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Title and author page

Full title

Vision Therapy Improves Binocular Visual Dysfunction in Patients with Mild Traumatic Brain Injury.

Short title

Vision therapy improves visual impairments after mild traumatic brain injury.

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Abstract

Objective: To evaluate benefits of binocular vision and ocular motility training in patients with long-term sequelae after mild traumatic brain injury (mTBI).

Methods: Twenty-eight mTBI (concussion) patients from 25 to 61 years of age with oculomotor dysfunction were selected by optometric examination. The vision therapy was designed to improve convergence, pursuit and saccades as well as to increase fusional reserves. The vision therapy was conducted by a neurooptometrist and a speech therapist, and took place weekly for 1 hour during 10 continuous weeks. Between vision training sessions, patients trained at home for 15-20 minutes daily. Before and after vision therapy, patients completed a test battery including the Groffman Visual Tracing Test, King-Devick test (K-D), a reading speed test, Multidimensional Fatigue Inventory (MFI-20) and patient interviews based on a modified version of the Canadian Occupational Performance Measure (COPM).

Results: Twenty-seven patients completed the vision therapy. After the therapy, improvements were measured on all test parameters, e.g. Groffman Visual Tracing Test ($p < 0.05$), K-D-Test ($p = 0.01$), Reading Speed Test ($p < 0.01$) and MFI-20 total ($p < 0.05$). The results for the modified COPM were significantly improved for both performance and satisfaction ($0.0001 < p < 0.01$).

Conclusion: Vision therapy improved fixation stability and endurance. Reading speed measured by the numbers of saccades and regressions time consumption per read word increased. There was also an improvement in visual attention, possibly making patients safer in traffic and outdoor activities.

Introduction

Mild traumatic brain injury (mTBI), also known as commotio cerebri or concussion, is defined as a shock or trauma to the head or body that typically results in transient neurological sequelae or symptoms. In Denmark, mTBI is common with an annual incidence among the adult population of approximately 180 pr. 100,000 (1). Approximately 10% of patients have long-term cognitive, physical and emotional consequences after mTBI, and about 80% of these patients experience vision problems such as loss of consciousness, confusion, disorientation, memory loss (amnesia), headache, nausea, dizziness and occasionally vomiting. (2-4).

For the majority of mTBI patients, spontaneous remission will occur within three months after symptoms onset. Unfortunately, for those with persisting symptoms the duration is unpredictable. Thus, the difference in duration of symptoms is extensive, and while some mTBI patients recover after a few days or weeks, other take years to regain pre-morbid functional levels. (5)

Consensus is lacking about the number of commotio patients with long-term post-concussion syndromes (PCS). For example, in one study 19 patients of 131 (15 %) patients had PCS one year after the injury (6), while in other studies approximately half of mTBI patients suffered long-term cognitive impairments. Furthermore, a large group of patients with mTBI had disabilities within several cognitive domains long after the concussion (7).

Precise mechanisms for long-term impairments following mTBI are not known. The brain is especially vulnerable to oxidative stress compared to other tissues, and following TBI an increase of reactive oxygen species (ROS), which are chemically reactive molecules containing oxygen, may contribute to and cause many harmful biological events (8-10). Although oxidative stress is considered an important pathogenic mechanism in traumatic brain injury and may be a driver of damage especially in repeated mTBI, studies are still scarce (11).

According to several studies, severe ocular motor dysfunctions often occur after head trauma. For example, investigators behind an eye-tracker study of 28 patients found that various oculomotor abnormalities occurred in 75 % of these patients. Abnormalities were imprecise vergence eye movements, slow and imprecise saccades, impaired reading eye movements compared to controls,

visual dysfunction as accommodation, etc. (8-10). In addition to blurred or double vision, there were indications of visual or ocular motor dysfunction being the cause of a wide range of symptoms, such as strained eyes, photosensitivity, difficulties reading and headache (3). The most common visual complaints after mTBI are described in table 1 (11).

Table 1. Post-concussion vision problems

Blurred vision
Avoids close work
Problems with reading
Intolerance for peripheral movement
Difficulties with over-viewing the surroundings
Asthenopia
Headache
Photosensitivity
Problems with concentration and awareness
Problems with balance/bodyposition/coordination
Vertigo/nausea

Common vision problems among mTBI patients.

In another study, investigators examined ocular motor dysfunction in 100 patients aged 11-17 years with PCS. Of these patients, 49 % were diagnosed with convergence insufficiency, 51% with accommodation anomaly and 29% with saccade dysfunction. More than one dysfunction was found among 69 % of patients (12). The weighted prevalence of ocular motor dysfunction, visual field defect and impaired visual acuity among patients with mTBI has been estimated in a meta-analysis from 2019 (13): among 2140 patients with PCS the weighted incidences of convergence insufficiency, accommodation insufficiency, visual field defect and impaired visual acuity were estimated to 36%, 43%, 7% and 0% respectively (14). Ocular motor problems often cause difficulties in daily life, for example, convergence- and accommodation insufficiency is known to cause blurring, horizontal diplopia when reading, headaches when reading, irritated eyes and letters that “move”, decreased ability to concentrate, and an impaired comprehension of read text (14-15).

The evidence for the treatment of visual problems after mTBI is still limited, although in recent years several studies have indicated that visual training with a relatively high success rate can improve rehabilitation of mTBI patients. One study presented better reading-related eye movement (16). Also the effect of spectacles to patients with mTBI has been tried with 50% success (17-18). It may be noted that the studies typically had small sample sizes and were uncontrolled.

In our present study, we therefore wanted to investigate whether vision therapy for patients with long-term consequences after mTBI can improve their micro-saccades, reading speed (saccades and regressions per minute), fixation stability and eye movements. We also wanted to investigate if patients' self-perception after vision therapy improved, and if they experienced less fatigue and increased quality of life.

Methods

The neuro-optometrist and the speech and language therapist at CSU-Slagelse recruited patients from December 2 2016 to January 1 2019.

Participants

Inclusion criteria-for patients were: adult (age>18 years) mTBI patients suffering from vision problems and referred by their home municipality or from the Speech & Brain Department of CSU-Slagelse.

Exclusion criteria were: patients who could not cope with long transport, who had mental illness, or who could not cope with training in a group due cognitive or physical problems causing insufficient motivation for vision therapy.

Interventions before and after the start of vision therapy

Before the vision therapy, a multidisciplinary inter-departmental team examined patients and was responsible for the coordination and selection of relevant patients. The multidisciplinary team consisted of a neuro-optometrist and a speech and language pathologist, both had extensive experience in treating patients with mTBI and PCS.

The aim of the neuro-optometrist's vision tests was to determine the state of the patient's binocular vision. The vision tests varied and were tailored to the patient sight functionality (19-20).

We provided a thorough mapping of symptoms, including previous treatments and general health conditions. This included status of stereopsis and motor skills (freedom of movement), phoria, fusional vergence, accommodation, refraction, spatial integration, visual field, contrast sensitivity, color vision and night vision (twilight vision). Before starting the vision therapy, the team held a conference for patients to ensure that patients would be motivated for and be able to complete the therapy. For each patient an individual plan was made. The plan was based on the patient's vision problems and rehabilitation goals, which meant that the exercises were monitored and adapted to the patient's abilities. Exercises were integrated and were based on oculomotor skills, for example agility, pursuit, and endurance level of difficulty were adjusted.

Vision therapy with 2-4 participants was provided 1 hour per week for 10 weeks. It was important for the success of the vision therapy that home training was performed every day for a minimum duration of 20 minutes except the day where the therapy was provided at CSU-Slagelse. After the vision training therapy, patients received a written plan for maintaining and continuing the therapy on their own.

Data collection and outcome measurements

Baseline examination was done using a combination of visual performance testing and a Canadian Occupational Performance Measure (COPM) interview. COPM is an individualized questionnaire for measuring a person's own perception of the meaning, performance and satisfaction of different chosen activities (21). COPM aims to promote high quality, activity-focused, evidence-based and

client-centered practices. COPM is therefore an important measuring tool for the patient's own experience. Normally COPM focuses on self-care, leisure and work, but this was less relevant, because most mTBI and PCS patients were unable to work. Therefore, COPM was modified to deal with three self-selected activities that had profound importance for the patient and was relevant for vision therapy.

Outcome results were collected immediately after the completion of the vision therapy. Thus, following the last vision therapy lesson, visual performance testing was repeated as well as the COPM interview with focus on the problems described before the start of the course.

To make an accurate study of oculomotor and habitual function levels, the following tests and assessments were completed:

The Groffman Tracing Test is a measure of both eye function and mobility of the eye muscles by testing abilities to trace lines using smooth pursuit eye movements. Patients simply had to follow a line from point to point in a complex pattern by only using eye movements (22).

King-Devick (K-D) is a test of saccadic eye movement. A saccadic movement is a quick, simultaneous movement of both eyes between two or more phases of fixation in the same direction. The K-D test is based on measurements of rapid number naming speed (reading aloud single-digit numbers from 3 test cards), which captures impairments of eye movements (23).

The Multidimensional Fatigue Inventory (MFI-20) is a questionnaire for screening fatigue/energy. It consists of 20 questions covering the domain of general fatigue, decreased activity, decreased motivation, and mental fatigue. Within each domain, 4-20 points can be obtained. The higher the score the greater the degree of fatigue. A score of 12 or more for "general fatigue" indicates presence of debilitating fatigue (24).

A Danish reading test with LIX (readability index used in Scandinavia) of 43 was used to measure reading speed in words per minute. Lix numbers between 35 to 44 are equal to sentences used in newspapers. The reading test is performed during 1 minute by reading aloud. The norm for spoken text is between 120-130 words per minute.

The patients' own assessments of their abilities to perform self-selected activities on a scale from 1-10 were measured before and after the vision therapy, high scores indicated increased importance, performance or satisfaction.

Anamnesis in schema form was obtained to map symptom profiles for vision problems. Before and after intervention, each patient assessed his visual symptoms as described in Table 1 on a scale from 0-4. A score of 4 indicating the most severe problems.

Sample size and power

The primary endpoint was the modified COPM test. We expected a 30% of the maximum score at baseline to increase to 50% at the end of the experiment, corresponding to a change from a score of 3 to a score of 5 on the COPM scale where 10 is best. As a basis for power calculation and sample size, $\alpha = 0.05$ and $\beta = 0.5$ were used. The minimum sample size was 14 participants. Due to age, transport difficulties and the time-consuming intervention, up to 25% dropout were expected, and thus at least 18 participants were considered the minimum sample size.

Data analysis

Comparisons of ranked pre- and post-performances were done using the Wilcoxon non-parametric test, which is the optimal test, when there are few participants and data cannot be expected to be normally distributed. Unless otherwise stated, results are reported as median values with associated 25th and 75th percentiles. A p-value below 0.05 was considered statistically significant. Incomplete and unused data was not included in the statistical evaluation and was treated as missing data, i.e. no calculations were made with such data. All statistical analyses were carried out by a person, who did not participate in data collection and had no personal knowledge of the patients.

Results

A total of 27 of 28 patients completed the vision therapy. Their median age was 45 (39-53) years. The youngest and oldest patients were respectively 25 and 62 years of age. The median number of

days between mTBI symptoms onset and the start of the vision therapy was 363 (237-599). Therefore, for many patients there was approximately 1 year from symptoms onset until the start of the vision therapy. The minimum time from symptom onset to the start of the vision therapy was 75 days, while the longest time was 1919 days. All patients had chronic PCS. A comparison of baseline and post-intervention results is shown in Table 2.

On all test parameters, significant improvements from baseline were measured after the vision therapy. Results from COPM showed highly significant improvements in terms of both performance and satisfaction for participant's self-chosen and particularly important chores. The patients' own assessments of vision problems were also improved. The patients experienced a lesser degree of vision problems, for example less degree of blurred vision, and less dizziness. MFI-20 showed significant fatigue reductions across several domains.

In performance-oriented tests such as Groffman Tracing Test, we measured a significant improvement, and similarly the K-D Test results improved. The reading speed significantly increased.

Table 2

Key results with associated p-values before and after vision therapy.

Measure (N = 27)	START	END	P-value
COPM1 Meaning	10 (9-10)	10 (9-10)	0.66
COPM1 Performance	3 (2 - 5)	7 (4 - 8)	0.00007
COPM1 Satisfaction	1 (1 - 4)	5 (2 - 7.5)	0.0009
COPM2 Meaning	9 (7.5-10)	9 (7.5 - 10)	1.0
COPM2 Performance	3 (2.5 - 4)	6 (5 - 8)	0.0001
COPM2 Satisfaction	2 (1 - 3)	7 (2 - 8)	0.0003
COPM3 Meaning*	9 (7.5-10)	9 (7.5-10)	1.0
COPM3 Performance*	4 (2.8 - 5)	7.5 (6 - 8)	0.01
COPM3 Satisfaction*	3,5 (1 - 4.3)	7.5 (4 - 8)	0.02
Total Vision Changes	31 (23 - 37)	21 (9.3 - 29)	0.0003
Concentration	3 (3 - 4)	2 (1 - 3)	0.002
Double vision	1 (0 - 3)	0 (0 - 2)	0.1
Blurred vision	2 (2 - 3)	1 (0 - 2)	0.007
Eye itching	1 (0 - 2)	0 (0 - 1)	0.04953
Screen work	4 (3 - 4)	3 (1 - 3)	0.02
Reading	3 (2 - 4)	2 (1 - 3)	0.02
Visual nuisance	3 (3 - 4)	2 (1 - 3)	0.02
Photosensitivity	3 (3 - 4)	3 (2 - 3)	0.06
Headache	3 (3 - 4)	3 (3 - 4)	0.01
Dizziness	3 (2 - 4)	2 (1 - 3)	0.003
Nausea	1.5 (0 - 3)	1 (0 - 3)	0.44
Fatigue	4 (3 - 4)	3 (2 - 4)	0.01
Groffman Tracing Test	28 (20 - 33)	34 (25 - 45)	0.02
K-D Test	83 (63 - 110)	65 (53 - 85)	0.01
Reading test	132 (110 - 151)	141 (131 - 175)	0.002
MFI-20 Total	73 (62 - 78)	67 (50 - 74)	0.02
General fatigue	17 (15 - 19.5)	16 (11.5 - 18.5)	0.15
Physical fatigue	16 (14 - 17.5)	14 (9.5 - 16)	0.01
Decreased activity	15 (11.5 - 17)	13 (10 - 15.5)	0.11
Decreased motivation	9 (6 - 11)	8 (6 - 9)	0.048
Mental fatigue	18 (15.5 - 20)	16 (14.5 - 17.5)	0.001

*N=10 due to few participants being able to identify a third important activity. *P*-values below 0.05 are in bold.

Discussion

Our results indicate that vision therapy improved visual dysfunction in patients with mild traumatic brain injury. Such significant improvements after vision therapy may be considered particularly important findings, because our study included patients with apparently chronic PCS. We combined objective

measurements with a qualitative questionnaire survey to uncover whether there was a correlation between the test results and the survey.

Regarding the physical examination findings, we found that symptoms associated with concussion were reduced, thus patients initially presenting with concentration problems, impaired reading abilities, headaches etc. improved. These recovery trajectories predict that convergence and oculomotor functions, as well as the autonomic system for accommodation, have a great influence in concussion rehabilitation.

Limitations

Our study was uncontrolled and patients were not randomized, which provide weaknesses and limitations. Still, single group studies evaluating outcomes longitudinally, like the current study, often may be the only feasible method and provide interesting exploratory results (25).

Only patients with chronic PCS were included, and it is our impression that the marked improvements after the vision therapy would be unlikely to occur spontaneously. Additionally, data collection was done by a multidisciplinary team, which may be considered a strength, even if the investigators were unblinded.

COPM results could be biased in case of patients wanting to please interviewers. The marked improvements in performance-based test results, such as results from the Groffman Tracing Test, the reading test and the K-D Test, where results cannot be exaggerated because patients' performances are objectively measured, indicated that the patients' outcome improvements in the surveys were genuine and not caused by a bias trying to please investigators.

Although our study has several limitations, evidence in favour of vision training has been supported by crossover studies, intervention studies without control groups and retrospective studies, which indicated positive effects of vision training in patients with visual symptoms after mTBI (26-27). It may be noted that due to difficulties recruiting patients control groups have been omitted in most similar investigations.

Furthermore, investigators have found that vision training can be used as rehabilitation for this group of patients with a relatively high success rate. For example, during a retrospective study of 160 patients,

results indicated that the majority of patients completing the vision training developed normal binocular vision (29).

Further findings and considerations

Scores in COPM indicated how a patient perceived her or his performance in important tasks of daily living, and these scores became markedly better after vision therapy, indicating that reading, screen work, and other close-up work were performed more effortlessly. Our hypothesis is that such improvements occurred because fusion reserves and binocularity were elevated. Fusion reserves are similar to the compensating fusion vergence, as eye movements have tendencies to deviate from bifoveal fixation (also called phoria) and such movements are controlled by fusional vergence (30). The magnitude of the fusion reserves can be measured using prisms. Improved ability to move eyes inward and outward, while maintaining binocular vision, indicate greater vision magnitude (31). Double vision may occur when fusion no longer can be maintained. Binocularity, also referred to as stereopsis, implies that by simultaneous coordination visual experience is achieved in 3D. 3D vision is measured in arc-seconds in various tests including Titmus Fly test, TNO Stereopsis Test etc. (32). When convergence insufficiency and accommodation insufficiency or other binocular anomalies have been cured by vision therapy, symptoms such as headache when reading, working at a PC-screen and participating in everyday activities are reduced (Table 1).

Another hypothesis was that patients achieved improvements in visual spatial integration. To be aware of our own location in space, we need to be spatially aware of surrounding objects and their relations to us, including movements and associated speeds. Visual spatial integration is an important function in understanding the surrounding world and demands intensive visual and perceptual cognitive processing (33). In some patients, severe vision problems prevent participation in, or benefitting from, other relevant rehabilitation, and therefore vision problems are important to treat.

Interactions between brain, body and extra personal space may be crucial to enhance integration of internal and external cognitive components by mechanisms of neural plasticity. Furthermore our current

results may be augmented, for example by the use of antioxidants to encounter an increase of reactive oxygen species and neuroinflammation (37-38).

We believe that our current results support that vision therapy increased visual awareness, and thus patients experienced less dizziness and motion sickness, and furthermore achieved better awareness, thereby increasing safety in traffic and in general outdoor activities.

Conclusions

The study objective was to investigate if vision therapy, based on binocular vision and ocular motility training in mTBI patients with chronic PCS, improves performances in visually demanding tasks and in overall quality of life. Thus, the investigation was focused on improving patients' visual endurance, peripheral attention and their experience of being able to solve important everyday tasks.

The results of our study are more positive than we anticipated, and we observed progress in all tests and surveys. None of the significant results indicated a worsening of a patient's health condition, thus the vision therapy had no adverse effect. The results therefore suggest that vision therapy for mTBI patients with PCS may lead to significant improvements in quality of life (34). Further research in this area will be needed to verify our results, as well as to investigate whether our results are long-term sustainable.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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