Oculomotor neurorehabilitation for reading in mild traumatic brain injury (mTBI): An integrative approach

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Abstract.

BACKGROUND: Considering the extensive neural network of the oculomotor subsystems, traumatic brain injury (TBI) could affect oculomotor control and related reading dysfunction.

OBJECTIVE: To evaluate comprehensively the effect of oculomotor-based vision rehabilitation (OBVR) in individuals with mTBI.

METHODS: Twelve subjects with mTBI participated in a cross-over, interventional study involving oculomotor training (OMT) and sham training (ST). Each training was performed for 6 weeks, 2 sessions a week. During each training session, all three oculomotor subsystems (vergence/accommodation/version) were trained in a randomized order across sessions. All laboratory and clinical parameters were determined before and after OMT and ST. In addition, nearvision-related symptoms using the Convergence Insufficiency Symptom Survey (CISS) scale and subjective visual attention using the Visual Search and Attention Test (VSAT) were assessed.

RESULTS: Following the OMT, over 80% of the abnormal parameters significantly improved. Reading rate, along with the amplitudes of vergence and accommodation, improved markedly. Saccadic eye movements demonstrated enhanced rhythmicity and accuracy. The improved reading-related oculomotor behavior was reflected in reduced symptoms and increased visual attention. None of the parameters changed with ST.

CONCLUSIONS: OBVR had a strong positive effect on oculomotor control, reading rate, and overall reading ability. This oculomotor learning effect suggests considerable residual neuroplasticity following mTBI.

Keywords: Traumatic brain injury, mTBI, reading dysfunction, oculomotor deficiency, nearvision symptoms, oculomotor rehabilitation, neuroplasticity, oculomotor learning, eye movements

1. Background

1.1. Reading: Basic concepts

Reading is a complex task that requires precise coordination of one's versional eye movements (especially saccades), synchrony between ocular accommodation and vergence, and maintained higher-level visual

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attentional aspects associated with text processing in conjunction with concurrently accurate comprehension. All of the above must be performed in an efficient manner to gain optimal benefits (Ciuffreda, 1994; Ciuffreda & Tannen, 1995).

Normal reading is comprised of precise, rhythmical, and automatically-executed sequences of saccadic eye movements interspersed with brief fixational pauses (Taylor, 1966; Ciuffreda & Tannen, 1995; Reichle & Raynor, 2002; Ciuffreda et al., 2005, 2006). The reading-related saccadic eye movements, typically being 1–3 degrees in amplitude and 30–60 msec in duration, progressively shift the eyes from left-to-right across the line of print. These saccadic shifts are interspersed with brief oculomotor fixational pauses of approximately 250msec duration to allow for the initial text processing (∼75 msec), followed by oculomotor positional programming (∼175 msec) of the subsequent saccade to the next word along with attentional allocation (Ciuffreda & Tannen, 1995; Abrams & Zuber, 1972; Reichle & Raynor, 2002). At times, the saccadic eye movements are regressive in nature, wherein the eyes either shift back briefly to a previously fixated word for informational confirmation or simply return to the beginning of the next line of text (i.e., return-sweep saccade). In addition, during each saccadic eye movement itself, there is a very small (<0.10 deg) dynamic alteration in the binocular vergence angle (i.e., dynamic fixation disparity), which must be corrected rapidly upon bifixation of the subsequent word (Clark, 1935; Taylor, 1966; Ciuffreda & Tannen, 1995). Hence, continuous small but highly accurate vergence adjustments are necessary to attain and maintain rapidly and fully, precise binocular alignment, and thus prevent either diplopia or partially overlapping images from intermittently occurring (Ciuffreda et al., 1996). Lastly, clarity of the text is critical for efficient visual information processing (Green et al., 2010, a,b), and hence the accommodative subsystem must function in a time-optimal manner to obtain and maintain an accurate focusing response. Thus, the version, vergence, and accommodative functions are essential for efficient oculomotor control during reading under a variety of naturalistic conditions. Furthermore, they must function in an *interactive* and *integrated* manner with precise *synchronization* for optimal reading performance to occur (Taylor, 1966; Ciuffreda & Tannen, 1995). In addition, this must be accomplished for a sustained period of time with a high level of attention, comprehension, and visual comfort (Taylor, 1966; Ciuffreda & Tannen, 1995).

1.2. Investigations on reading in brain injury: Diagnosis

Reading dysfunction is a major problem, and hence symptom, in individuals with mTBI (Ciuffreda et al., 2006, 2007; Goodrich et al., 2007, 2013; Lew et al., 2007; Brahm et al., 2009; Stelmack et al., 2009; Capó-Aponte et al., 2012; Bulson et al., 2012). A major source of this reading problem is *oculomotor-based* (Ciuffreda et al., 2005, 2006, 2007). Any failure in one or more of these oculomotor systems will likely result in problematic reading, especially as these three subsystems are interactive and integrative in nature (e.g., an accommodative problem will also impact on vergence via accommodative vergence) (Ciuffreda & Kenyon, 1983).

Based on earlier investigations, it was estimated that the majority (>60%) of individuals with mTBI manifest a range of oculomotor abnormalities (Baker & Epstein, 1991; Suchoff et al., 1999; Ciuffreda et al., 2007). Of particular interest is a recently completed retrospective study in a civilian clinic, in which Ciuffreda et al. (2007) found that *90%* of the visually-symptomatic, adult, mTBI group sampled (*n* = 160) exhibited some form of oculomotor dysfunction, when investigated comprehensively and in detail clinically. This is consistent with five recent reports from VA hospitals, in which many of the mTBI patients were warfighters (Goodrich et al., 2007, 2013; Lew et al., 2007; Brahm et al., 2009; Stelmack et al., 2009). Most relevant was the very high frequency of saccadic inaccuracy (i.e., saccadic dysmetria), convergence insufficiency, and accommodative insufficiency uncovered in each study. These basic oculomotor anomalies transfer to one's naturalistic setting to affect adversely both sensory and motor-based aspects of the reading process (Taylor, 1966; Ciuffreda & Tannen, 1995; Ciuffreda, 1994; Han et al., 2004; Ciuffreda et al., 2005, 2006), and in turn text processing and comprehension (Solan et al., 2003), as well as desynchronize the attentional aspect and its spatial allocation (Posner, 1980).

In addition, general attentional and more specifically visual attentional deficits are frequently present in individuals with TBI (Mateer & Mapou, 1996; Nag & Rao, 1999; Park & Ingles, 2001, Hibbard et al., 2001; Bonnelle et al., 2011; Kim et al., 2012). Traditionally, attention has been broadly categorized as follows (Pashler, 1998): *selective attention*, which involves the selection of relevant stimuli with disregard for irrelevant distracting or competing ones; and, *divided attention*, which involves the simultaneous monitoring of, and

response to, more than one relevant sensory stimulus. Both types are important to be normally functioning for successful completion of one's activities of daily living (ADL), including reading. This is evidenced in a current model of reading (E-Z Reader) (Reichle & Rayner, 2002), which incorporates two primary components: the *oculomotor* loop, which is activated once the fixated word is recognized to subsequently saccade to the next word of text; and, the *attentional* loop, which is activated following lexical completion and attention (but not gaze), is shifted to the next word of text per Posner's attentional spotlight hypothesis (Posner, 1980). A significant component of our basic tracking and reading-related oculomotor training involves, by its very nature, aspects of both sustained selective and divided attention. That is, visual attention per se is a significant underlying component in the overall oculomotor training process (Ciuffreda, 2002). This notion is consistent with the findings of Solan (Solan et al., 2003), in which both oculomotor and attentional training impacted positively on reading ability.

1.3. Oculomotor rehabilitation for reading in TBI

The area of reading in mTBI has been addressed using objective recording techniques in a series of studies, including its remediation, but using *version only* training protocols (fixation, saccade, simulated reading, and pursuit) (Han et al., 2004; Kapoor et al., 2004; Ciuffreda et al., 2005, 2006). Briefly, the results of these four investigations demonstrated large, consistent, and statistically significant improvements in all subjective aspects and many objective oculomotor aspects of reading in the mTBI group following a total of 9.6 hours of laboratory-based, versional eye movement training distributed over an 8-week period. First, all individuals ($n = 9$) reported significant increases in overall reading ease and ability, with subjectively-based increased attentional aspects transferring to their other vocational and avocational task domains. Of these, 55% demonstrated an increase in reading rate of 10–30%. Second, there were marked objective improvements in saccadic tracking ability during simulated reading (i.e., they executed fewer saccades). Third, there were objectively-based improvements in many of the reading eye movement parameters for the Visagraph grade 10, adult-level paragraphs, especially with respect to reduction of the number of progressive saccades executed, which is a major limiting factor in reading speed (Taylor, 1966; Ciuffreda & Tannen, 1995; Ciuffreda

et al., 1996). However, there were study limitations: (1) relatively small sample sizes, (2) lack of a vergence eye movement testing and training component, (3) lack of an accommodative testing and training component, (4) lack of a validated method to assess critical aspects of visual attention and (5) lack of a validated questionnaire to assess the oculomotor training effects on reading ability and quality of life.

Thus, the purpose of the present investigation was to perform oculomotor training (OMT) in adults with mTBI with the aforementioned past study limitations in mind. There were two critical questions: (1) Can OMT improve reading rate in this population, and (2) what oculomotor parameters correlated with the improved reading rate and related factors?

2. Methods

2.1. Subjects

Twelve subjects between the ages of 23 and 33 years (mean age: 29 [±3] years) with documented mTBI, and having a brain injury onset of greater than 1 year (1–10 years post-insult), participated in the study. Only younger, non-presbyopic individuals participated in the study to assure that sufficient accommodation was present for our testing. The training effects for the study were hypothesized to be moderate to large based on our earlier related laboratory studies as well as extensive clinical experience. Thus, this sample size was calculated using a power analysis program (G-Power software) at an alpha level of 0.05, with a power set at 0.80 using key parameters of vergence (i.e., near point of convergence, NPC) and accommodation (i.e., near point of accommodation, NPA). Inclusion and exclusion criteria are presented in Table 1. Subjects were identified by their university-based health care provider and were recruited from the Raymond J. Greenwald Vision Rehabilitation Center at the State University of New York (SUNY), State College of Optometry, Optometric Center of New York (OCNY), New York City. All were referred from local hospitals with detailed medical records regarding their diagnosis. Each subject received a comprehensive vision examination in the Raymond J. Greenwald Vision Rehabilitation Center prior to participating in the experiment. The vision examination included detailed refractive, oculomotor, and ocular health assessment. The study was approved by the SUNY Institutional Review Board (IRB) and the US Army Department of Defense (DoD) IRB. Written

Table 1
Inclusion and exclusion criteria for study subjects

Inclusion criteria	TBI onset at least one year post-incident to ensure that any subsequent changes during training *are not* secondary to their natural neurological recovery function period (~6–9 months)
	Exhibit at least one symptom (e.g., skipping lines while reading, blur, diplopia, etc.,) and one clinical sign (e.g., receded near point of convergence) of a non-strabismic oculomotor dysfunction related to impaired sustained reading
	Intact cognitive ability to perform the required tasks for the study
	Stable systemic health
Exclusion criteria	Persons over the age of 40 years, as they typically will not have sufficient accommodation to measure reliably
	Best corrected visual acuity poorer than 20/30 in either eye
	Constant strabismus, amblyopia, or ocular disease in either eye
	Medications that alter oculomotor function and/or attentional state

Table 2
Stimulus parameters for objective evaluation of simulated reading with saccadic tracking (Han et al., 2004)

Stimulus	Total amplitude (degrees)	Target amplitude (degrees)	Frequency	Test period duration (seconds)
Full-screen Simulated Reading Multiple-Line (SRML)	±10 horizontally	1, 2, or 3 randomly	Every 2 seconds	220
Simulated Reading Single-Line (SRSL)	±5 horizontally	2.5	Every 2 seconds	50

informed consent was obtained from all subjects prior to their participation.

2.2. Study design

A cross-over, interventional experimental design of a single-blinded nature (for the subject) was used. In essence, in such a design (Hatch, 1988), each subject acts as their own control, thus negating undesirable intersubject variability. In addition, each subject received the OMT, as well as ST. During phase 1, every odd-numbered subject first received OMT, and every even-numbered subject first received ST, and vice-versa during phase 2. This was an intervention study of 15 weeks duration. It consisted of 12 weeks of the 2 treatment phases, 6 weeks each phase, separated by a week, for a total of 9 hours of OMT and 9 hours of ST. In addition, there were 3, one-week measurement periods: one week before phase 1 treatment, one week after phase 1 treatment, and one week following phase 2 treatment. During these testing and training periods, subjects did not perform any other oculomotor-based vision rehabilitation to avoid contamination of test results. All testing and training of the subjects was performed by the first author, who is an optometrist with experience in oculomotor rehabilitation.

The study consisted of the following phases:

1. Week 1 – *Initial baseline measures* - All "Evaluative Procedures" (described later) were recorded over two separate test sessions (each session lasting for up to 1.5 hours, including rest periods to prevent fatigue) separated by at least two days.

2. Weeks 2–7 - *Phase 1 treatment* – 6 weeks of either the OMT or ST. Subjects received 2 training sessions per week. Each session was 60 minutes in duration, involving 45 minutes of actual training with the remainder of time consisting of short and interspersed rest periods for the subject. Total training time of 9 hours.

3. Week 8 – *Repeat baseline measures* - All "Evaluative Procedures" were repeated over two separate test sessions (each session lasting for up to 1.5 hours including rest periods to prevent fatigue) separated by at least two days.

4. Weeks 9–14 – *Phase 2 treatment* - 6 weeks of either the OMT or the ST. The subjects received 2 training sessions per week. Each session was 60 minutes in duration, involving 45 minutes of actual training with the remainder of time consisting of short and interspersed rest periods for the subject. Total training time of 9 hours.

5. Week 15 – *Repeat baseline measures* - All "Evaluative Procedures" were repeated over two separate test sessions (each session lasting for up to 1.5 hours including rest periods to prevent fatigue) separated by at least two days.

2.3. Evaluative procedures

A range of clinically-based subjective and laboratory-based objective measures, along with subjective visual attention and near vision symptoms,

were assessed (Thiagarajan, 2012; Thiagarajan & Ciuffreda, in press). All clinical parameters were measured using conventional standardized clinical techniques (Borish, 2006). All laboratory-based objective measures were performed using commercially-available instrumentation with well-established test protocols (Han et al., 2004; Green et al., 2010b; Szymanowicz et al., 2012, for version, accommodation, and vergence, respectively). All measures were non-invasive and were recorded with their habitual distance correction in place. Order of testing was randomized over the 2 days of measurements. See Thiagarajan (2012) for details of the parameters assessed. For the purpose of the present paper, the primary oculomotor parameters (clinical and laboratory-based), as well as nearvision symptoms and visual attentional aspects, involved in reading ability will be considered.

2.3.1. Clinical parameters

This included the near point of convergence (NPC), near point of accommodation (NPA) using the push-up method, and reading eye movements. While the NPC and NPA were recorded using standardized clinical procedures (Borish, 2006), reading eye movements were recorded using the Visagraph objective eye movement recording system as described below.

Reading eye movements (horizontal position of both eyes) to standardized text paragraphs (grade-10 level equivalent) were recorded using the Visagraph reading eye movement system (Taylor Associates, Huntington, NY). It consists of an infrared, limbal-reflection eye movement recording system, which has become a standard clinical test in optometry (Ciuffreda & Tannen, 1995), to assess oculomotor-based reading dysfunctions objectively (Ciuffreda et al., 2003). The system has a resolution of <1°, a sampling rate of 50 Hz, and a linear range of at least ±10°. This sampling rate is sufficient for appropriate saccadic detection during reading (Ciuffreda & Tannen, 1995). Subjects wore test goggles incorporating the infra-red sensors and emitters. They read silently the standardized 100-word text binocularly at their habitual reading distance in primary position. Following two practice paragraphs at level 10 to assure the attainment of a stable baseline (Ciuffreda et al., 2003; Griffin & Grisham, 2002), each subject then silently read a new level 10-paragraph at each test session, and they then answered 10 yes/no questions related to details of the paragraph to assess for adequate comprehension (≥70%) (Taylor, 1966). Subjects were instructed to read the paragraphs using their normal reading strategy, and furthermore to pay attention to text details, as they were tested for comprehension at the end of reading, but not to reread. The following selected conventional reading eye movement parameters (Taylor, 1966) were compared both within and between subgroups before and after training: reading rate in words per minute (wpm), number of progressive saccades as fixations/100 words, number of regressive saccades as regressions/100 words, comprehension in percentage calculated from the number of correct answers, fixation duration in seconds, and grade-level efficiency based on a weighted average of the aforementioned parameters. The Visagraph software automatically calculated the values for each parameter.

2.3.2. Laboratory parameters

Binocular horizontal versional eye movements were recorded objectively using the Arrington eye movement recording system, which is a table-mounted, infrared, binocular camera system having a 220 Hz sampling rate and 0.01° resolution, with a linearity of ±44° horizontally (Chiu & Yantis, 2009). Its sampling rate satisfies the Nyquist criterion (Khan, 2005). A 12-point calibration was performed at each test session to assure response linearity across the tested field, as well as after any rest period during which the subject removed their head from the headrest/chinrest assembly. The computer-controlled test stimuli were comprised of a 1° bright square target displayed on a high-resolution computer monitor at a 40 cm test distance, with the target either remaining stationary at a given screen position for a specified period of time or being displaced stepwise horizontally. Subjects were instructed to fixate the center of the target. These test stimuli and paradigms were developed in our laboratory over the past decade (Han et al., 2004). Subjects either binocularly fixated or executed saccades based on the laboratory parameter tested (Thiagarajan, 2012). A range of basic versional parameters (e.g., saccadic latency, saccade ratio, amplitude, peak velocity, horizontal and vertical fixation) were measured. For the purpose of the present paper, the parameter of *saccade ratio* alone is described as related to reading (Han et al., 2004; Kapoor et al., 2004; Ciuffreda et al., 2006).

The *saccade ratio* is defined as the number of tracking saccades executed divided by the number of test target step displacements; a ratio of 1.0 indicating one saccade for each target step displacement would be optimal (Han et al., 2004). This was calculated using a simulated reading single line (SRSL) (±5° horizontal range) and a simulated reading multiple line (SRML)
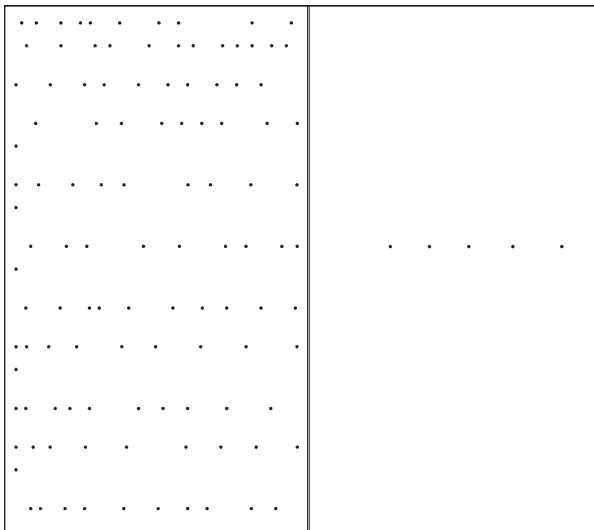
Fig. 1. Full-screen multiple lines stimulus pattern for simulated reading (left). Single-line stimulus pattern for simulated reading (right). In both cases, at any given time, only an isolated, single 1° square target appeared on the screen at the positions shown by the dots that the subject tracked with saccades.

(±10° horizontal range) paradigms (Fig. 1). While the former paradigm consisted of both spatially and temporally predictable stimulus changes (2.5° steps, every 2 seconds), the latter paradigm consisted of a spatially randomized (1, 2, or 3 degree steps) and temporally predictable (every 2 seconds) stimulus. For SRML, the

subject followed the single square 1° target as it randomly moved across the screen to simulate reading a paragraph of text. For SRSL, the subject followed the same target as it predictably moved across the center of the screen in a repeated pattern. See Table 3 for related stimulus parameters. While the SRSL simulated reading on a single line repetitively to develop accuracy and automaticity, the SRML simulated reading of a 10-lined text paragraph to develop accuracy and global visual scanning ability during reading. However, considering the test target used (e.g., a black square), both paradigms tested pure saccadic tracking in the absence of any cognitive component (e.g., word recognition or text comprehension). Subjects were instructed to execute saccades that were as accurate as possible as the target was displaced laterally on the screen, while fixating the target center once it was foveally acquired. The total number of saccades executed by the subject was determined off-line manually on the high resolution display monitor. Any saccade greater than or equal to 0.25 degrees in amplitude was counted as a saccade for both the SRML and SRSL paradigms.

2.3.3. Subjective visual attention test

A subjective correlate of visual attention was assessed using the Visual Search and Attention Test (VSAT). It involves a visual search (for a letter or a symbol) and cancellation (cross-out) task that was

Table 3
Stimuli for oculomotor training protocol

Stimulus	Stimulus parameter	Training period duration (seconds)	Total training duration (minutes)
Version			
Fixation	Central (midline)	60	5
	Left (10 degrees)	60	
	Right (10 degrees)	60	
	Up (10 degrees)	60	
	Down (10 degrees)	60	
Predictable Saccades	Horizontal (±5 degrees)	50	5
	Horizontal (±10 degrees)	50	
	Vertical (±5 degrees)	50	
	Vertical (±10 degrees)	50	
Simulated Reading	Full-screen	75	5
(repeated twice)	Single-line	75	
	Full-screen	75	
	Single-line	75	
Vergence			
	Step amplitude (BO/BI)	7	15
	Step facility (BO/BI)	5	
	Ramp	3	
Accommodation			
	Step amplitude right eye plus/minus lenses	5	15
	Step amplitude left eye plus/minus lenses	5	
	Step facility	5	

developed by Trenerry et al. (1989). It assesses global sustained visual attention, while scanning to search for selected letters/symbols. Test-retest reliability for the VSAT was found to be 0.95, using the Pearson product-moment correlation. Calculated sensitivity and specificity were 0.88 and 0.86, respectively (Trenerry et al., 1989). The test was performed binocularly at the subject's habitual near work distance.

2.3.4. Symptom scale

Individual symptoms related to near-work were rated by the subjects using the Convergence Insufficiency Symptom Survey (CISS), whose sensitivity (0.98) and specificity (0.87) have been demonstrated to be high (Rouse et al., 2004). The test-retest reliability was found to be 0.88. It is comprised of a 15-item questionnaire specifically probing reading-related symptoms, such as intermittent blur, diplopia, headache, skipping lines, losing concentration, etc. Severity of symptoms is scaled from 0 to 4, i.e., from least symptomatic to most symptomatic. The total score was compared before and after the 2 training phases. A reduction in overall score

of 10 or more was considered to reflect a significant reduction of symptoms. A score of zero would indicate being absolutely symptom-free, and a score of 60 would represent maximal symptomatology.

3. Treatment protocol

3.1. Phase 1 and phase 2 treatment phases

3.1.1. OMT procedures

This oculomotor rehabilitation was performed along the midline at 40 cm, 2 sessions per week, for a total of 6 weeks. Training was performed with constant verbal and visual feedback, motivation, repetition, and maintained attention by involving active participation of the subject (Ciuffreda, 2002). At each session, each oculomotor component (version, vergence, and accommodation) was trained for 15 minutes, interspersed with 5 minute rest periods. Each session lasted for 1-hour, with 45 minutes of total training and 15 minutes of rest periods, for a total of 9 hours of training over the 6 week period (Fig. 2).
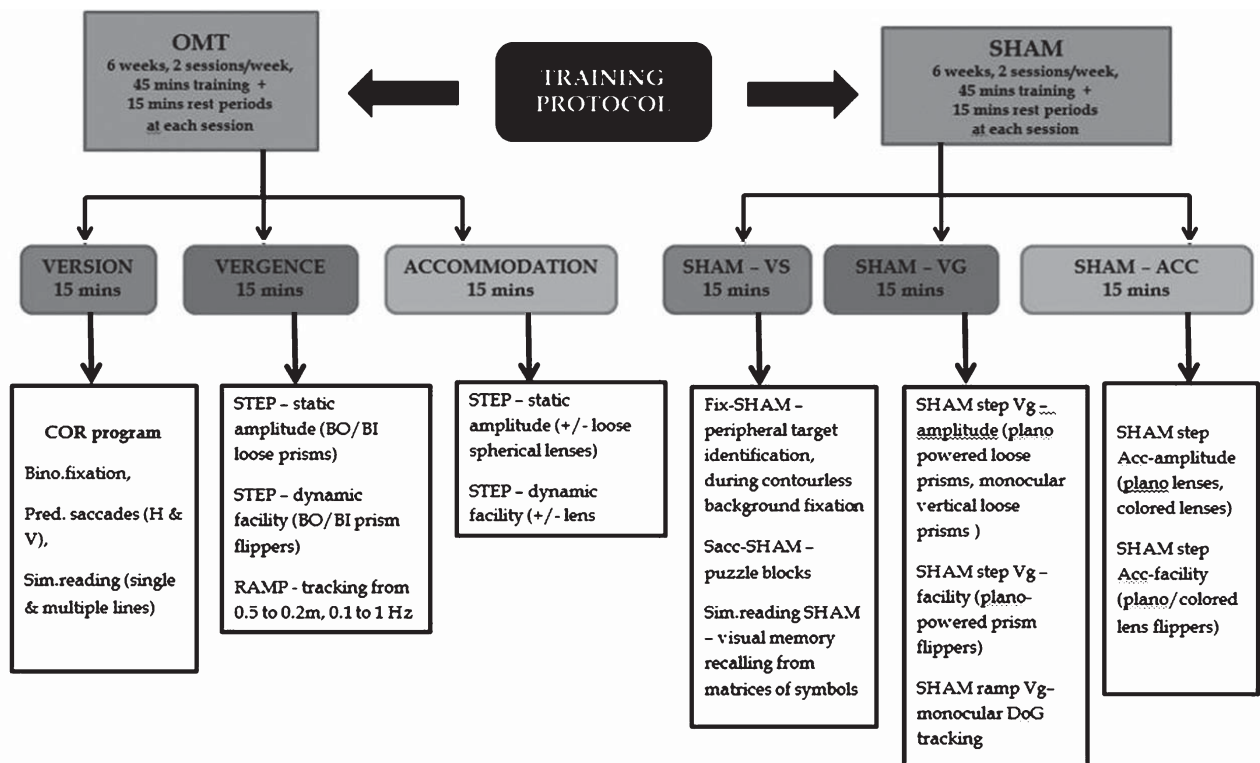

Fig. 2. Overview of oculomotor training (OMT) and sham training (ST) protocols, see text for details. VS = version; VG = vergence; ACC = accommodation; COR = computerized oculomotor rehabilitation; Bino = binocular; Pred. = predictable; Sim. = simulated; BO = base-out; BI = base-in; Fix. = fixation; DoG = difference of Gaussian.

3.1.1.1. Version. Version (fixation, predictable saccades, and simulated reading) was trained via the computerized oculomotor rehabilitation (COR) software developed in our laboratory (Thiagarajan, 2012) using a rapid-serial visual presentation (RSVP) paradigm (Xu et al., 2009) with binocular viewing. The COR program allows for training of versional, vergence, and accommodation. For version, it can train fixation, saccades, pursuit, vestibular (VOR), and simulated reading by appropriate target selection. Targets can be altered with respect to size, color, detail, test duration, etc. For vergence and accommodation, the same versional target selection is used, but the changes in vergence and accommodative demand levels are introduced manually by the experimenter. Targets in the form of pictures, numbers, symbols, letters, color patches, etc., of varying sizes were presented rapidly for different presentation times. Subjects either fixated a stationary target to train fixation or executed saccades to track the target to train predictable saccades. At the beginning of each training component, a sample target (e.g., picture) was presented to the subject. While maintaining either binocular fixation or tracking of the target, the subject was instructed to count the number of times the sample target appeared in the array of possible targets presented during the stipulated training duration (i.e., RSVP). Subjects were constantly motivated to achieve the maximum number of correct responses. The subject's numerical response was compared with the actual number of presentations (provided by the software). Verbal feedback related to subject's performance was also given by the software in the form of a female voice. See Table 3 for the versional training stimuli.

3.1.1.2. Vergence. Similar to version, at each training session, horizontal vergence was trained for 15 minutes. While rapid step vergence was trained for 12 minutes, slow ramp vergence was trained for 3 minutes (Hung et al., 1986). During the step tracking, both amplitude (7 minutes) and facility (5 minutes) were trained to attain both response accuracy and speed (Scheiman & Wick, 2008), respectively. See Table 3 for the vergence training protocol.

For step vergence amplitude training, base-out and base-in (BO/BI) prisms were used. The fusional targets were comprised of pictures, symbols, numbers, letters, tumbling E, and colors displayed on a computer screen at 40 cm. While the subjects bifixated the target, loose prisms were introduced manually by the experimenter in 2 prism diopter (pd) increments either in front of one eye or divided equally between the two eyes. The total amount of prism was determined by the subject's task performance level. After introducing each BO/BI prism, subjects were instructed to fuse the target as rapidly as possible and sustain single/fused vision for 15–20 seconds. For step vergence facility training, combinations of BO/BI prism flippers (3ΔBO/1ΔBI, 6ΔBO/2ΔBI, 9ΔBO/3ΔBI, and 12ΔBO/3ΔBI) were used, while maintaining the accommodative stimulus constant at 0.4 m (2.5D). Based on the subjects' ability to fuse the target, the magnitude of prism flipper was chosen. Subjects bifixated targets displayed on a computer screen and were instructed to fuse and focus as rapidly as possible and to achieve the maximum numbers of cycles of prismatic stimulus change as possible.

For ramp vergence training, subjects binocularly tracked a 20/30 letter on an X-Y plotter in free space over a range of 0.5 m to 0.2 m at the rate of 0.1 to 1 Hz. Task difficulty was increased as performance improved by tracking at closer distances in combination with increased target speed.

3.1.1.3. Accommodation. At each training session, accommodation was trained for 15 minutes. Step accommodative amplitude was trained for 10 minutes (5 minutes each eye), binocular step accommodative facility was trained for 5 minutes (Hung & Ciuffreda, 1988). See Table 3 for the accommodative training protocol.

For step accommodative amplitude training, positive and negative spherical lenses were used. The accommodative targets were comprised of texts of various sizes ranging from 20/60 to 20/20 displayed on a computer screen at 40 cm. While the subjects monocularly fixated the target, lenses were introduced manually at 0.5D increments in front of the eye. The lens magnitude was selected based on the subject's task performance level. After introducing each lens (positive/negative), subjects were instructed to focus the text as rapidly as possible and to sustain clarity of vision for 15–20 seconds. For step accommodative facility training, combinations of ± lens flippers (±0.5, ±0.75, ±1.00, ±1.50, and ±2.00D) were used, while maintaining the vergence stimulus demand constant at 0.4 m (2.5MA) (Scheiman & Wick, 2008). Subjects bifixated targets displayed on a computer screen and were instructed to fuse and focus as rapidly as possible and to achieve the maximum number of cycles possible.

3.1.2. Analogous ST procedures

Similar to the OMT, ST was performed along the midline at 40 cm, 2 sessions per week, for a total of 6 weeks (Thiagarajan, 2012). Again, training was

performed with constant verbal feedback, motivation, repetition, and involving active participation of the subject to maintain attentional awareness (Ciuffreda, 2002). At each session (lasting for 1 hour), the sham analogue of version, vergence, and accommodation training was performed for a total of 45 minutes with interspersed rest periods for 15 minutes, for a total of 9 hours of training over the 6 week treatment phase. For version, there was no formal, programmed, and repetitive fixation (with foveal feedback) or saccades per se. It rather involved intermittent and random saccades interspersed with random fixational pauses that would not be effective in training the versional system (Ciuffreda, 2002). Similarly, vergence sham did not involve any disparity stimulation, and accommodative sham did not involve any blur stimulation, as these are the primary drives to the respective systems (Ciuffreda, 1992, 2002; Hung et al., 1996).

3.1.2.1. SHAM version. For *fixation* ST, subjects bifixated the estimated center of a contourless blank computer screen at a 40 cm distance for 2 seconds before two targets (1 inch square picture/symbol/letter) were presented for 100 msec on either one or both sides (±10 degrees either horizontally or vertically) of the estimated fixation point. The subject attempted to identify the two peripheral targets presented. Peripheral target presentation time (100 ms) was shorter than the mean saccadic latency (~200 ms) (Ciuffreda & Tannen, 1995) to prevent target foveation. *Saccade sham* involved completion of perceptual puzzle blocks, in which subjects completed the puzzle by arranging individual puzzle blocks into an appropriate pattern both monocularly and binocularly. Visual concentration was the sham analogue of the *simulated reading* training. The subject viewed and randomly scanned with saccades an array (varying from 3 × 3 to 5 × 5) of pairs of pictures for a 10-second period. Then, the pictures were removed, and the subject was requested to recall by visual memory the location of a specific picture in the array.

3.1.2.2. Sham vergence. For sham-step stimuli, binocular or monocular plano-powered loose prims, prism flippers, and/or monocular vertical prism (0.5 or 1pd) flippers were used. The targets were comprised of pictures, a vertical column of letters/numbers of varying sizes, and a cartoon movie displayed on a computer screen at 40 cm. The training was comprised of repetitive and systematic manual alternation of the flippers/loose prisms every 15–20 seconds, but without

any actual prismatic power changes horizontally, while bifixating static targets or watching a cartoon movie. For sham-ramp stimuli, subjects tracked a difference of Gaussian (0.2cycles/degree) target through a 0.5 mm pinhole monocularly for 5 minutes (2.5 minutes each eye) in an otherwise dark room (Ciuffreda, 1992). This target does not have any blur or disparity stimulation when viewed monocularly (Kotulak & Schor, 1987).

3.1.2.3. Sham accommodation. This ST involved repetitive and systematic manual alternation of the lens flippers, monocularly and binocularly, but without any spherical lens power changes (i.e., plano/colored lenses). Subjects read a text paragraph or watched a cartoon movie at 40 cm on a computer screen, similar to that performed for the OMT.

4. Results

Figure 3 presents the group mean findings related to reading rate before and after the OMT, with comparison to the grade-level normative data of Taylor (1966). There was a significant 25% increase in reading rate following the OMT. It increased from 142 to 177 words per minute, with it closely approaching the lower normal limit (Taylor, 1966). However, it did not normalize.

Table 4 presents the key group mean Visagraphic oculomotor-based parameters, including reading rate as described above. Grade-level efficiency significantly
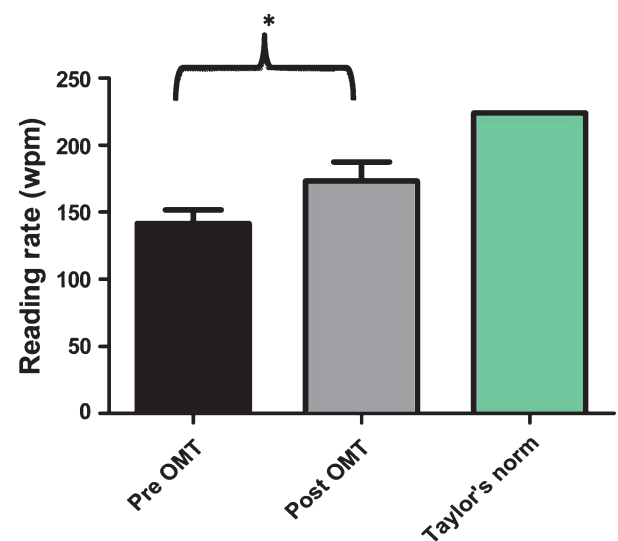

Fig. 3. Mean reading rate before (Pre-OMT) and after (Post-OMT) in mTBI compared to Taylor's norm. Error bar indicates +1SEM; * = statistically significant.
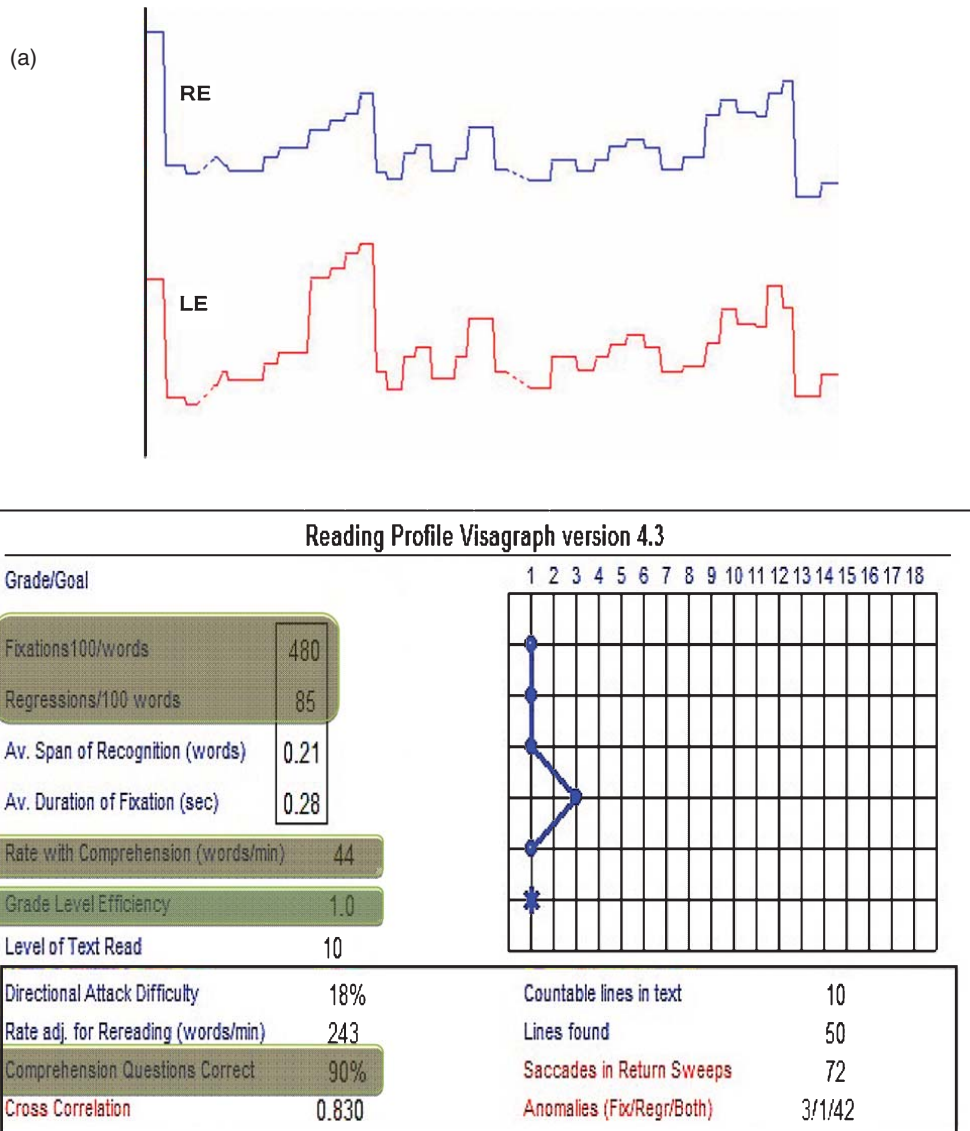
(a)

Fig. 4(a). Visagraph output in a mTBI subject at baseline who showed the best post-OMT Visagraph-based reading gains: Top - Horizontal eye position as a function of time (8 seconds data); RE = right eye; LE = left eye; Upward inflection = progressive saccade; downward inflection = regressive saccade. Bottom – On the left = Various Visagraph parameters assessed for grade-10 reading material; Graph plot on the right = Taylor's grade level efficiency (from 1–18; >12 is normal), showing a level of 1.0 (star) in this subject before OMT. Relevant parameters are highlighted.

increased following the OMT by over 2 grade levels, which is considered to be clinically significant (Ciuffreda et al., 2003). Similarly, the number of fixations per 100 words (i.e., number of progressive saccades) reduced significantly. However, neither parameter normalized. The number of regressions per 100 words decreased by 23% in the predicted direction, but this large change was not statistically significant, presumably due to the relatively large inter-subject variability found. Lastly, the comprehension level did not change significantly, as it was already normal at baseline ($\geq 70\%$) (Taylor, 1966).

With regard to the saccade ratio, there was a marked reduction in the number of progressive and regressive saccades, following the OMT. The group mean saccade ratio for the SRML paradigm reduced significantly ($p < 0.05$) from a mean value of 2.1 to 1.7 ($\sim 20\%$), thus demonstrating improvement in pure sequential saccadic tracking ability. With respect to the simulated reading single line (SRSL) ratio, it reduced from 2.7 to 2.2 ($\sim 20\%$), but this change was not statistically significant, presumably due to the relatively large inter-subject variability found. However, its decreasing trend is suggestive of improvement. Neither
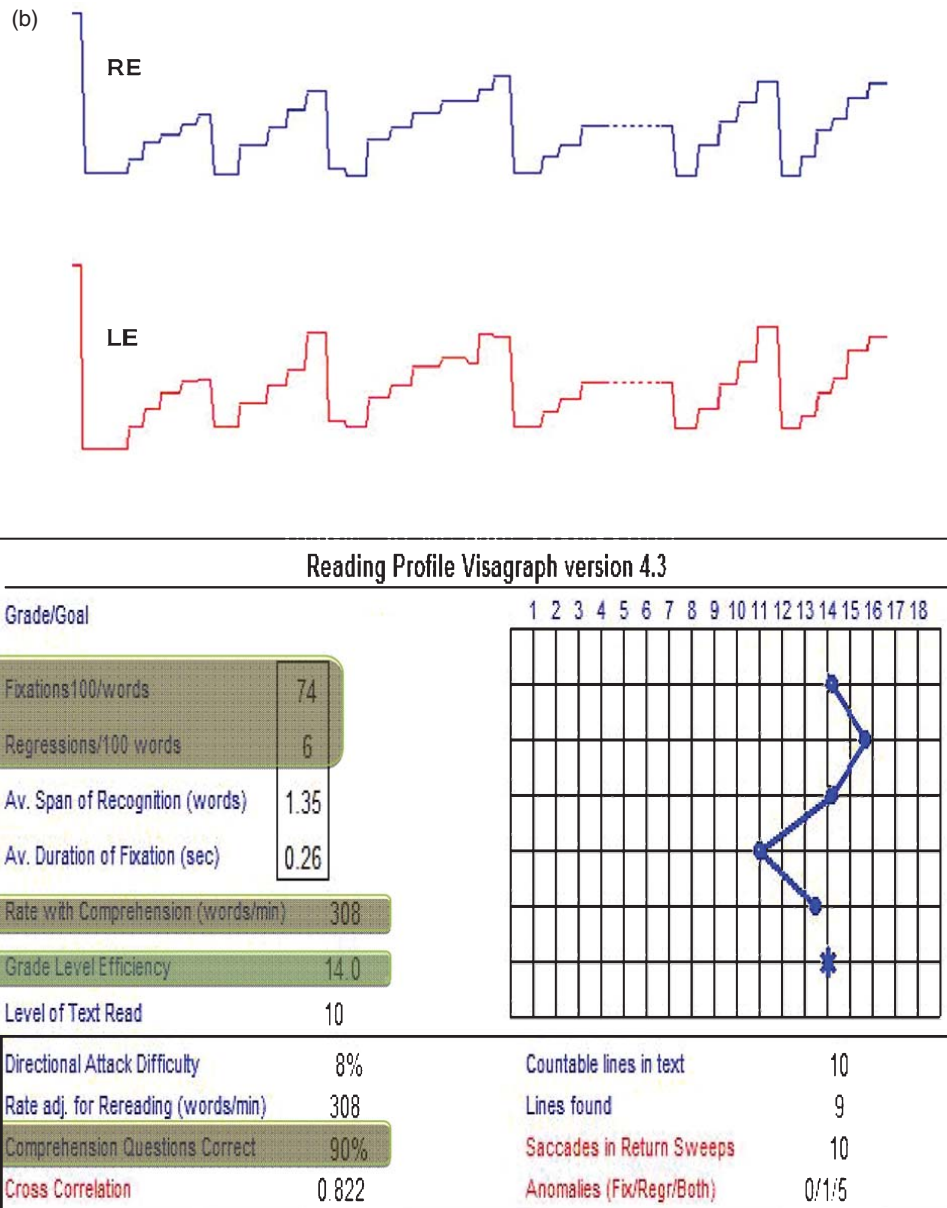
Fig. 4(b). Visagraph output in the same mTBI subject after OMT: Top - Horizontal eye position as a function of time (8 seconds data); RE = right eye; LE = left eye; Upward inflection = progressive saccade; downward inflection = regressive saccade. Bottom – On the left = Various Visagraph parameters assessed for grade-10 reading material; Graph plot on the right = Taylor's grade level efficiency (from 1–18;>12 is normal, based on weighted average of the reading parameters), showing a level of 14.0 (star) in this subject. Relevant parameters are highlighted.

saccade ratio correlated with the increase in reading rate (Table 5).

Figure 4a and b present Visagraphic reading eye movement traces before and after OMT, along with the related tabular reading-related analysis (see highlighted areas), in the subject who demonstrated the most dramatic improvements. Notably, reading rate increased from 44 to 308 words per minute, and hence it normalized (Taylor, 1966). Related to this, grade-level efficiency increased markedly, and it normalized going from grade 1 to grade 14 (college level), with a high comprehension level present at each test phase (90%). The global reading eye movement pattern became more regular and "staircase-like" following the OMT, a desirable profile (Taylor, 1966; Ciuffreda & Tannen, 1995).

The change in reading rate with OMT was also significantly correlated with two key clinical parameters, which are typically abnormal at baseline

Table 4
Mean (±1SEM) Visagraph parameters of reading eye movements before (baseline) and after oculomotor training (post-OMT) for grade-10 level text. wpm- words per minute; fixations/100 words – number of progressive saccades; regressions/100 words – number of regressive saccades. BOLD, italicized = statistically significant. * - normal at baseline

Visagraph parameter	Baseline	Post-OMT	Significant	*p* value
Reading rate (wpm)	142 (10)	177 (14)	*yes*	*<0.01*
Comprehension (%)	81 (4)*	85 (3)	no	0.31
Fixations/100 words	164 (10)	135 (11)	*yes*	*0.02*
Regressions/100 words	30 (3)	23 (4)	no	0.11
Fixation duration (sec)	0.27 (0.008)*	0.27 (0.10)	no	0.91
Grade level efficiency	4.1 (0.7)	6.3 (1.2)	*yes*	*0.01*

Table 5
Correlation of critical oculomotor parameters for reading

Correlated parameters	*R* value	Significant	*p* value
SRML ratio vs. reading rate	0.13	No	0.52
SRSL ratio vs. reading rate	0.27	No	0.19
Binocular accommodative amplitude vs. reading rate	0.43	*Yes*	*0.03*
NPC break vs. reading rate	−0.51	*Yes*	*0.01*
Binocular accommodative facility vs. reading rate	0.23	No	0.26
Vergence facility vs. reading rate	0.31	No	0.14
Reading rate vs. CISS score	−0.37	*Yes*	*0.03*
Reading rate vs. VSAT percentile	0.35	*Yes*	*0.04*

(i.e., prior to any OMT) in individuals with mTBI (Green et al., 2010b; Szymanowicz et al., 2012; Thiagarajan, 2012; Ciuffreda et al., 2007) (see Table 5). Binocular accommodative amplitude (i.e., the maximum accommodative amplitude), which increased significantly and normalized following OMT, significantly correlated with reading rate. Similarly, the near point of convergence (i.e., the maximum convergence amplitude), which increased significantly following OMT but did not normalize, significantly correlated with reading rate (Thiagarajan, 2012).

The change in reading rate also significantly correlated with two key non-oculomotor-based, but related, visual parameters (Table 5). Nearwork symptoms significantly decreased, and visual attention significantly increased, with increase in reading rate following OMT.

This aforementioned change in reading rate did not significantly correlate with two key clinical dynamic parameters, which are frequently abnormal at baseline

in mTBI (Green et al., 2010b; Szymanowicz et al., 2012; Ciuffreda et al., 2007). These were lens facility and prism facility (Table 5).

Lastly, and of considerable interest and importance, was the frequency of occurrence of an abnormality in one or more of the three oculomotor subsystems based on dual categorization, namely clinically-based and laboratory-based parameters. The summarized findings are presented in Table 6 for each of the 12 subjects at baseline. For each subject, there are 6 possible categories of oculomotor abnormalities across the three oculomotor subsystems tested (2 for each, i.e., clinical and laboratory). If all subjects exhibited an abnormality for all three subsystems for both the clinical and laboratory-based parameters, there would be 72 boxes checked in Table 6. First, across subjects, 60 out of the 72 possible boxes were checked as "abnormal" (84%). Second, 11 of the 12 subjects (92%) had at least one of the categorized parameters (clinical/laboratory) abnormal for all three subsystems. Only one subject (CR04) demonstrated abnormality in two systems (version and vergence). Accommodation was found to be normal in this subject. Third, no subject had an oculomotor abnormality in only one oculomotor subsystem. Lastly, the greatest number of abnormalities was found in the versional system and the least number in the accommodative subsystem.

In contrast to that found for the OMT, the ST did not have a significant effect on *any* parameters assessed (Thiagarajan, 2012). In the odd group of subjects who performed oculomotor training first, there was no significant difference ($p > 0.05$) between post-OMT and post-ST measures, thus showing no effect of the ST. Similarly, in the even group of subjects who performed ST first, there was no significant difference ($p > 0.05$) between baseline and post-sham measures, again thus showing no effect of the ST.

5. Discussion

Reading constitutes one of the most important activities of daily living (ADLs) (Ciuffreda et al., 2006). As mentioned in the Introduction, efficient reading requires the precise coordination of both the lower-level, oculomotor (version, accommodation, and vergence) and the higher-level, non-oculomotor (e.g., attention, linguistic, cognitive, memory) processes (Reichle & Rayner, 2002). Since TBI produces a diffuse/global kind of brain injury (e.g., coup-contrecoup) (Suchoff et al., 2001; Greve et al., 2009), deficits in either the oculo-

Table 6
Baseline abnormal oculomotor subsystems. Symbols: √ = presence of abnormality; grey filled box = absence of abnormality

	VERGENCE		ACCOMMODATION		VERSION	
	Clinical	Lab	Clinical	Lab	Clinical	Lab
JM01		√		√	√	√
TB02	√	√	√		√	√
BR03	√	√	√		√	√
CR04		√			√	√
EK05	√		√	√	√	√
KO06	√	√		√	√	√
DB07	√	√	√	√	√	√
AN08	√	√	√	√	√	
DJ09	√	√	√	√	√	√
SR10	√	√	√	√	√	√
AK11	√	√	√	√	√	√
NM12	√		√	√	√	

motor and/or non-oculomotor systems could adversely affect reading. If an individual cannot read efficiently with comfort for a sustained period of time, their ability to perform many routine ADLs (e.g., computer work), as well as one's overall quality of life (QOL), will likely be compromised (Ciuffreda et al., 2006).

Following head trauma, the diffuse axonal injury (DAI) causes the axons to stretch, twist, and tear, which results in overall disrupted white matter (WM) integrity (Greve et al., 2009). As a consequence, the strength, number, and organization of the neuronal synapses are reduced, thus causing the neuronal synchrony and firing rate to be compromised (Warraich & Kleim, 2010). These structural changes along the affected neural pathways are reflected in the functional abnormality as a response that is *inaccurate, variable,* and *slowed.* In particular, the "automaticity" or "reflexive nature" of a particular function is lost, and hence the affected individual cannot respond in a time-optimal manner. Thus, an individual whose functional automaticity is compromised will need to constantly exert considerable effort simply to perform this necessary but *lower-level* actions (e.g., basic saccadic oculomotor control), which in turn will adversely impact upon and compromise higher-level aspects, such as comprehension, sustained

attention, and short-term visual memory, as well as visual comfort.

One of the main motor systems that is commonly affected subsequent to a TBI is the oculomotor system (Ciuffreda et al., 2007; Capó-Aponte et al., 2012). Considering the vulnerability of the brain stem structures (Greve et al., 2009) that primarily house neurons related to accommodation, vergence, and version, the frequency of disorders in one or more of these three subsystems is not surprising (Ciuffreda et al., 2007). Since reading involves synchrony within and between each of these three oculomotor subsystems and their related aspects, it is not surprising that "*difficulty with reading*" is the primary symptom in individuals with TBI (Ciuffreda et al., 2007; Goodrich et al., 2007, 2013; Lew et al., 2007; Brahm et al., 2009; Stelmack et al., 2009). A combination of intermittent blur/ diplopia due to accommodative and/or vergence dysfunctions, and skipping words/lines and loss of place due to a saccadic dysfunction, would adversely affect reading. More importantly, higher level attentional aspects, of necessity, would now be allocated to perform basic oculomotor functions during reading (e.g., intermittently focusing/fusing the words), thus resulting in compromised comprehension. However, individu-

als with oculomotor abnormalities may modulate their reading speed and frequently reread to attain an acceptable level of comprehension (Ciuffreda & Tannen, 1995). All of the above would significantly reduce reading speed and impact adversely on overall reading efficiency, thus producing nearvision symptoms.

In the present study, reading eye movements recorded using the Visagraph system revealed several interesting results. Taylor's normative data (Taylor, 1966) show that the expected average adult values to be 224 wpm for reading rate, 101 fixations per 100 words, 19 regressions per 100 words, and grade-level efficiency to be 14. However, those with mTBI in the present study demonstrated significantly reduced reading rate, an increased number of fixations/100 words, a higher number of regressions/100 words, and decreased grade-level efficiency. An excessive (i.e., unwanted) number of saccades, both progressive and regressive in nature, are the main determinants of slow reading (Ciuffreda & Tannen, 1995). The more saccades that are executed, the slower the reading rate based on sampled-data theory alone (Stark, 1968); that us, after a saccade is completed, the refractory period for initiation of the next saccade is approximately 180 msec. The present finding of an increased number of unwanted/unnecessary, inaccurate saccades is consistent with that of the significantly elevated saccade ratio found in these subjects. However, the fixation durations were within normal limits, and thus did not contribute to the reduced reading rate of the subjects (Table 3).

Following training, there was a significant 25% improvement in reading rate. Figure 3 shows reading rate values before and after training in comparison to Taylor's age-normed values. This reading rate increase was also significantly correlated with the reduction in CISS score, along with the increase in VSAT percentile, thus suggesting concurrently improved subjectively-based visual comfort and visual attention, respectively, in the process. In addition, the number of fixations/100 words reduced by 18%, thus demonstrating a reduced number of excessive and unnecessary saccades after the training. The simulated reading training protocol was purposely designed, so that subjects could not make a "regression", by extinguishing the previous target when the new target appeared. While this reduces the number of purely oculomotor-based regressive saccades, however, it might not reduce regressions made to reconfirm a particular text component during actual reading. In the present study, the number of regressions/100 words decreased by 23% in the predicted direction following the training. However, it was not significant due

to the relatively large intersubject variability. As far as comprehension was concerned, it was normal at baseline, and hence no large change was expected following the training. Since comprehension did not change after the training, it suggests that the increased reading rate was primarily oculomotor-based, and an effect of OMT training. Based on the present results, it is clear that the oculomotor-based training had a significant positive effect on reading rate and related aspects.

The correlational analyses provided several important insights into the OMT effects and their functional significance (Table 5). First, improvement in reading rate was correlated with two key clinical, *amplitude*-based, *static* oculomotor parameters: the maximum amplitude of accommodation and the maximum amplitude of convergence, following OMT. In contrast, reading rate was not correlated with two key clinical, *facility*-based, *dynamic* oculomotor parameters: lens facility and prism facility, following OMT. There is a logic to these findings. Reading requires a sustained level of accommodation and convergence, as the reading material is maintained at a relatively constant near distance for prolonged periods of time. This suggests that a considerable amount of both accommodation and vergence must be exerted, as well as be maintained "in reserve" to allow for sustained and comfortable reading and nearwork in general, as has been hypothesized for the relationship between "accommodative reserve" and the onset of symptomatic presbyopia (Rabbetts, 2007). That is, according to this notion, the maximum amplitude of accommodation should be at least twice the near dioptric demand for sustained and comfortable nearwork. Second, there were correlations between reading rate, and both the CISS and VSAT score changes, following OMT. It is not surprising that the reading rate would increase, once the three oculomotor subsystems were significantly remediated, as the presumption was that all/most of the reading problems at baseline (i.e., pre-OMT) had a primary oculomotor basis in the sample population (Ciuffreda et al., 2007; Capó-Aponte et al., 2012). Thus, following the OMT, there was presumably less effort allocated to the low-level oculomotor-based reading components. Related to this was the significant increase in visual attention with OMT, as well as its correlation with the training-related increase in reading rate. This finding suggests that overall attention could now be directed to the task of comprehending the text rather than to the low-level control oculomotor aspects. Furthermore, it has been established that the task of oculomotor remediation per se has embedded into it an underly-

ing attentional training component (Solan et al., 2003; Ciuffreda, 2002). That is, with the associated high level of attention and continuous task demands (e.g., keeping the target in focus at all times) and related visual feedback involving the concept of "perceptual learning" (Ciuffreda, 2002) in the training process, visual attention was heightened and improved. This was demonstrated several years ago by Ciuffreda et al. (2006), in which the training of basic versional eye movements and simulated reading resulted in marked improvement of the attentional state under a variety of environmental conditions (e.g., quiet versus noisy room) in individuals with mTBI using a simple rating-scale questionnaire.

The lack of correlation of reading rate with the saccade ratio is interesting. An improvement in basic saccadic tracking ability, as evident from the reduction in saccade ratio, was expected to correlate with the increased reading rate. However, the present study results revealed lack of correlation with either the single-line or multiple-line saccade ratios. Although improved tracking ability was reflected in the reduction of fixation/100 words and regressions, the finding could be attributed to the individual subject variability. The reduction in saccade ratio was smaller than the magnitude reported by Ciuffreda et al. (2006), although the baseline ratios reported in their study were larger than in the current study, and thus there was more room for a significant improvement to occur.

Neurophysiologically, the observed changes in oculomotor behavior could be attributed to residual oculomotor/visual neuroplasticity in the present subjects. This training-induced recovery process involves functional recovery via a "relearning" process (Chen et al., 2010; Munoz-Cespedes et al., 2001). Vision rehabilitation acts as a critical part of the relearning process, in which the trained system gains its accuracy and automaticity through feedback and repetition. With regard to the results of the present study, an overall improvement in the oculomotor behavior was observed in *all* 12 individuals with mTBI to some degree, and it is a consequence of "oculomotor learning" (Abernathy et al., 1997; Ciuffreda, 2002). A combination of repeated stimulation with various amounts and types of blur (via negative and positive lens), horizontal disparity (crossed and uncrossed), target step displacements (horizontal and vertical), etc., as well as increasing task level difficulty (e.g., progressively reducing target size), active participation of the subjects, heightened attentional state, presence of visual and verbal feedback, and high motivation of the subjects to perform

the task over the 6 week training period resulted in a significant oculomotor training effects (Ciuffreda, 2002). This marked functional improvement shows great promise for future rehabilitation in these and other such individuals. Based on the existing knowledge of oculomotor control neurology (Leigh & Zee, 2006), it is difficult to definitely state what specific areas of the brain have regained activity, since the brain utilizes different strategies (restoration/recruitment/retraining) to recover from the functional loss (Warraich & Kleim, 2010). Functional neuroimaging studies are thus necessary to assess for correlation with these relearned oculomotor behavioral changes. To date, there is only one pilot study (Alvarez et al., 2010) that evaluated brain activity changes in 2 individuals with mTBI associated with oculomotor rehabilitation involving solely the vergence subsystem. Their fMRI results showed increased amount of voxels and correlation within several regions of interest (ROI) (i.e., brain stem, cerebellum, FEF, and SEF) following a total of 18 hours of both clinically-based and laboratory-based *vergence only* rehabilitation. While increased cortical activity was attributed to neural recruitment, increased correlation was attributed to improved synchronization of the involved subsystem's population of neurons. Similar future studies are required to evaluate the neural correlates of oculomotor rehabilitation and improved function in individuals with mTBI.

Related to the above notion of residual brain neuroplasticity was the finding that the vast majority of the oculomotor parameters significantly improved/increased following the OMT, but many did not normalize except for the accommodative facility rate (Thiagarajan, 2012). Perhaps increasing the oculomotor rehabilitative time by two-fold or more would have resulted in an even more positive outcome: that is, a greater number of parameters that were abnormal at baseline would have both increased significantly and normalized. This remains to be tested. The present study is on-going, and the study individuals are being followed-up at 3 and 6-month intervals. Results from this follow-up investigation will be used for planning more efficient and targeted future vision therapies (both active and maintenance). However, there may be an alternative explanation given the global and pervasive damage to the brain (e.g., coup-contrecoup): complete restoration of oculomotor control may be beyond the scope and ability of such a damaged brain. This notion warrants future investigation via anatomical, physiological, and brain imaging studies in individuals with TBI before and after such remediation.

Although the present investigation was intended to be relatively comprehensive, there were some study limitations. First, it was primarily restricted to those with mTBI. Investigation of the oculomotor system in moderate TBI with respect to baseline dysfunctions and their remediation would add considerably to our knowledge in this area, especially with respect to oculomotor/visual system plasticity in a more damaged brain. Second, due to our experimental crossover design and related practical aspects, only 9 hours of true training could be performed. Future studies on remediation should be conducted to determine how effective longer training durations might be. And, third, long-term follow-up was not performed. Follow-up should be at least one year, at 3 month intervals, and then perhaps as long as 4 additional years with full testing occurring annually.

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Declaration of interest

Authors have no direct or indirect affiliation with any organization with a financial interest in the subject matter or materials discussed in the manuscript.

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