Effect of oculomotor vision rehabilitation on the visual-evoked potential and visual attention in mild traumatic brain injury

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Abstract

Primary objective: The purpose of the experiment was to investigate the effect of oculomotor vision rehabilitation (OVR) on the visual-evoked potential (VEP) and visual attention in the mTBI population.

Research design and methods: Subjects (n = 7) were adults with a history of mild traumatic brain injury (mTBI). Each received 9 hours of OVR over a 6-week period. The effects of OVR on VEP amplitude and latency, the attention-related alpha band (8–13 Hz) power (μV²) and the clinical Visual Search and Attention Test (VSAT) were assessed before and after the OVR.

Results: After the OVR, the VEP amplitude increased and its variability decreased. There was no change in VEP latency, which was normal. Alpha band power increased, as did the VSAT score, following the OVR.

Conclusions: The significant changes in most test parameters suggest that OVR affects the visual system at early visuo-cortical levels, as well as other pathways which are involved in visual attention.

Introduction

Traumatic brain injury (TBI) is a major medical and public health problem in the US [1, 2]. According to the Centers for Disease Control and Prevention (CDC), every year 1.7 million people suffer from a TBI [3]. There are three categories of TBI: mild, moderate and severe. Approximately 75% of the TBIs that occur every year are of the mild type [4]. The recent increase in the prevalence of TBI is mainly due to the past Iraq/Afghanistan wars [5] and the newly-recognized, sports-related concussions (e.g. football) [6].

Mild traumatic brain injury (mTBI) results from the initial mechanically-based, pervasive, coup–contrecoup injury of the brain within the cranium, which involves rapid and powerful acceleration, deceleration and rotational forces, thus causing diffuse axonal injury (DAI) [7–9]. The DAI affects neural transmission; it is responsible for slowing and delays in cortical processing, including vision [10]. Based on the aforementioned global brain insult, it is not surprising that a range of visual deficit occurs following an mTBI (e.g. oculomotor problems, visual-field defects, visual attention deficits and increased motion sensitivity) [11–15]. More specifically, individuals with mTBI frequently report oculomotor-based problems [16–19], as well as concurrent slowed visual information processing [20, 21] and visual distractibility [22]. These visual dysfunctions may have an adverse impact on their activities of daily livings (ADLs), as well as vocational and avocational goals [23, 24]. Oculomotor-based vision rehabilitation has been provided to these patients to improve these and related visual deficits with a high degree of success [16].

Oculomotor vision rehabilitation (OVR) is commonly prescribed for remediation of the resultant and common symptomatic oculomotor deficits prevalent in mTBI [16, 25–29]. This remediation typically includes the versional (e.g. fixation and saccades), vergence and accommodative systems, but it may also involve the vestibular system and its interaction with vergence [30, 31]. OVR incorporates the use of targeted, repetitive, specific and sequenced visual stimulus-based manipulation and prescribed protocols to obtain and maintain single, clear and stable vision at all times, by incorporating the principles of motor and perceptual learning [30, 32]. In addition, embedded in OVR is the heightening of general/visual attention [30, 33–35], as the patient is trained to become more acutely aware of changes in the visual stimulus (e.g. blur) and then respond motorically to optimize the resultant visual percept. With repetition, the oculomotor responsivity becomes automatic and reflexive in nature, with transfer to the real world environment such as the classroom and work place. The effect of successful OVR on the oculomotor system can be assessed both subjectively in the clinic [30, 36] and objectively in the laboratory [29, 37].

There has been only one study in the mTBI population which used the VEP to assess objectively the effect of OVR on visuo-cortical responsivity. Freed and Hellerstein [26] tested two groups of adult patients with mTBI: Group 1 was...
comprised of 18 individuals (mean age = 32.5 years) who received OVR, which included the prescription of lenses, prisms, partial occlusion and oculomotor-based vision therapy [14, 30]. Group 2 included 32 age-matched (mean age = 32 years) individuals, but who did not receive any form of OVR and served as controls. The OVR and VEP were performed in group 1, on average 1.7 years post-injury, and in group 2, on average 1.35 years post-injury, to circumvent contamination of results via natural recovery (up to 6–9 months post-injury [38]). To measure the VEP responses, a black-and-white checkerboard pattern stimulus, with a check size of 56 min arc, was used with modulation at a rate of 1.88 reversals/second. Stimulus contrast was not specified. They used the following criteria to specify that the VEP waveform was ‘abnormal’: if the P100 latency was delayed by more than 15% and/or the VEP amplitude was decreased by more than 50% over the three trials, as compared to their normative clinical VEP response data pool. Freed and Hellerstein [26] found that 71% of those in group 1 and 81% of those in group 2 presented with an ‘abnormal’ VEP waveform at baseline. In contrast, 12–18 months after the OVR, there was a 33% decrease in abnormal waveforms in the treated group 1, but only a 3% decrease in abnormal waveforms in the non-treated group 2. However, Freed and Hellerstein [26] only categorized and did not quantify in detail the VEP responses following the OVR; furthermore, they did not assess the effect of the OVR on visual attention.

Visual attention is processed by different cortical (i.e. visual cortex, frontal and parietal lobes) and subcortical (i.e. thalamus) areas of the brain [12, 39]. For example, Kastner and Ungerleider [40] suggested that the mechanism of visual attention processing was initiated in the visual cortex before being transmitted to higher cortical areas. Therefore, assessing visual attention at the visual cortex area using the VEP method provides critical, early information about the attentional state in humans, be it normal or abnormal [41–43]. Researchers have confirmed that the alpha band (8–13 Hz) activity of the VEP (0.5–30 Hz) generated from the primary visual cortex (V1) is related to human thalamo-cortical attention [41, 42, 44–47]. Synchronous and asynchronous cortical neuronal activities occur in V1 related to different attentional states, which modulate the alpha band power [42, 43]. For example, attenuation of alpha power occurs when comparing the ‘eyes-closed’ to the ‘eyes-open’ viewing conditions, which is a normal phenomenon: inability to suppress alpha suggests an attentional deficit [41–43]. Currently, there are no studies in mTBI which have used the VEP method to assess visual attention objectively before and after OVR.

Therefore, the purpose of the present study was to investigate the effect of OVR on VEP responsivity in the mTBI population. Furthermore, the effect of OVR on visual attention was assessed both objectively and subjectively. Objective visual attention was quantified using the alpha band (8–13 Hz) responsivity of the VEP [37, 41–43], whereas subjective visual attention was quantified using the clinical Visual Search and Attention Test (VSAT) [42]. Changes in the VEP amplitude and latency and visual attention both objectively and subjectively following OVR would suggest its effects at the early visuo-cortical level.

Methods

Subjects

Seven individuals (one male, six females) with medically-documented mTBI, and having oculomotor and/or visual attentional deficits based on case history and clinical assessment, participated in the study. They had a mean age of 29.5 ± 4.3 years, with a range from 25–38 years. Time of injury ranged from 1–6 years prior to the VEP and VSAT testing, as well as the OVR. The insult occurred either from a motor vehicle accident or fall. See Table 1 for subject demographics. The following criteria were used for the diagnosis of mTBI [48]: (1) loss of consciousness for less than 30 minutes or an altered state of consciousness, (2) a score of 13 or greater on the Glasgow Coma Scale (GCS) and (3) post-traumatic amnesia (PTA) lasting less than 24 hours. Each had a comprehensive vision examination at the SUNY/State College of Optometry, which included evaluation of refractive, binocular/oculomotor and ocular health status, prior to participating in the study. All had best corrected visual acuity of 20/20 in each eye at both distance and near. Exclusion criteria were history of seizures, strabismus and amblyopia, as well as any ocular, systemic or neurological disease. They were not taking any drugs or medications that would affect either their visual or attentional states. Subjects were enrolled from the Raymond J. Greenwald Rehabilitation Center/Brain Injury Clinic at the State University of New York (SUNY), State College of Optometry, the Institutional Review Board (IRB) at the SUNY, State College of Optometry, approved the study. Each subject provided written informed consent.

Apparatus

The VEP amplitude, latency and alpha band (8–13 Hz) power were assessed with the DIOPSYS™ NOVA-TR system (Diopsys, Inc., Pine Brook, NJ) [41–43, 49]. The DIOPSYS™ system generated a checkerboard stimulus, as well as analysed the VEP and alpha power responses using custom-designed software programs. A single computer processing unit controlled the entire system. It included a 17” LCD stimulus test monitor with a refresh rate of 75 Hz, which was used for presentation of the test stimuli. The system also had a real-time response monitor, which was used by the experimenter for on-line viewing and graphical display of the VEP and alpha responses. The DIOPSYS system is approved by the FDA for use with clinic patients. This VEP system has been used extensively in the laboratory for the past 3 years [41–43, 49, 50].

Procedures

VEP and alpha recordings

The VEP and alpha recordings were performed immediately before and after successful OVR [51–53] to assess both VEP responses and the visual attentional state objectively. The recordings were performed by using three standard GRASS (Grass Technologies, Astro-Med, Inc., West Warwick, RI) gold cup electrodes (i.e. active, reference and ground), each of 1 cm in diameter [41–43, 49, 50].
The following two test conditions were used to measure the VEP amplitude and latency, as well as to modulate the visual attentional state and in turn alpha (8–13 Hz) responsivity as quantified via power spectrum analysis [41–43, 54]; that is, at each frequency, the amplitude component contribution to the overall complex VEP waveform was assessed (i.e. \( m V^2 \) = power, where \( V \) is voltage). Three trials for each of the two test conditions were performed. Test duration was 20 seconds for each trial.

(1) Full-field VEP (‘eyes-open’): In this test condition, conventional full-field (17° H × 15° V) VEP testing was employed (64 × 64, black-and-white checkboard pattern, 20 minute arc check size, 85% contrast, 74 cd m\(^{-2}\) luminance, 1 metre distance, binocular viewing with spectacle correction). The stimulus was modulated at a temporal frequency of 1 Hz (two reversals per second). To control fixation and maintain visual attention, a small (0.5° diameter) red, rotating, annular fixation target was presented in the centre of the test stimulus per the manufacturer’s software. In this ‘eyes-open’ condition, subjects fixated the small target as they gazed at the checkboard visual stimulus. From these responses, the alpha band (8–13 Hz) power (\( \mu V^2 \)) was mathematically extracted, displayed and quantitatively assessed using power spectrum analysis [54]. This eyes-open condition was always tested first. This was done to assure VEP response normalcy. An average of the three test trials was used in the analysis for each subject, which was then combined across the group.

(2) ‘Eyes-closed’: In this test condition, the subjects were instructed to close their eyes, relax and ‘clear their mind’ for 60 seconds before starting the recording. This helped them to attain a relaxed attentional state [37, 41–43]. In addition, they were instructed to imagine ‘gazing’ straight ahead where the rotating fixation target was previously presented to maintain steady gaze. During this condition, the alpha (8–13 Hz) power (\( \mu V^2 \)) was assessed using power spectrum analysis [54]. An average of the three trials was obtained and used in the analysis for each subject, which was then combined across the group.

**Alpha attenuation ratio (AR)**

The alpha AR is related to the visual attentional state [37, 41–43]. The alpha AR is defined as the alpha power (\( \mu V^2 \)) measured during the ‘eyes-closed’ condition divided by the alpha power measured during the ‘eyes-open’ condition [42, 43]. In a recent paper from this laboratory [42], an AR of 2.0 or greater suggested normal visual attenuation; that is, there was considerable and normal suppression of the alpha activity in the ‘eyes-open’ condition as compared to the ‘eyes closed’ test condition [41–43].

**Subjective visual attention test**

A conventional visual attention test was performed immediately before and after the 6 weeks of OVR. The Visual Search and Attention Test, or VSAT test (© Psychological Assessment Resources, Inc., Lutz, FL), assessed visual attention subjectively as performed clinically in many disciplines [42, 55]. Test–re-test reliability for the VSAT was 0.95 [55]. Sensitivity and specificity were 0.88 and 0.86, respectively [55]. It involves a visual search and cancellation task that assesses the subject’s global sustained visual attention [55]. This test was performed binocularly in a quiet room, per manual instructions, at the individuals habitual near working distance with refractive correction in place. Following two practice trials, two test trials are performed. An average of the two test trials was used to calculate the mean VSAT percentile.
score for each subject, which was then combined across the group. These percentile scores were compared with the age-matched normative table.

Oculomotor vision rehabilitation (OVR)
Oculomotor vision rehabilitation (OVR) was provided by the second author. It included training of the three oculomotor systems, i.e. version, vergence and accommodation, with an embedded and indirect visual attentional training component [30, 33–35]. OVR training was performed twice a week for 6 weeks for a total of 9 hours, 3 hours for each oculomotor system [51–53].

Data analysis
There were several aspects to the statistical data analysis. The group mean VEP amplitude and latency before and after the OVR were compared. Then, the effect of the OVR on visual attention was assessed both objectively and subjectively. The VEP technique was used to assess the effects objectively in two ways. First, the group mean alpha AR at each alpha frequency (i.e. 8, 9, 10, 11, 12 and 13 Hz) before and after the OVR was compared. Second, the combined alpha AR across all frequencies (i.e. 8–13 Hz) before and after OVR was compared. The VSAT was used to assess the OVR effect subjectively. The VSAT percentile scores were compared before and after the OVR. For all data analyses, either a two-way, repeated-measures ANOVA or a paired, two-tailed, t-test was performed on the group data using GraphPad Prism 5 software.

Results
VEP analysis
Amplitude
The mean VEP amplitude and its variability before and after the OVR are presented in Figures 1(a) and (b) for each subject, respectively. A paired, two-tailed, t-test for the group results revealed a significant increase in VEP amplitude after the OVR \( t(6) = 3.60, p = 0.01 \). Furthermore, a paired, two-tailed, t-test for the group results revealed a significant decrease in amplitude variability after the OVR \( t(6) = 3.08, p = 0.02 \) (see Table II).

Latency
The mean VEP latency (P100 ms) before and after the OVR is presented in Figure 2 for each subject. A paired, two-tailed, t test for the group results revealed no significant change in VEP latency before and after the OVR \( t(6) = 0.12, p = 0.90 \). Similarly, a paired, two-tailed, t-test for the group results revealed no significant change in latency variability before and after the OVR \( t(6) = 0.52, p = 0.61 \) (see Table II). Latency values were normal before and after the OVR.

Alpha attenuation ratio (AR)
Individual alpha frequency AR
The group mean AR for each alpha frequency (i.e. 8, 9, 10, 11, 12 and 13 Hz) before and after the OVR is presented in Figure 3. A two-way, repeated-measures ANOVA was performed for the factors of AR and alpha frequencies. There was a significant effect on both the AR \( F(1, 5) = 97.7, p < 0.05 \) and alpha frequencies \( F(5, 5) = 18.83, p < 0.05 \). The post-hoc Bonferroni multiple comparisons revealed a significant increase in AR following the OVR at three of the six alpha frequency sub-bands (i.e. 10, 11 and 13 Hz) \( p < 0.05 \) (see Table II).

AR combined across the alpha frequency band
The AR combined across the alpha frequency band (i.e. from 8–13 Hz) before and after the OVR is presented in Figure 4 for each subject. A paired, two-tailed, t-test for the group results revealed a significant increase in the combined alpha AR after the OVR \( t(6) = 3.81, p = 0.008 \). The combined AR increased in each subject following the OVR (see Table II).

Visual search and attention test (VSAT)
The VSAT percentile scores before and after the OVR are presented in Figure 5 for each subject. A paired,
two-tailed, t-test for the group results revealed a significant increase in the VSAT percentile scores after the OVR \(t(6) = 3.13, p = 0.02\). Before OVR, subject S3 had an abnormal VSAT 2nd percentile score and subject S6 had a borderline VSAT 3rd percentile score. After OVR, all subjects had normal VSAT percentile scores (see Table II).

Table II. Group results before and after the oculomotor vision rehabilitation (OVR).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before OVR</th>
<th>After OVR</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>VEP amplitude (µV)</td>
<td>17.10 (SEM = ±3.85)</td>
<td>19.15 (SEM = ±3.80)</td>
<td>Yes</td>
</tr>
<tr>
<td>VEP amplitude variability (µV)</td>
<td>Range = 6.43–33.87</td>
<td>Range = 8.52–33.99</td>
<td></td>
</tr>
<tr>
<td>VEP latency (ms)</td>
<td>1.89</td>
<td>1.03</td>
<td>Yes</td>
</tr>
<tr>
<td>VEP latency variability (ms)</td>
<td>Range = 0.96–3.18</td>
<td>Range = 0.60–1.99</td>
<td></td>
</tr>
<tr>
<td>8 Hz AR</td>
<td>1.26</td>
<td>1.72</td>
<td>No</td>
</tr>
<tr>
<td>9 Hz AR</td>
<td>2.33</td>
<td>2.55</td>
<td>No</td>
</tr>
<tr>
<td>10 Hz AR</td>
<td>2.00</td>
<td>3.07</td>
<td>Yes</td>
</tr>
<tr>
<td>11 Hz AR</td>
<td>1.41</td>
<td>2.87</td>
<td>Yes</td>
</tr>
<tr>
<td>12 Hz AR</td>
<td>1.14</td>
<td>1.66</td>
<td>No</td>
</tr>
<tr>
<td>13 Hz AR</td>
<td>1.12</td>
<td>2.69</td>
<td>Yes</td>
</tr>
<tr>
<td>Combined alpha AR</td>
<td>1.54 (SEM = ±0.14)</td>
<td>2.43 (SEM = ±0.31)</td>
<td>Yes</td>
</tr>
<tr>
<td>VSAT percentile</td>
<td>40.25 (SEM = ±12.31)</td>
<td>59.5 (SEM = ±9.25)</td>
<td>Yes</td>
</tr>
</tbody>
</table>

AR, Attenuation ratio; OVR, oculomotor vision rehabilitation; Hz, Hertz; VSAT, Visual Search and Attention Test; statistical significance, \(p < 0.05\).

**Discussion**

The results of the present investigation confirmed and extended that of Freed and Hellerstein [26], which represented the sole study in this area. Using a dichotomous waveform categorization, they found that the VEP waveform was normal in ∼30% and 60% of the subjects before and after the OVR, respectively, thus showing a large and significant 2-fold increase immediately after the visual intervention. In the present study, the results were even stronger: nearly all primary VEP and alpha test parameters significantly improved in each subject (except for the parameter AR), as well as across the group. Latency was normal both before and after the intervention, so no change was expected. Lastly, the assessment of visual attention, both objectively and subjectively, before and after OVR has never been performed and, thus, the present results in this area represent a significant extension of their earlier findings, as will be discussed later.

Several factors related to the visual intervention may have contributed to the observed changes in the objective measures for both the VEP and alpha aspects. First, more accurate and stable bifoveal eye alignment (i.e. vergence) following the OVR would result in more precise stimulation of corresponding retinal points. This would in turn enhance binocular summation [56], thus increasing the VEP amplitude [57]. Second, more accurate and stable accommodation following the OVR would produce, on average over time of the test trial, less retinal defocus, and this too would once again result in an
increase in the VEP amplitude [58]. Third, and lastly, there is suggestive evidence from recent brain-imaging studies [32] that vergence-based OVR results in an increase in neural synchronization in relevant regions of the brain (e.g. frontal areas, cerebellum and brain stem), which would increase the resultant neural signal, as was earlier suggested by Ciuffreda [30]. This would produce a larger signal-to-noise ratio, which would be reflected in increased VEP amplitude and decreased VEP variability.

As discussed in the Introduction, embedded in all OVR/general vision therapy is an ‘indirect’ attentional aspect. Although general/visual attention was not formally trained [33, 35], it is an underlying component of such therapy [30, 33–35]. That is, as part of the OVR process, the individuals were instructed to take careful note of the quality of the stimulus, such as the presence and relative degree of blur, and then to respond appropriately and rapidly motorically to improve the resultant visual percept, e.g. to reduce the blur. In the present investigation, the improvement of visual attention, as assessed both subjectively and objectively, suggests and is consistent with the above notion.

Related to the above, one might wish to ascertain the relative contribution of the OVR and the attention component to the post-therapy increase in VEP amplitude: was it due to OVR, enhanced attention or both? At least two arguments suggest that OVR was primary. First, the OVR-related aspects were directly trained and not the visual/general attentional aspects per se. Second, the findings of Solan et al. [33, 59] would be consistent with this conclusion. In children with oculomotor-based reading problems, they performed either oculomotor, cognitive (comprehension) or attentional training in three matched groups. They found that all three types of training improved reading ability, but with the attentional training showing considerably lower gains than for either the oculomotor or cognitive ones. Such a study incorporating the test vehicles of the Solan et al. [33, 59] group should be performed to tease out more directly this important question in the mTBI population.

The present findings have important clinical implications. First, both the VEP and alpha information can be used to assess objectively baseline normalcy in those with mTBI. Second, both the VEP and alpha information can be used to assess objectively the effects of OVR in mTBI, as performed by Freed and Hellerstein [26] for the VEP, as well as perhaps other types of visual interventions (e.g. prisms). If objective changes are not found after the OVR, as was the case for the present study and that of Freed and Hellerstein [26], then one might either extend the course of the OVR or re-assess the case to search for factors that might have predicted a poorer prognosis and/or VEP-alpha electrophysiological response than would be expected.

Acknowledgement

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References


