *Journal of Eye Movement Research, 2*(5), 1–13.

Semmlow, J. L., Chen, Y.-F., Pedrono, C., & Alvarez, T. L. (2008). Saccadic behavior during the response to pure disparity vergence stimuli I: General properties. *Journal of Eye Movement Research, 1*(2), 1–11.

Semmlow, J. L., Hung, G. K., Horng, J. L., & Ciuffreda, K. (1993). Initial control component in disparity vergence eye movements. *Ophthalmic and Physiological Optics, 13*(1), 48–55.

Semmlow, J. L., Yuan, W., & Alvarez, T. L. (1998). Evidence for separate control of slow version and vergence eye movements: Support for Hering's Law. *Vision Research, 38*(8), 1145–1152.

Shiffrin, R. M., & Schneider, W. (1977). Controlled and automatic human information processing II. Perceptual learning, automatic attending and a general theory. *Psychological Review, 84*(2), 127–190.

Shrout, P. E., & Fleiss, J. L. (1979). Intraclass correlations: Uses in assessing rater reliability. *Psychological Bulletin, 86*(2), 420–428.

Sreenivasan, V., & Bobier, W. R. (2014). Reduced vergence adaptation is associated with a prolonged output of convergence accommodation in convergence insufficiency. *Vision Research, 100*, 99–104.

Sreenivasan, V., & Bobier, W. R. (2015). Increased onset of vergence adaptation reduces excessive accommodation during the orthoptic treatment of convergence insufficiency. *Vision Research, 111*(Pt A), 105–113, doi: 10.1016/j.visres.2015.04.001.

Thiagarajan, P., Lakshminarayanan, V., & Bobier, W. R. (2010). Effect of vergence adaptation and positive fusional vergence training on oculomotor parameters. *Optometry and Vision Science, 87*(7), 487–493.

van Leeuwen, A. F., Westen, M. J., van der Steen, J., de Faber, J. T., & Collewijn, H. (1999). Gaze-shift dynamics in subjects with and without symptoms of

convergence insufficiency: Influence of monocular preference and the effect of training. *Vision Research, 39*(18), 3095–3107.

Wolf, K. S., Bedell, H. E., & Pedersen, S. B. (1990). Relations between accommodation and vergence in darkness. *Optometry and Vision Science, 67*(2), 89–93.

Ying, S. H., & Zee, D. S. (2006). Phoria adaptation after sustained symmetrical convergence: Influence of saccades. *Experimental Brain Research, 171*(3), 297–305.

Yuan, W., & Semmlow, J. L. (2000). The influence of repetitive eye movements on vergence performance. *Vision Research, 40*(22), 3089–3098.

Yuan, W., Semmlow, J. L., Alvarez, T. L., & Munoz, P. (1999). Dynamics of the disparity vergence step response: A model-based analysis. *IEEE Transactions on Biomedical Engineering, 46*(10), 1191–1198.

Yuan, W., Semmlow, J. L., & Muller-Munoz, P. (2001). Model-based analysis of dynamics in vergence adaptation. *IEEE Transactions on Biomedical Engineering, 48*(12), 1402–1411.

Zee, D. S., Fitzgibbon, E. J., & Optican, L. M. (1992). Saccade-vergence interactions in humans. *Journal of Neurophysiology, 68*(5), 1624–1641.

Zuber, B. L., Semmlow, J. L., & Stark, L. (1968). Frequency characteristics of the saccadic eye movement. *Biophysical Journal, 8*(11), 1288–1298.