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# THE NECESSITY TO CONSIDER VISUAL DYSFUNCTIONS AFTER ACQUIRED BRAIN INJURY

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# THESIS FOR DOCTORAL DEGREE (PhD)

By

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To my four-leaf clover:

To my patients for teaching me perspectives of life

To my team at Huddinge for support and comradeship

To Inger Grönberg for always being there

And to my husband, Claes-Henric Berthold, for love.

## POPULAR SCIENCE SUMMARY OF THE THESIS

The brain receives its information concerning the outside world from our senses: vision, hearing, smell, taste and sensation. Vision is the dominant sense in man and the basis for important functions such as reading, avoiding obstacles, detecting danger, or being able to drive a car or ride a bicycle. Both directing the gaze and interpret visual information are complicated processes involving widespread networks in the brain, and thereby easily injured in connection with an acquired brain injury, ABI. The impact of an ABI can be divided into damage directly to the flow of visual information, such as loss of visual field or glare, or damage to the eye motor system, making it difficult to direct the gaze. This doctoral dissertation has focused on detecting and defining different types of visual deficits after an ABI, as well as evaluate vision rehabilitation. The patients who participated had suffered moderate to severe ABI, in most cases caused by stroke, and were 18-67 years old.

In the first study 170 patients responded to a structured interview intended to define whether there was a visual impact and, if so, the type of symptom. More than half of the patients experienced a change in vision. This result was consistent with other studies. The most common problems were the effect on reading, 53%, glare, 35%, and blurred vision, 35%. One tenth of the patients did not experience any change in vision but answered yes to 4–9 of the questions about visual symptoms. It seems that sometimes it is difficult to determine whether a problem is due to changes in vision or not. However, if the patients are posed more specific questions about their situation, the difficulties are revealed.

In the second study 123 patients were examined concerning if increased vision problems were associated with other common and severe symptoms after an ABI such as fatigue, anxiety and depression. The study revealed a correlation between medium to severe fatigue and increasing visual problems, but no such correlation was found with anxiety or depression.

In the third study 73 patients were interviewed concerning visual changes and were examined by an optometrist. Both types of assessments showed high levels of vision deficits in accordance with the first study. The most common oculomotor deficits found were problems in adjusting the gaze or shifting a clear and steady gaze between near and far. These symptoms are difficult to diagnose in a regular medical examination. Thus, a vision specialist examination is needed. The conclusion of the study was that both subjective and objective assessments are required for a good quality vision examination.

In the fourth study 48 patients with ABI received visual rehabilitation and, compared to a control group with 41 patients, there was a statistically significant improvement in vergence abilities. The control group also showed some improvement, but except for fusion at distance, the changes was not statistically significant.

## ABSTRACT

Visual information is processed in wide and extensive networks in the brain, and forms part of executive functions, emotions and memories. An acquired brain injury (ABI) often brings about a disruption of these networks and around half of the patients develop visual dysfunctions. Due to these injuries, patients may have a diminished ability to handle an environment full of impressions, to react quickly to danger, or they develop impaired reading-social- or working abilities. Despite these common effects, visual dysfunctions have not been central in neurorehabilitation. The purpose of this thesis was to examine the occurrence of visual dysfunctions after ABI as well as evaluate vision therapy and discuss its effect on neurorehabilitation. All patients included in the studies suffered from medium to severe ABI.

In study I the frequency and type of visual deficits were examined. In study II visual dysfunction and their association with fatigue, anxiety or depression were examined. In study III, two different types of subjective and one objective assessment of visual dysfunctions were undertaken in order to evaluate if these assessments correlated or supplemented each other. In study IV the effect of vision therapy (VT) of vergence dysfunctions was examined.

*Results:* In study I, the answers of 170 patients to a questionnaire, Visual Interview (VI), revealed that half of the patients experienced visual changes, mostly reading disorder (53 %), followed by blurred vision and glare (both symptoms 35%). A fourth of the patients had visual field disorders and a fifth suffered from double vision. Two-tenths of the patients, who did not experience any vision change, answered “yes” 4–9 times to specific questions concerning visual dysfunctions.

In study II, with 123 patients included, an association between increased visual dysfunctions and medium to severe fatigue was found. However, there was no such correlation found between increased visual dysfunctions and anxiety or depression.

In study III 73 patients answered two questionnaires, VI, and Convergence Insufficiency Symptom Survey (CISS) and underwent a visual examination. All three assessments showed high scores of visual dysfunctions. VI and the visual examination correlated to some extent although VI also covered activity. Two-thirds of the patients who did not report visual changes turned out to have visual dysfunctions when measured objectively.

In study IV 48 patients with ABI received visual rehabilitation and, compared to a control group with 41 patients, there was a statistically significant improvement in vergence abilities. The control group also showed some improvement, but except for fusion at distance the changes was not statistically significant.

*Conclusion:* More than half of the patients experienced visual changes after ABI, regardless of the type of examination, and some of the patients are not aware of their problems. This strongly indicates a need for visual screening as a part of a neurorehabilitation assessment. VT improved the vision function trained, but more research is needed to examine the effect on activity and participation level.

## LIST OF SCIENTIFIC PAPERS

- I. Berthold-Lindstedt M, Ygge J, Borg K (2017): Visual dysfunction is underestimated in patients with acquired brain injury, J Rehabil Med 2017, doi: 10.2340/16501977-2218
- II. Berthold-Lindstedt M, Johansson J, Ygge J, Borg K (2019): Visual-related symptoms after acquired brain injury and the association with mental fatigue, anxiety and depression, J Rehabil Med 2019, doi: 10.2340/16501977-2570
- III. Berthold-Lindstedt M, Johansson J, Ygge J, Borg K (2020): How to assess visual function after acquired brain injury – Asking is not enough! Brain Behav 2020 Nov 23; e01958, doi: 10.1002/brb3.1958
- IV. Johansson J, Berthold-Lindstedt M, Ygge J, Borg K: Vision rehabilitation as part of neurorehabilitation after acquired brain injury – a clinical study in an out-patient setting. Brain inj. 2020 Dec 9;1-8, doi:10.1080/02699052.2020.1858495

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## LIST OF ABBREVIATIONS

ABI	Acquired Brain Injury
ACRM	American Congress of Rehabilitation Medicine
BI	Base In
BIV-IQ-15	Brain Injury related Vision Impairment questionnaire
BIVSS	Brain Injury Vision Symptom Survey
BO	Base Out
CI	Convergence Insufficiency
CISS	Convergence Insufficiency Symptom Survey
Cpm	cycles per minute
CVQS	Cerebral Vision Screening Questionnaire
D	Diopter
DAI	Diffuse Axonal Injury
DSI	Dual sensory impairment
EMDR	Eye Movement Desensitization and Reprocessing
GOSE	Glasgow Outcome Scale Extended
HADS	Hospital Depression and Anxiety Scale
HADS-A	Hospital Depression and Anxiety Scale- Anxiety section
HADS-D	Hospital Depression and Anxiety Scale- Depression section
ICF	Classification of Functioning, Disability and Health
MFS	Mental Fatigue Scale
mTBI	Mild Traumatic Brain Injury
NFV	Negative (divergent) Fusional Vergence
Pd	Prismdiopter
PFV	Positive (convergent) Fusional Vergence
PTSD	Post-Traumatic Stress Disorder
Q	Question
QoL	Quality-of-life
RCT	Randomized Controlled Trial
RM	Rehabilitation Medicine
SAH	Subarachnoid Hemorrhage

SC	Superior colliculus
SPSS	Statistical Package for the Social Sciences
TBI	Traumatic Brain Injury
VFD	Visual Field Deficit
VI	Vision Interview
VISA	Vision Impairment Screening Assessment,
VT	Vision Therapy

# **1 INTRODUCTION**

Vision is so taken for granted, it's just there, but at the same time, extremely complicated. Vision guides movements and is fundamental to social behavior and emotions. Vision forms part of our thoughts, memories and dreams. Because of this overwhelming, ongoing input, and its vulnerability to injury, visual function ought to constitute an important factor in brain injury rehabilitation. My hope is that this doctoral dissertation will contribute to such a development.

## **1.1 ACQUIRED BRAIN INJURY**

Acquired brain injury (ABI) affects approximately 40,000 people in Sweden each year and often leads to lifelong disability. Of this total, 25,000 people are affected by stroke (1) and 15,000 by traumatic brain injury (TBI) (2). Four other less common diagnoses are relevant in neurorehabilitation: subarachnoid hemorrhage (SAH), anoxic injuries, encephalitis, and brain tumors.

## **1.2 INJURY MECHANISMS IN ABI**

ABI affects the brain's communication capacity by distorting neural networks. However, the injury mechanism differs in different diagnoses. Stroke is caused by an obstruction or bleeding in a blood vessel. The primary injury gives rise to a secondary reaction, leading to increased cell death and oedema (3). TBI is caused by trauma to the head, such as a fall, assault, or road accident. The injury can be both focal and diffuse. Damage to the white matter, diffuse axonal injury, DAI, is the main reason for chronic impairments after a TBI (4-6). SAH results in the risk of acutely raised pressure in the brain and encephalitis can lead to both necrotic injuries and secondary damage due to immune reactions.

ABI activates the brain's immune system through microglia. These immune reactions are extremely complicated and mostly unknown (7). They can be protective or lead to the destruction of brain tissue. The reaction of the immune system of the brain after injury/illness is a growing area of research and may in the future contribute to the development of new strategies for treating ABI (7, 8).

## **1.3 VISION AND THE BRAIN**

All information about the outside world enters the brain via our sensory systems: vision, hearing, smell, taste and sensation, and in humans, vision is the dominant sensory system (9, 10). Visual impressions arise from reflected light from the environment which is imaged optically in the eye. Processing visual information involves widely spread networks and several areas of the brain (11). Through this process, information about objects, people and their spatial relationships is acquired. The information is used in different ways, to enable the brain to plan movements or other executive functions, form thoughts, or give rise to emotions. It is an ongoing feed-forward and feedback system, and is also connected to memories and other cognitive processes for more complex planned actions (12).

In the next part of this chapter the intention is to provide an overview of the anatomy and the sensory and motor features of visual function.

#### **1.4 THE SENSORY-MOTOR COOPERATION FOR VISUAL PROCESSING**

The cooperation between visual input and the oculomotor system enables processing of visual impressions. These systems function and cooperate continuously to make it possible to direct the gaze to objects of importance, interpret visual impressions and connect them to higher cognitive, emotional and executive functions.

#### **1.5 IMPORTANT CONCEPTS OF SENSORY INPUT IN VISION**

- *Visual acuity* denotes the eye's ability to form a sharp picture on the fovea, i.e. the central part of the retina, and the ability of the eye to resolve details. Changes in the transparent media of the eye, its refractive properties, can be remedied by spectacles (13).
- *Visual field*: The visual field of humans is 170 degrees. The overlapping part, as seen by both eyes, is about 120 degrees (14). All information from the left vision field goes to the right side of the brain and vice versa. Lesions in the retina or along the visual pathways may cause loss of sensitivity in the visual field.
- *Contrast sensitivity*: Contrast sensitivity refers to the ability to discriminate differences in brightness (13). In dimmer light, people or objects may become difficult to detect. When assessing visual acuity, high contrast vision charts are often used so that low contrast sensitivity may go undetected (12). Refractive errors, eye diseases or lesions along the visual pathways may cause reduced contrast sensitivity.
- *Stereopsis*: The ability to analyze the three-dimensional world is of fundamental importance in all visual activities. Since the eyes are separated laterally, each eye provides a slightly different view of an observed object. This difference gives rise to depth perception, or stereopsis. (13). Issues concerning visual acuity, major visual field deficits or oculomotor functions may cause problems with depth perception, asthenopic symptoms or double vision.

#### **1.6 IMPORTANT CONCEPTS OF OCULOMOTOR FUNCTION**

The oculomotor system has three purposes

- stabilizing the gaze
- control of gaze eye movements
- obtaining vergence eye movements

Oculomotor activities depend on complex and cooperating networks present in large parts of the cerebral cortex, the basal ganglia, the cerebellum, and the brain stem. The superior colliculus, SC, is an important hub in these interactions (12).

### **1.6.1 Stabilization of the gaze**

Visual fixation is essential for the ability to keep the gaze steady, so that the image of an object is held firmly on the central part of the retina, the fovea. Failure to maintain visual fixation will cause a decline in visual acuity, for example nystagmus may cause a marked decline in visual acuity and a sense of movement in the visual percept, oscillopsia.

The stabilization of the gaze during brief head movements is secured by the vestibulo-ocular-reflex (VOR). VOR is a combination of networks connecting cerebellum, nuclei in the brain stem and the balance organs (12). Issues concerning the VOR function may cause blurred vision or a sense of movement in the visual percept, self-motion.

### **1.6.2 Control of gaze eye movements**

When the eyes move in the same direction, i.e., conjugate movements, the purpose is to maintain the image of a moving object on the fovea, that is, to track a moving object with the eyes. The eye movements providing this consist of pursuit movements, for following objects, and saccades for fast redirection. The purpose of pursuit movements is to maintain the image of a moving object on the fovea, that is, to track a moving object with the eyes.

Pursuit movements also maintain the image on the fovea during self-motion.

Saccades bring the image of an object to the fovea, e.g., when an object of interest appears in the visual field the eyes are redirected with a saccade to point at the object. There are different subtypes of saccadic movements: reflexive, voluntary, anti, memory guided and self-paced saccades (15). Reflexive saccades are a direct response to a stimulus through redirection of the gaze, anti-saccades involve the ability to voluntarily direct the gaze contralaterally from the stimuli and memory saccades direct the gaze to something known to have been there earlier. When reading, small saccades enable progression through a text and change of line. In a medical examination one often just assesses the self-paced saccades.

### **1.6.3 Vergence**

Vergence eye movements, i.e., disconjugate movements, is when the eyes move in opposite directions. The purpose is to hold the image on the fovea in both eyes simultaneously when viewing objects at different distances. Vergence eye movements comprise convergence, vergence facility and fusion vergence, and are essential for maintaining binocular vision close up or far away. Issues concerning vergence may cause asthenopic symptoms, blurred or double vision, and difficulties in shifting a sharp focus in different directions.(13). If the gaze falls out of focus, fusion vergence redirects the gaze centrally.

## **1.7 VISUAL PATHWAYS**

### **1.7.1 The Retina**

Visual processing starts in the retina. Light passes through the different media of the eye and reaches the retina where two types of photoreceptors are present, rods and cones. Rods are sensitive to weaker light (16) and more frequent in the periphery (16). Cones are sensitive to bright light and colors, with highest density in the fovea, and this concentration

of cones enables high resolution of details. The fovea corresponds to only about 1,5 degrees of the central visual field; hence eye movements are needed to hold the image of an object in the fovea in tasks that require detailed resolution, such as recognition and reading.

There are several layers of neurons in the retina in which a primary processing occurs. Axons from the approximately one million retinal ganglion cells form the optic nerve (13). The two optic nerves meet at the optic chiasm. At this point nerve fibers partly cross over; nerve fibers originating from the nasal retina (corresponding to the temporal visual field) cross over while fibers from the temporal retina remain on the original side. This reorganization of nerve fibers is part of the visual brain's mapping of overlapping visual fields and is the basis for binocular vision.

### **1.7.2 Pathways after the optic chiasm**

The part of the vision tract after the optic chiasm, the optic tract, is divided into two different pathways. Ninety per cent of the nerve fibers end up in the primary visual cortex, V1. It runs through the lateral geniculate nucleus, a part of the thalamus, and then through the temporal, parietal and occipital lobes. This pathway transmits information for interpretation to networks dealing with pattern, color and motion recognition and forward information to other higher cognitive areas (9).

Ten percent of the fibers enter the superior colliculus (SC) in the brain stem, proceed to the pulvinar nucleus of the thalamus and to the visual areas in the parietal and temporal lobes forming parts of feed-forward and feedback networks for orientation of the gaze (9). The two different pathways are constantly communicating (17).

## **1.8 VISUAL PROCESSING**

Visual processing was originally described as a hierarchic process (18). Currently this idea has been extended to embrace a more interconnected system of networks with both hierarchical and multiple parallel pathways (9, 19). The same information is transformed in parallel to different parts of the brain with different endpoints that act in various behavior programs.

Two models describing the brain's processing of visual impressions are described below

### **1.8.1 The ventral and dorsal stream model**

In 1982 Ungerleiden & Mishkin (18) described a visual process divided into a ventral and dorsal pathway. Both pathways have their origins in the occipital lobe, the ventral pathway leading to the inferior temporal lobe, and a dorsal pathway, leading to the parietal lobe. The ventral pathway is crucial for identifying objects and the dorsal pathway for spatial relationships. The two pathways are described as answering respectively to the questions "What" and "Where" (19). The model has been determined anatomically (20), and is commonly accepted. Milner and Goodale (19) have developed the model further. They suggested a more executive interpretation and change "What" and "Where" to "What" and

“How”. They described the dorsal pathway as intended for action and therefore dependent on information about object recognition which involves a close connection between the two pathways (21). Lauwereyns (22) describes a further extension of the model, the dorsal stream reaches the dorsolateral prefrontal cortex, and the ventral stream reaches the ventrolateral prefrontal cortex. These connections constitute the feedback and feed-forward systems required, for example, when reaching for objects, moving or avoiding danger (23).

### **1.8.2 The bi-model of visual processing**

A bi-model of the visual process was presented by Padula et al 2017 (23), based on experiences from TBI research. Two different connecting processes were described, the ambient process and the focal process. The ambient process develops in early childhood and arises from the brainstem and cerebellum. It is “gravity specific” and connected to the proprioceptive input from what the authors define as the “base of support” (BOS). Eye motor control adds to this process, establishing a platform for vision that is preconscious and matches information from BOS. The ambient process maintains balance and a sharp gaze. To do so it responds dynamically to movements.

The focal process provides information for attention, higher cognitive processing, executive functions and movement planning, with networks in multiple locations.

The two processes are connected in the SC, which matches the information from BOS with spatial information from the focal process. This information goes to the binocular coordination cells “to provide a spatial context for the fusion process and ultimately binocularity”. By maintaining the balance, the ambient process liberates the focal process, to concentrate freely on items of interest (23). In connection with TBI or other brain injuries a disruption of the balance between the two processes, leads to a disturbed feed-forward system which entails difficulty in adapting to environmental changes and gives ocular motor dysfunctions. Padula et al. (23) defined visual rehabilitation as a treatment to re-establish the balance between the two processes.

## **1.9 VISUAL ATTENTION**

The stream of visual impressions is processed unconsciously. The total visual input is too extensive for the brain to interpret. Visual attention refers to the process of simplifying, concentrating and selecting impressions which enables the brain to interpret the environment. In doing so visual attention becomes an important part in behavior programs, facilitating activity. The visual attention is both unconscious and goal directed (10), or is described in relation to demands: focused, sustained, selective, alternating and divided attention (24). This modification of visual input from visual attention, appears both subcortically and at all different levels of the visual cortex (10).

Around 40–60% of ABI patients displayed attention deficits after ABI (25, 26). Ponsford et al. (27) carried out a follow-up of TBI patients 10 years after injury and found that half of the patients still suffered from attention deficits.

## 1.10 VISUAL SYMPTOMS AFTER ABI AND ITS IMPACT ON QUALITY OF LIFE

Visual processing is widely distributed in the brain which entails that an ABI results in high levels of visual dysfunctions (17). The reports show a frequency of visual dysfunctions from 50–70%. Most common are reduced visual acuity, visual field defects (VFD), double vision, photophobia, blurred vision, and oculomotor disturbances (28-34). (Oculomotor function is here defined as convergence, smooth pursuits movements, saccades, fusion, vergence facility and VOR) (33, 35-37). For a description of the symptoms see table 1.

**Table 1.** Visual symptoms after ABI

Visual functions	Typical symptoms after ABI
<b>Visual acuity</b>	Manifest or intermittent blurred. Headache. Fatigue.
<b>Visual Field Defect</b>	Difficulties with visual overview and to move freely. Risk of fall. Reading difficulties. Danger in traffic situations.
<b>Convergence, Vergence facility</b>	Intermittent double vision close up, eye strain, headaches. Delayed clarity of vision if focus shifts between near and far. Tired after reading or doing close work.
<b>Fusion vergence</b>	Intermittently blurred or double vision, floating words, Apparent movement of objects. Difficulties in maintaining eye contact, eye strain, headache.
<b>VOR</b>	Balance problems and insecurity. Inactivity, decreased physical activity, neck pain.
<b>Saccades</b>	Lower speed of overview and reaction to objects or people in the environment. Reading difficulties.
<b>Double vision</b>	Difficulties to move around in and to interpret the environment. Reading difficulties. Headache.
<b>Glare</b>	Avoidance of bright environments, difficulties in dark environments, driving, reading, close up work.
<b>Hypersensitivity</b>	Isolation. Avoidance of social activities and environments with lots of people and impressions.

Rowe et al. (38) performed a qualitative study in order to investigate the impact of visual dysfunctions after stroke, most commonly VFD. The impact on everyday life was loss of confidence, panic attacks, fear of falling, being startled by sudden appearances from the blind side, loss of driving license, increased bumps/collisions, assistance required outdoors, inability to pursue hobbies, fear of dark evenings/nights (which was worse in wintertime),

fear of crowded places, and misjudgments of distances. A study by Smith et al. (39) found difficulties in reading, increased risk of falls and inability to work and drive as a consequence of visual dysfunctions (39). Gall et al. (40) found mental distress in 25% of 122 patients with VFD. These findings indicate that visual dysfunctions have a considerable impact on everyday activities (38, 39).

### **1.11 MODELS FOR ASSESSMENT OF VISUAL IMPAIRMENT AFTER ABI**

Neurorehabilitation has no common model for assessing visual dysfunction. Furthermore, there is no consensus on what symptoms need referral to a vision specialist. Vision specialists, e.g., ophthalmologists, opticians, orthoptists and optometrists, have mainly been active concerning illnesses or trauma to the eye, and rehabilitation specialists have not been aware of the complicated impact of vision deficits on rehabilitation. Rowe et al (41), interviewed professionals active in stroke rehabilitation at centers with high-quality vision care. They identified success factors for the provision of good vision rehabilitation. The factors were: good communication between vision specialist and rehabilitation professions, “open access” for referrals by every active team member, use of standardized screening forms, information to the patients both written and oral as well as support for the visual aspect of rehabilitation by the physicians.

During recent years several different screening methods and proposals for cooperation between vision and rehabilitation specialist have been suggested by different authors.

### **1.12 THE ACRM MODEL (42)**

In 2016 the American Congress of Rehabilitation Medicine (ACRM), drew up a structured model for joint visual assessment and rehabilitation. Roberts et al. (42), summarized knowledge about vision and ABI in the article “A conceptual model for vision rehabilitation”. The starting point was that although visual impairment is common and of fundamental importance for rehabilitation, there is no agreement upon training methods to offer to the patients. They found a need to provide a concept for assessment and rehabilitation to fill this gap. They began by defining certain terms to create a standard vocabulary:

- *Visual function* is defined as the function of the eye and lower-order cerebral mechanism.
- *Visual impairment* is defined as injuries to these areas.
- *Functional vision* is defined as the function of higher-order cerebral mechanisms.
- *Visual dysfunction* is defined as injuries to these areas.

Finally, they define tasks for the two different professions – visual specialists and non-visual specialists – in the rehabilitation team. Visual specialists have mainly acted as consultants. The ACRM model makes them part of the rehabilitation team because they consider the inclusion of a vision specialist is a postulate for high-quality care. The visual specialists are mainly active in assessing the visual impairment level. The neurorehabilitation team, is mainly active in assessing visual dysfunction, analyzing patients with regard to activity level.

After assessing and integrating the results, a treatment plan can be established. After treatment, an evaluation of changes in function, activity and quality of life is made. The results of the evaluation are applied in future assessments and a circle of learning in this new area of rehabilitation is formed. ACRM points out that the combination of the two specialties may lead to research in the area and will eventually offer recommendations for visual rehabilitation which are based on this shared experience (42).

### **1.12.1 Additional assessment models**

There are other studies valuating different ways of assessing visual dysfunctions. Neumann et al (43) validated the Cerebral Vision Screening Questionnaire, CVQS. The questionnaire has nine items about vision deficits. It had high sensitivity and specificity and took about ten minutes to perform. Laukkanen et al (44) have developed a multidimensional scale, Brain Injury Vision Symptom Survey, BIVSS, mostly covering the functional level but also some questions about activity. The subheadings are visual acuity, visual comfort, double vision, light sensitivity, dry eyes, stereovision, visual field and reading. Hepworth et al (45) have constructed the Brain Injury related Vision Impairment questionnaire, BIV-IQ-15, with 15 items. This scale focuses more on how vision deficits interfere with activities. Vision Impairment Screening Assessment, VISA (46), is a structured way to assess visual dysfunctions, and consists of case history, clinical observations of visual signs, visual acuity, eye alignment position, assessment of eye movement, VFD, visual neglect, functional vision and reading. In the recommendations for a specialist vision examination, all the above is included in addition to a binocular vision assessment and a quality-of-life questionnaire. The ability to reach an agreement of what screening instruments to be used in research and clinical practice, would be a step forward in the development of vision rehabilitation.

## **1.13 VISUAL REHABILITATION**

### **1.13.1 Rehabilitation medicine (RM)**

RM perform the rehabilitation of patients suffering from long-term disabilities after injury or disease. A sub-specialty of RM is neurorehabilitation.

Neurorehabilitation can be separated into three main components which run simultaneously.

- *Functional training* to regain brain control by refining or creating new networks through structured rehabilitation methods.
- *Strategy training* to teach the patient to support the brain by internal or external strategies such as memory aids, resource management to cope more, planning activity level for greater endurance, or the use of different aids to facilitate everyday activities.
- *Coping with the consequences of the injury or illness* to provide support for the patients in the grieving process and to help them move forward in life. Here,

information about the injury and its effects is a way of strengthening self-confidence and regaining one's self-image.

ABI has a complex impact on emotion, cognition, physical function, language and speech. The assessment must be broad as various injuries impact different aspects of human life. In order to define disability after ABI, the International Classification of Functioning, Disability and Health (ICF) is used in rehabilitation medicine (47). The ICF is divided into three main domains: bodily function and structure, activity and social interaction, environmental and personal factors. Vision dysfunction is covered under Body Structure, chapter 1 and 2 (47).

There are few studies concerning visual rehabilitation after ABI but there is extensive and long-standing clinical experience of vision rehabilitation among vision professionals, mainly optometrists. The technique for training oculomotor disorders is based on this experience (48).

### **1.13.2 Visual rehabilitation of visual field deficit (VFD)**

VFD is a common symptom, 20%–57%, (31, 49) and is mostly an effect after stroke. It has impact on driving, mobility, reading and everyday activities (50). There are three different methods of rehabilitation for VFD: restitution, compensation and substitution. Restitution therapy involves repetitive stimulation of the border zone of the VFD to restore this part of the visual field. Compensatory therapy involves exercise to achieve automatic eye movements in the injured visual field to improve the ability to scan the environment and facilitate reading. Substitution is the use of devices or extraneous modifications to cope with VFD. The Cochrane Library published two reports in 2011 and 2019 (51, 52) concerning visual rehabilitation after VFD, in which the three different types of rehabilitation were analyzed. The studies included in the review reported variations in terms of treatment models and intensity. The Cochrane Library report (52) found only limited low-quality evidence of the effect of compensatory training and found no generalized conclusion concerning the effects of restitution or substitution. Other reviews (53, 54) clearly recommend compensatory therapy. In a review by Hanna and Rowe 2017 (55), visual scanning was recommended for both visual neglect and VFD. The same conclusion was drawn in a review by Berger et al. in 2016 (54) and also by Rowe et al. in a study published in 2019 (53).

Compensatory therapy involves top-down training and one limitation is that most visual searching entails automatic unconscious processes. A few studies (56, 57) used a bottom-up profile for visual training with an audio-visual approach and found stronger outcomes for reading and exploration after training with this method than with top-down strategies. However, these studies included few patients.

### **1.13.3 Visual rehabilitation of oculomotor disorders**

Rowe et al. (58) assessed the effectiveness of any intervention for oculomotor disorders due to ABI. They found only five relevant studies and of these only one, by Thiagarajan and Ciuffreda 2014 (59), that focused on visual rehabilitation. Another review by Hanna and

Rowe (55) did not find any studies concerning oculomotor training after stroke. However, the authors recommended different treatments for double vision: occlusion, prism, surgery and botulinum toxin. They comment that these are clinically established treatments with known good results and there is no need of clinical trials. In 2018 Simpson-Jones et al. (60), reviewed the literature regarding visual interventions after mild TBI. Eight studies dealt with visual rehabilitation. Five of these studies included fewer than 15 patients. The other three involved 40, 95 and 137 patients respectively. None of them had a randomized controlled trial (RCT) design. All studies were performed by optometrists and all reported improvement in oculomotor function. The authors (60) conclude that interventions for vision rehabilitation and optical devices ought to be tested (60) in patients after TBI.

It appears that there is evidence that oculomotor training has an effect on the ocular movement itself (37, 59, 61), but the impact on visual processing and everyday activities is still unexplored.

#### **1.13.4 Rehabilitation of vestibulo-ocular reflex (VOR) dysfunction**

VOR is often affected after ABI leading to symptoms like vertigo, nausea, visual motion sensitivity (62) and difficulties in stabilizing the gaze. There are several physiotherapeutic methods for regaining balance, but few combine vision and balance. Schow et al. (63) evaluated a 4-month program for group rehabilitation of balance dysfunction after stroke. Visual therapy was combined with balance therapy. Statistically significant improvements were found in stereopsis, vergence, saccadic movements, burden of visual symptoms, balance, gait speed, fatigue and health-related quality of life. In a 6-month follow-up all improvements were stable and the proportion of patients who could return to work rose from 23% to 60% (63).

#### **1.13.5 Reading difficulties**

One of the most serious effects of visual dysfunction is its impact on reading capacity. Reading is a complex activity that has impact on daily life and reading difficulties are common after ABI (64). The incidence varies between 20% to 80%, commonly at a level higher than 50% (31, 32, 65-68). Reading ability plays a central role for communication skills by cell phone or computer and is required in nearly all types of work. In rehabilitation medicine reading difficulties are thereby of high importance.

The visual dysfunctions underlying reading insufficiency are VFD, oculomotor disorder, (such as saccade insufficiency and fusion), visuospatial disorder, visual neglect, altered contrast sensitivity and/or color perception (69). Thiagarajan et al. (64) summarizes the demands of the oculomotor system as the ability to perform fixation and precise, rhythmical saccadic eye movements. But reading also holds different cognitive demands. Schuett (69) describes it as dependent on visual abilities, attentional processes, eye movement control and intact language functions. All these functions, motor and cognitive, need to be synchronized with each other and be sustainable over time (64).

VFD influences reading in many ways. The beginning or the end of the line disappears, the prompts to switch line and form saccadic movements across the page are disturbed and the oculomotor reading strategy falls apart (69). It ends up in a slow reading with a disorganized eye-movement pattern. Nearly the same problems have been assessed after TBI; with loss of pace, difficulties in switching line and line skipping (37). Limited studies of both training oculomotor movements in reading (64) and rehabilitation using reading strategies have, however, shown improvement (70).

Another study by Schuett et al (67) examined whether explorative training after VFD could be generalize to reading. They found no generalization and concluded that reading must be trained by reading. Although there is a difference between reading disturbances due to oculomotor dysfunctions or cognitive issues, many of the patients suffer from both.

#### **1.14 SUMMARY OF VISION REHABILITATION**

- Function:
  - Vision dysfunctions are common after ABI
  - Compensation therapy for VFD is recommended and may be enhanced by bottom-up methods
  - Vision Therapy improves oculomotor function
- Activity and participation interaction:
  - Vision dysfunctions hamper and reduce the level of activity and social interaction.
  - There are few research reports regarding the effect of vision therapy on activity and participation level.
  - Reading disturbances are common after ABI and there are positive reports of reading improvements after VT.



## 2 RESEARCH AIMS

*General aim:* To investigate the occurrence of visual dysfunctions in patients with medium to severe ABI and evaluate different assessment models to identify these dysfunctions for further use in neurorehabilitation.

- I. To analyze the frequency and type of self-reported visual changes in an out-patient group with medium to severe ABI.
- II. To explore whether increased experience of visual dysfunctions in ABI patients is associated with self-perceived mental fatigue, anxiety and/or depression.
- III. To estimate the frequency and type of visual dysfunctions objectively measured in an out-patient group with medium to severe ABI.  
To evaluate the correlation between subjectively reported visual changes and objectively measured visual dysfunctions.  
To evaluate if a questionnaire concerning reading and near work, CISS, would give more information than just VI.
- IV. To investigate the effects of vision therapy after ABI.



### 3 MATERIALS AND METHODS

For overview of material and methods see Table 2

**Table 2.** Overview of the studies, design, data collection, statistics.

Study	I	II	III	IV
<b>Study design</b>	Descriptive	Cross-sectional	Cross-sectional	Observational
<b>Participants:</b>				
<i>Number</i>	170	123	73	48 intervention/41control
<i>Women/men</i>	79/91	56/67	31/42	19/29, 16/25
<i>Age 18-68, Mean</i>	47 years	47 years	50 years	49,5/52 years
<b>Data collection from medical records</b>	Yes	Yes	Yes	Yes
<b>Questionnaires</b>	VI	VI, HADS, MFS	VI, CISS	VI, CISS
<b>Objective measurement</b>	No	No	Yes	Yes
<b>Statistical methods</b>	Descriptive statistics Chi-square test Fisher's exact test	Descriptive statistics Mann-Whitney <i>U</i> -test Kruskal-Wallis test Chi-square test Fisher's exact test Binary logistic regression	Descriptive statistics Chi-square test Non-parametric statistic	Descriptive statistics Chi-square test Fisher's exact test Wilcoxon signed rank or Student's t-test

#### 3.1 PARTICIPATIONS AND STUDY DESIGNS

In all four studies the patients were recruited from the out-patient day-care units of the Department of Rehabilitation Medicine, at Danderyd University Hospital, Stockholm, Sweden. The day-care units offer team-based rehabilitation. The rehabilitation program is based on the assessment of cognitive, motor and emotional changes after ABI. The patients were 18 – 68 years old and the main diagnoses were stroke or TBI. Most patients had a

moderate to severe brain injury using the definition of Glasgow Outcome Scale Extended, GOSE (71).

***Inclusion criteria:***

- All patients diagnosed with ABI and admitted to the day-care unit.

***Exclusion criteria:***

- Patients with severe aphasia or great difficulties in understanding Swedish.
- The assessment discovered that other diagnoses than ABI were causing the symptoms.
- The patient did not fill out the questionnaires or did not complete the assessment.
- Patients who did not agree to participate.

**3.2 PROCEDURE:**

**3.2.1 Study I**

170 patients were included, 79 women and 91 men. Most patients suffered from moderate to severe ABI using the definition from GOSE see table 3. The most common diagnoses were stroke, 45%, and TBI, 22%, see table 4. The mean age was 47 years, for the division between age groups see table 4. There were 26 excluded patients: due to severe aphasia (n = 1), VI missed at admission (n = 14), symptoms not primarily caused by ABI (n = 4), direct entry to the rehabilitation program based on an assessment elsewhere (n = 3), and interview interrupted or refused by patient (n = 4).

The Vision Interview, VI, (72, 73) was performed by a physician on admission. Demographic information from the medical records including diagnosis, age, sex, time since onset of injury/illness was collected and analyzed in comparison with the described visual changes in the VI.

**Table 3.** Degree of severity of the brain injury. Published with consent of Journal of Rehabilitation Medicine

	GOSE 4	GOSE 5	GOSE 6	GOSE 7	Missed
Patients, n (%)	10 (6)	90 (53)	62 (37)	6 (4)	2 (1)

4 = upper severe disability, 5 = lower moderate disability, 6 = upper moderate disability,

7 = lower good recovery.

**3.2.2 Study II**

The study included 123 patients with medium to severe ABI, 56 women and 67 men. The diagnoses varied, most frequent were stroke, 46 %, and TBI, 27%. For demographic data see table 5. Of the 165 patients initially included 42 were excluded due to: severe aphasia (n = 5),

the patient did not complete the admission ( $n = 7$ ), symptoms not primarily caused by ABI ( $n = 5$ ) or the patients did not fill out all three questionnaires ( $n = 25$ ).

**Table 4.** Demographics of patients in study I. Published with permission of Journal of Rehabilitation Medicine

	Sex			Age group, years		
	Total <i>n</i>	Women <i>n</i>	Men <i>n</i>	18 – 35 <i>n</i>	36 – 55 <i>n</i>	55 – 68 <i>n</i>
<b>Stroke</b>	77	27	50	9	35	33
<b>TBI</b>	37	15	22	13	14	10
<b>SAH</b>	15	9	6	0	9	6
<b>Infection</b>	10	7	3	3	2	5
<b>Tumor</b>	11	7	4	3	6	2
<b>Anoxia</b>	7	2	5	3	2	2
<b>Other*</b>	13	12	1	4	4	5
<b>Total</b>	170	79	91	35	72	63

\*Other: different surgical interventions in the brain ( $n = 6$ ), post-radiation of tumor (1), epilepsy (1), multi-organ failure (1), NMDA encephalitis (1), sinus thrombosis (1), a. vertebral dissection (1), late effects of intracerebral hemorrhage (1); TBI: traumatic brain injury; SAH: subarachnoid hemorrhage.

The patients were interviewed by a physician using the VI. The answers to the VI were dichotomous, yes = 1 and no = 0. The outcome of VI was presented as a score, 0 – 17p, the question on whether an eye examination had been performed was excluded. On admission the patients also answered two questionnaires, Hospital Anxiety and Depression Scale (74), HADS, and Mental Fatigue Scale (75), MFS.

Demographic information from the medical records about diagnoses, age, sex, time since onset of injury/illness was compared with visual changes in VI, anxiety, depression or fatigue

as reported in HADS and MFS questionnaires. Correlation between depression, anxiety and fatigue in relation to self-reported vision symptoms was analyzed.

**Table 5.** Demographics of patients included in study II. Published with permission of Journal of Rehabilitation Medicine

Diagnosis	n	Women/Men	Mean age and standard dev. (years)	Age range (years)	Mean value time post-injury (months)	Time range post-injury (months)
<b>Stroke</b>	57	17/40	51.5 ± 10.3	21 – 65	6.1	1 – 30
<b>TBI</b>	33	14/19	39.0 ± 13.6	19 – 65	10.3	1 – 62
<b>SAH, Infection, Tumor</b>	24	19/5	47.4 ± 11.7	19 – 65	7.1	3 – 18
<b>Other</b>	9	6/3	41.7 ± 15.7	20 – 62	7.9	2 – 18
<b>Total</b>	<b>123</b>	<b>56/67</b>	<b>46.6 ± 13.0</b>	<b>19 – 65</b>	<b>7.6</b>	<b>1 – 62</b>

### 3.2.3 Study III

The study included 73 patients with moderate to severe ABI, 31 women and 42 men. The diagnoses varied, most common were stroke, 46%, and TBI, 16%. For demographic data see table 6. Of the 79 patients included originally, 6 patients were excluded: 4 because of incomplete data and 2 patients did not complete the admission, for demographics see table 6.

The patients included answered the CISS questionnaire and were assessed concerning visual deficits by an optometrist. The VI was performed by the physician. The objectively measured visual functions were visual acuity, refractive error, eye motility and eye teaming. The answers to the questionnaires and the objectively measured findings were summarized and analyzed with regard to correlations and group differences. Six patients did not possess binocular vision due to ocular health issues (n=3) and amblyopia, (n=3). Thus, objective assessment of eye teaming of these patients could not be carried out.

**Table 6.** Demographics of patients included in study III. Published with consent of Brain and Behavior

	All	Stroke	TBI	Infection	Hypoxia	Tumor	SAH	Other
	n = 73	n = 32	n = 12	n = 9	n = 6	n = 6	n = 4	n = 4
<b>Women/Men</b>	31/42	10/22	4/8	7/2	1/5	3 / 3	3/1	3/1
<b>Median age, years (min-max)</b>	50 (20-64)	51 (29-63)	35 (21-50)	50 (27-57)	53.5 (20-64)	56 (46-63)	54 (38-59)	40 (25-58)
<b>Time since injury</b>								
<b>0 – 3 months</b>	14	8	5				1	
<b>4 – 6 months</b>	21	11	4	2	2	1	1	
<b>7 – 12 months</b>	20	9	1	3	3	3		1
<b>13 – 24 months</b>	10	3	2	1	1	1	1	1
<b>&gt;24 months</b>	8	1		3		1	1	2
<b>Glasgow Outcome Scale Extended</b>								
<b>GOSE 4</b>	6	3	1	1	1			
<b>GOSE 5</b>	40	20	8		4	3	3	2
<b>GOSE 6</b>	25	9	3	8	1	3	1	
<b>GOSE 7</b>	2							2

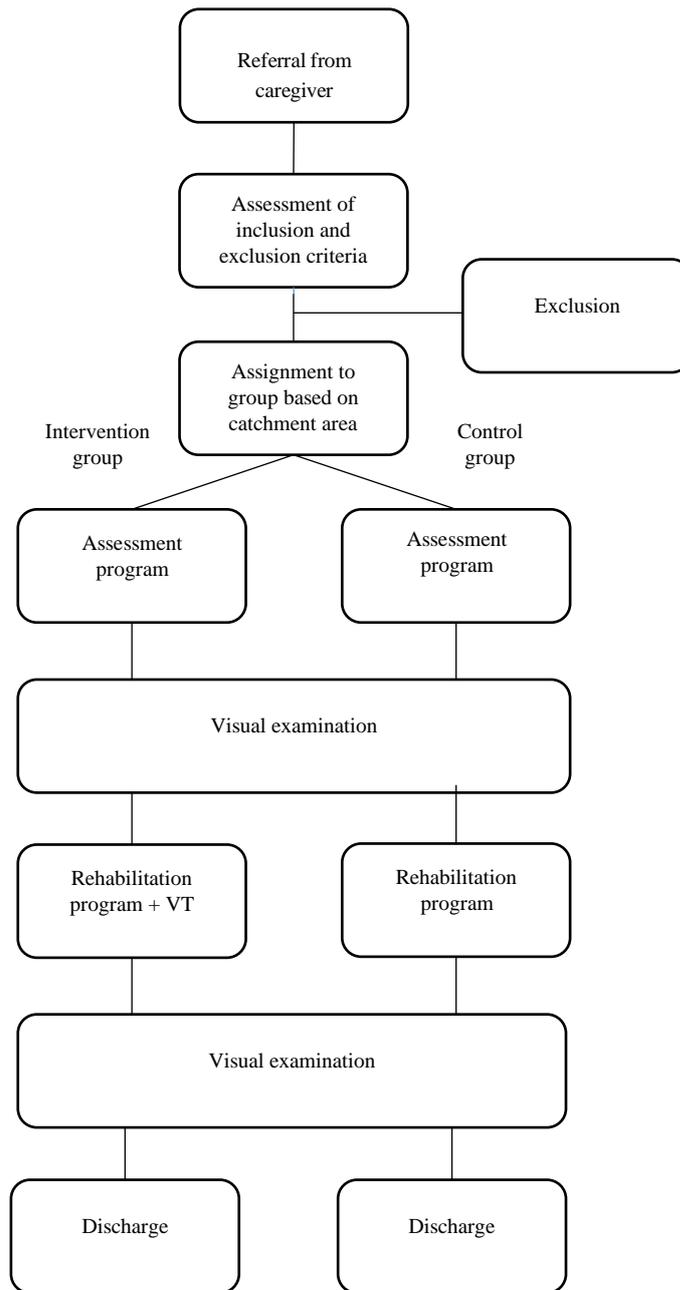
GOSE 4: Upper severe disability; GOSE 5: Low moderate disability; GOSE 6: Upper moderate disability;  
GOSE 7: Low good recovery

### 3.2.4 Study IV

The study included 89 patients with medium to severe brain injury, 48 in the intervention group (19 women and 29 men) and 41 in the control group (15 women and 25 men). In the intervention group the median age was 49.5, range 27–63, and median age in the control group 52, range 18-67. The diagnoses varied: most common were stroke, 50% of the intervention group and 66 % of the control group. For demographic see table 7. All patients in the intervention group also participated in study III. The examination found 5 in the intervention group and 8 in the control group who did not possess binocular vision and thus could not be assessed concerning eye teaming, see table 17. Finally, 43 patients remained in

the intervention group and 33 in the control group. All patients received neurorehabilitation according to individually adapted programs. The patients admitted to the intervention group received visual rehabilitation (VT) if the assessment had revealed visual dysfunction. The visual rehabilitation focused on eye teaming issues, convergence, vergence facility and fusion vergence both near and far.

The control group was only assessed but did not receive visual rehabilitation.



**Figure 1.** Flow chart of study IV, Published with permission of Taylor & Francis in Journal of Brain Injury.

Some differences, although not statistically significant, were found between the two groups regarding age, distribution of gender, diagnosis and time after injury, see table 7.

**Table 7.** Demographic data of patients in study IV, published with permission of Taylor & Francis in Journal of Brain Injury.

		Intervention group n = 48	Control group n = 41
<b>Women/Men</b>		19/29	15/25
<b>Time since injury, n (%)</b>	0 – 3 months	9 (18.8%)	2 (4.9%)
	4 – 6 months	17 (35.4%)	15 (36.6%)
	7 – 12 months	10 (20.8%)	17 (41.5%)
	13 – 24 months	7 (14.6%)	5 (12.2%)
	> 24 months	5 (10.4%)	2 (4.9%)
<b>GOSE, median (range)</b>		5 (4 – 7)	5 (4 – 6)
<b>Diagnosis, n (%)</b>	Stroke	24 (50.0%)	27 (65.9%)
	Trauma	7 (14.6%)	3 (7.3%)
	Infection, SAH, Tumor	13 (27.1%)	8 (19.5%)
	Other†	4 (8.3%)	3 (7.3%)

†Other diagnoses: hydrocephalus, arteriovenous malformation, idiopathic intracranial hypertension

All patients were assessed with regard to visual dysfunctions by an optometrist, both on admission and at discharge, and answered the CISS and VI questionnaire. The objectively measured visual functions included visual acuity, refractive error, stereovision, eye motility and eye teaming. The intervention group received vision therapy specifically targeted to the dysfunctions detected. The training was performed three times a week, a total of 60 minutes/week and carried out by an occupational therapist. The degree of difficulty of the training was adapted to the patient’s ability. When there was improvement the exercises became more demanding.

### **3.3 SCALES, QUESTIONNAIRES AND ASSESSMENTS**

#### **3.3.1 Vision interview (VI) (72, 73)**

1990, Kerkhoff et al. (72) compiled an “Interview Questionnaire” assessing visual disorders after ABI. The interview was translated into Norwegian by Wilhelmsen 2003 (73) and Jacobsson and Hamelius translated it from Norwegian to Swedish 2010 (see supplement). The Vision Interview (VI) was used in all studies. In 2015, VI was revised, and the new version was used in paper III and IV. The questionnaire is not validated, however, 2016 Neuman et al, (among whom was Kerkhoff) (43) validated the Cerebral Vision Screening Questionnaire, CVQS, (43). It contains nine questions, two of which have an a and b section (=11 questions) and takes about ten minutes to complete. VI has 10 questions identical to those of CVQS.

Study I and II: The first version of VI comprised 18 questions concerning visual changes after ABI. Two questions were more general and the other 16 addressed specific visual symptoms at both function and activity levels. The two general questions concerned experienced changes in vision after the ABI or completed eye examination since becoming ill. The specific questions concerned common visual symptoms (Q2, Q8–17), impact of visual deficits on activity (Q4–7) and reading disturbances (Q3). The answers to all questions were dichotomous, “yes” or “no” (see supplement).

Study III and IV: The revised VI now contained 20 questions and was structured for greater compliance with the ICF concept: function, activity and participation. Two questions were added, one about neck pain, and the other a Visual Analog Scale (VAS) scale in order to capture the patient’s own experience of the impact of their vision deficits on everyday life (see supplement). Completing the interview takes about 5-10 minutes.

#### **3.3.2 Hospital depression and anxiety scale (HADS) (72)**

HADS is a validated questionnaire intended to test levels of depression and anxiety. The scale is not intended for ABI and addresses psychological disturbances. It has 14 items, 7 about symptoms of depression, and 7 about anxiety. There are four-scale responses according to the severity of the symptom, 0–3. The maximum sum is 21 points for depression, HADS-D, and 21 points for anxiety, HADS-A. The total sum is interpreted on a three-level scale: no problem (0–7), some symptoms, (8–10) and finally, medical treatment required, (>10). In paper II a cut-off level of >7p was used.

#### **3.3.3 Mental Fatigue Scale (MFS) (75)**

There are several fatigue scales but MFS is aimed at patients with neurological diseases, among them TBI and stroke. It uses a multidimensional scale and includes 15 questions, of which one is analyzed separately. The total sum is graded on a four-level scale: no problem,

light fatigue, moderate fatigue and severe fatigue. In paper II a cut-off level of medium-severe fatigue. (>14.5p) was used. This level was used to catch the more severe problems.

### **3.3.4 Convergence Insufficiency Symptom Survey (CISS) (76)**

The CISS was originally introduced to detect convergence insufficiency and is directed to near work such as reading and computer use, > 20 p indicates convergence insufficiency, (CI). It is intended for ABI but has been applied for mild TBI patients (33, 61).

### **3.3.5 Glasgow Outcome Scale Extended, (GOSE) (71)**

GOSE is a valid scale for measuring the severity of a brain injury. It has 8 levels of severity: 1 = dead, 2 = vegetative state, 3 = lower severe disability, 4 = upper severe disability, 5 = lower moderate disability, 6 = upper moderate disability, 7 = lower good recovery, 8 = upper good recovery.

### **3.3.6 Objective assessment**

The objective assessment of vision deficits was made by a licensed optometrist. The assessments were conducted 1–2 weeks after admittance or, in paper IV, at discharge as well. The assessment included visual acuity, refractive error, stereovision, eye motility, and eye teaming. For types of criteria and impairment, see table 8.

**Table 8.** Visual function, impairment, diagnostic criteria

Visual function	Type of impairment	Criteria
<b>Visual acuity</b>	Uncorrected refractive error, amblyopia, damaged visual pathways	Monocular visual acuity below decimal 1.0
<b>Visual field</b>	Partial or complete loss of peripheral vision due to damaged visual pathways	As determined with standard visual field testing at the ophthalmologist's office, mainly via Humphrey Visual Field Analyzer
<b>Accommodation</b>	Defective amplitude (near point)	Accommodative amplitude (D) less than minimum expected according to the Hofstetter formula ( $15 - 1/4 \text{ age}$ )
	Infacility	<4.5 cpm with age- appropriate lens power ( $\pm 1 \text{ D}$ to $\pm 2 \text{ D}$ lens flipper)
<b>Convergence</b>	Defective near point	Near point > 10 cm
	Infacility	< 11 cpm with 3 pd BI / 12 pd BU prism flipper (pre-presbyopia, age < 40) < 7 cpm with 3 pd BI / 12 pd BU prism flipper (presbyopia, age $\geq 40$ )
<b>Fusional vergence</b>	Paper III: Below minimum expected amplitudes for break point for either NFV or PFV  Paper IV: Below minimum expected amplitudes of vergence reserve width	NFV at far: minimum 6 pd BI PFV at far: minimum 13 pd BO  NFV at near: minimum 13 pd BI PFV at near: minimum 19 pd BO  Width at distance viewing < 19 prism diopters (pd)  At near viewing < 27 pd

D = diopter; cpm = cycles per minute; PFV = positive (convergent) fusional vergence; NFV = negative (divergent) fusional vergence; BI = Bas In; BO = Base Out; pd = prism diopter.

### 3.4 STATISTICS

*Study I:* Descriptive statistics were used for individual values and frequencies. Chi-square tests and Non-parametric statistical analyzes were used to evaluate differences between groups. The statistical package SPSS, version 22, was used.

*Study II:* Descriptive statistics were used for individual values and frequencies. The Mann-Whitney U-test and the Kruskal-Wallis test were used to compare outcome values between sex and diagnosis groups, respectively. The Chi-square or Fisher's test was used for analysis of cross-tabulations of frequencies. Binary logistic regression was used for the analysis of links between reported visual changes and fatigue (MFS), depression and anxiety (HADS).

The dependent variables, HADS and MFS, were treated as dichotomous values based on a cut-off score. The statistical package SPSS, version 23, was used.

*Study III:* Descriptive statistics were used for individual values and frequencies. Non-parametric statistics were used to evaluate differences between groups. The Chi-square or Fisher's test was used for analysis of links between VI-items and the presence of objectively measured vision dysfunctions. The statistical package SPSS, version 23, was used.

*Study IV:* Descriptive statistics were used for frequencies and percentages. Analysis of results was performed with IBM SPSS Statistics 26 and Originlab Origin 2017. Distribution-tests were performed with Chi-square or Fisher's test and for pairwise analysis the Wilcoxon signed rank or Student's t-test were applied. The Mann-Whitney U- test was used for non-pairwise tests.

### **3.5 ETHICAL CONSIDERATIONS**

All studies adhered to the tenets of the Declaration of Helsinki and were approved by the regional ethics review board. For study I and II, with approval in 2013, the ethical board did not demand written consent from the patients. They defined the study as a follow-up of the department's regular work. In study III and IV, written consent from the patient was required.

Every patient was given an identifying number and the code key was handwritten and stored in the medical record archive of the department. None of our assessments were upsetting or disturbing in any way for the patients.

## 4 RESULTS

### 4.1 STUDY I

The study included 170 patients who answered the VI, for results see table 9. Half of the patients reported visual changes after ABI (54%) which conforms with earlier reported data (33, 34, 77). The most common visual changes reported were reading dysfunction (53%), light sensitivity (35%) and blurred vision (35%). The most affected aspects were the risk of bumping into objects while walking (31%) and/or the unexpected appearance of objects (24%), see table 9.

**Table 9.** Results of the Visual Interview, published with permission of Journal of Rehabilitation Medicine.

Self-reported visual changes after ABI	Yes n (%)
Q1. Have you noticed any visual change?	91 (54)
Q2. Do you suffer from double vision?	33 (19)
Q3. Do you have problems while reading	90 (53)
Q4. Do people and objects suddenly appear before you in an unexpected way?	41(24)
Q5. Do you crash into people and objects when you are on the move?	52 (31)
Q6. Do you find it difficult to estimate depth or heights in a stairway?	19 (11)
Q7. Do you find it difficult to grasp a glass, a door handle or to shake hands?	33 (19)
Q8. Do you find it difficult to recognize faces?	19 (11)
Q9. Do you interpret familiar faces in the way that differs from before?	15 (9)
Q10. Does light blind you more than before?	60 (35)
Q11. Do you need stronger light now than before in order to obtain distinct vision?	43 (25)
Q12. Do you need stronger light now while reading?	63 (37)
Q13. Is your vision more blurred than before?	60 (35)
Q14. Have you experienced that color has changed?	3 (2)
Q15 Have you experienced any sight phenomena?	36 (21)
Q16. Have you had any other unexpected sight experiences?	23 (14)
Q17. Are there areas of reduced sight in your vision field?	46 (27)
Q18. Have your eyesight been examined after you fell ill?	83 (49)

Light sensitivity, Q10, and the experience of sight phenomena, Q15, were more common in women ( $p < 0.002$  Fisher Exact test,  $p < 0.001$  Fisher Exact test).

TBI patients suffered more often from light sensitivity, Q10, ( $p < 0.004$ , Pearson X<sup>2</sup>), and stroke patients had fewer problems with sudden appearance of objects, Q4, ( $p < 0.012$ , Pearson X<sup>2</sup>).

Reading capacity had declined in 90 of the patients (53%). The level was higher in connection with VFD, light sensitivity, blurred vision and double vision, see table 10.

**Table 10.** Total number of patients with reading difficulties in combination with VFD, light sensitivity, blurred vision and double vision.

	VFD	Light sensitivity	Blurred vision	Double vision
<b>Total n of patients</b>	46	60	60	33
<b>Reading difficulties, n (“yes” Q3)</b>	35	45	43	26
<b>% with reading disturbance</b>	76%	75%	72%	79%

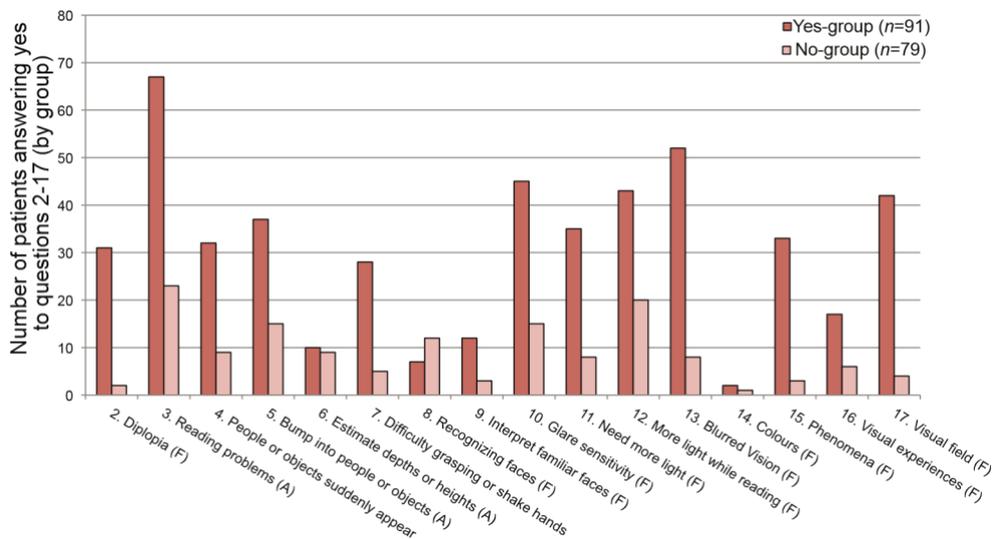
VFD was found in 46 of the patients (27%), and of these patients 31(67%) had VFD in combination with either, light sensitivity, blurred vision or double vision (Q2, Q10 or Q13) see table 11.

**Table 11.** The number and % of patients reporting VFD in combination with light sensitivity, blurred vision and double vision.

VFD, 46 patients	Light sensitivity	Blurred vision	Double vision
<b>n combination with VFD and</b>	14	11	7
<b>% of VFD patients</b>	30%	24%	15%

An ophthalmologic assessment was performed prior to admission in 83 patients (49%). Of these about 2/3 had experienced visual changes according to Q1 in VI. The patients suffering from VFD, were ophthalmologically assessed in 72% of the cases, the patients with double vision in 61%, and two of these 20 patients were referred to an orthoptist.

Of the 170 patients, 79 (46%) did not report experiencing any visual change (Q1), but 53 of these answered “yes” to one of the nine questions concerning vision problems in the VI, and 16 of them (20% of 79 patients) “yes” to four or more questions, see figure 2.



**Figure 2.** The patients having experienced visual changes, “yes-group”, not experienced visual changes “no-group”. Published with permission of Journal of Rehabilitation Medicine.

## 4.2 STUDY II

The study included 123 patients who were interviewed according to the VI and answered to MFS and HADS.

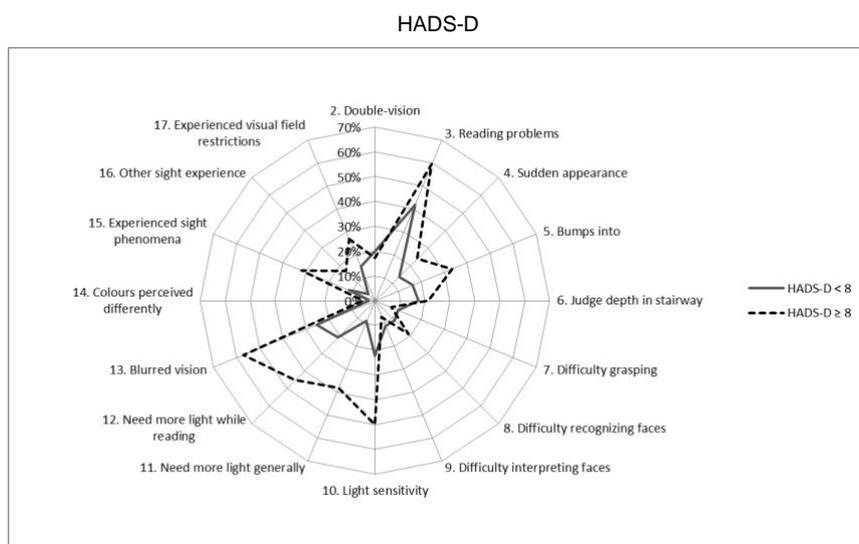
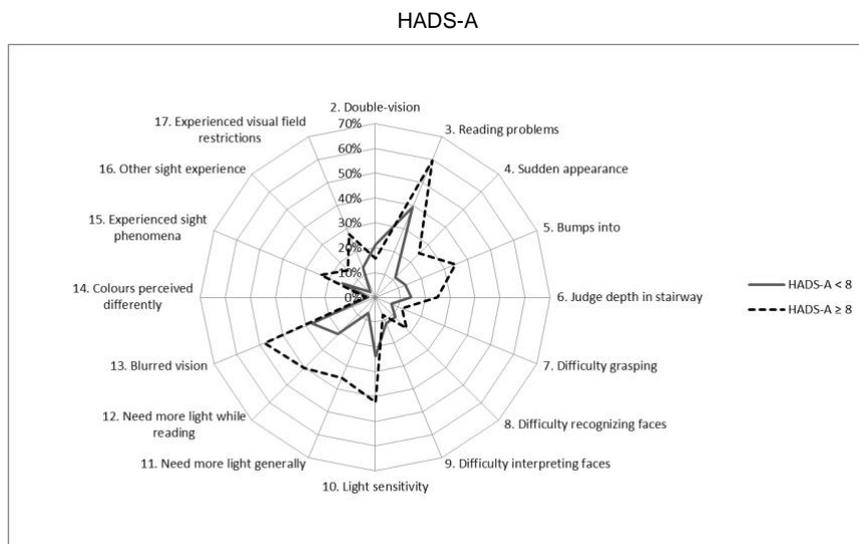
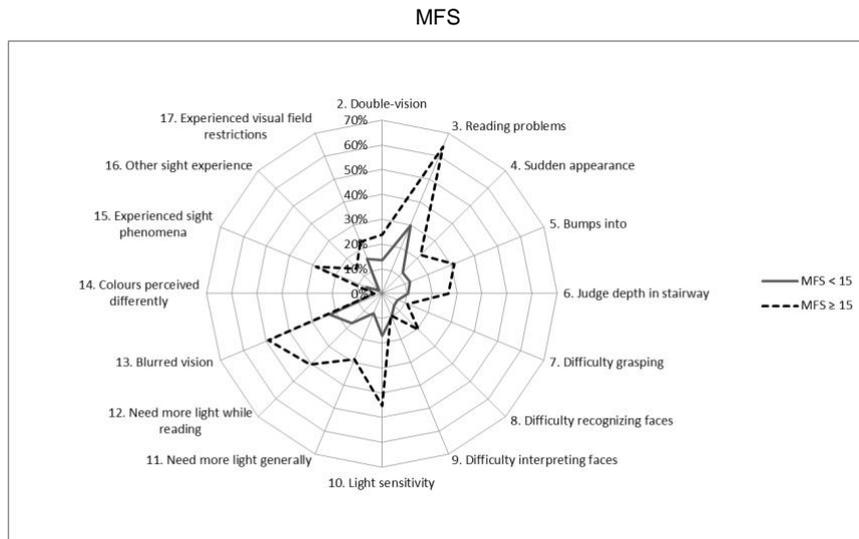
At least one experienced visual dysfunction was reported by 100 (81 %) patients. The mean VI-score was 4 (range 1–15). There was a statistical difference between women and men, mean 4 and 3 respectively, (Mann-Whitney U-test,  $p=0.026$ ). There was no statistical correlation between VI-score and age group or VI-score and diagnosis group (Kruskal-Willis).

In the MFS, 64 patients reported a level of moderate to severe fatigue  $>14,5p$  (52%). Of these patients, 35 reported moderate fatigue, 15-19,5p, (29%), and 29 severe fatigue,  $>19,5 p$ , (23 %).

In the HADS-A, 52 patients reported a level of anxiety  $> 7p$ , (42%). Of these 23 (19%) between 8–10p, and 29 (23%)  $>10p$ .

In the HADS-D, 43 patients (35%) reported a level of depression  $>7p$ , 23 (19%) between 8–10p, 20 patients (16%)  $>10p$ .

The questions concerning reading problems (Q3), light sensitivity (Q10) and blurred vision (Q13) revealed a large difference between those who had or did not have problems with fatigue, anxiety or depression. See figure 3.



**Figure 3.** Share of patients responding with a yes to each symptom in the Visual Interview depending on if exhibiting mental fatigue (top), anxiety (middle), or depression (bottom). Published with permission of Journal of Rehabilitation Medicine.

Logistic regression was used to find correlations between VI-score and fatigue, anxiety and depression.

#### *Mental fatigue*

The model used was statistically significant ( $\chi^2$  71.138,  $df=8$ ,  $p=0.000$ ). It explained 58.6% of the variance (Nagelkerke R<sup>2</sup>) and correctly classified 82.9% of the cases. Medium to severe mental fatigue was associated with increased VI-score and HADS-D (cut-off >7), see table 12.

#### *Anxiety*

The model used was statistically significant ( $\chi^2$  53.092,  $df=8$ ,  $p=0.000$ ) It explained 47.1% of the variance (Nagelkerke R<sup>2</sup>). It correctly classified 79.7% of the cases. H HADS-D (cut-off >7) and TBI were associated with higher rates of anxiety. The logistic regression showed no correlation with increasing VI- score and anxiety.

#### *Depression*

The model used was statistically significant ( $\chi^2$  64.394,  $df=8$ ,  $p=0.000$ ) It explained 56.4% of the variance (Nagelkerke R<sup>2</sup>), and correctly classified 82.1% of the cases. MFS (cut-off >14,5p) and HADS-A (cut-off >7p) were linked to a propensity to exhibit depression. The logistic regression showed no correlation with increasing VI- score and depression.

**Table 12.** Logistic regression predicting likelihood of *mental fatigue* ( $MFS \geq 15$ ) based on gender, age group, diagnosis group, visual interview score, HADS-A and HADS-D. Gender is for women compared to men, diagnosis group is compared to stroke. Published with permission of Journal of Rehabilitation Medicine.

Variable	Wald	Df	Odds ratio	Sign
Gender (female)	1.227	1	1.822	0.268
Age group	2.378	1	0.567	0.123
Diagnosis (stroke)	4.933	3		0.177
Diagnosis (TBI)	2.916	1	3.150	0.088
Diagnosis (SAH/Inf./Tum)	3.575	1	3.781	0.059
Diagnosis (other)	0.129	1	1.467	0.720
VI score	6.598	1	1.261	0.010
HADS-A	3.388	1	2.927	0.066
HADS-D	11.361	1	10.347	0.001
Constant	2.226	1	0.217	0.136

### 4.3 STUDY III

The study included 73 patients. All assessments, both subjective and objective, revealed a high occurrence of visual dysfunctions.

#### VI

Forty-four patients (60%) reported visual dysfunctions.

Most common were reading difficulties, difficulty in remembering what you have read, glare and blurred vision, see table 13.

#### CISS

Mean CISS-score was 23 (min1, max 49) with 54 % scoring 21 or above. For the stroke group it was 45.2 %, for the other diagnoses 50% or more.

#### Objective measurement

Nineteen patients (26.4%) had subnormal acuity, due to uncorrected or insufficiently corrected refractive error (n = 12), ocular health issues (n = 3), amblyopia (n = 3), and

damage to the visual pathways associated with the ABI (n = 1). Visual field defects were found in 15 patients (20.8 %). Accommodative function was measured in 22 patients of whom five showed insufficient accommodation. For oculomotor findings in the patient group, see table 14.

**Table 13.** Visual dysfunctions as reported in VI of the 73 patients. Published with permission from Brain and Behavior

Item (Item no)	Number of responses	Percentage of patients
Reading difficulties (Q16)	47	64%
General vision concern (Q1)	44	60%
Difficulty remembering just read (Q17)	39	53%
Hypersensitivity to glare (Q4)	31	42 %
Blurred vision (Q7)	31	42 %
The need for light become greater while reading (Q6)	24	33 %
Frequently bumping into people or objects (Q13)	24	33 %
Difficulty evading people and objects moving towards you? (Q12)	21	26 %
Visual field affected (Q3)	19	26 %
Neck pain (Q11)	19	26 %
Headache when reading (Q18)	19	26 %
Difficulty with depth perception (Q14)	18	24 %
Needing more light in general to see well (Q5)	17	23 %
Other visual concern (Q10)	11	15 %
Double vision (Q2)	10	14 %
Problems with recognizing faces (Q9)	8	11 %
Difficulty with eye-hand coordination (Q15)	8	11 %
Affected color perception (Q8)	4	5 %

**Table 14.** Oculomotor findings of the visual examination. Published with permission of the Journal of Brain and Behavior.

Eye alignment issues	All (n = 73)	Stroke (n = 32)	TBI (n = 12)	Infection (n = 9)	Hypoxia (n = 6)	Tumor (n = 6)	SAH (n = 4)	Other (n = 4)
Near point of convergence	18 25.0 %	8 25.8 %	4 33.3 %	2 22.2 %	0 0 %	1 16.7 %	1 25.0 %	2 50.0 %
Vergence facility	35 48.6 %	14 45.2 %	7 58.3 %	4 44.4 %	3 50.0 %	3 50.0 %	3 75.0 %	1 25.0 %
Fusion vergence	60 83.3 %	25 80.6 %	10 83.3 %	8 88.9 %	6 100.0 %	3 50.0 %	4 100 %	4 100 %
Strabismus	2 2.8 %							

Evaluation of subjectively reported visual dysfunctions, according to VI, and objectively measured ones, revealed seven associations, see table 15.

**Table 15.** Associations between symptoms identified with VI and visual dysfunctions found by optometric assessment. Published with permission of the Journal of Brain and Behavior.

Visual changes in VI (Question No)	Objective findings of optometric examination				
VI	Visual acuity	Positive fusional vergence at far	Positive fusional vergence at near	Vergence facility	Visual field defect
General vision concern (Q1)		Chi-square 5.228, Df = 1, p = 0.022, Phi = 0.29	Chi-square 10.397, Df = 1, p = 0.001, Phi = 0.409		
Double vision (Q2)			Fisher Exact p = 0.005, Phi = 0.261		
Visual field affected (Q3)				Fisher Exact p = 0.01, Phi = 0.343	Fisher Exact p = 0.000, Phi = 0.487
Problems with recognizing faces (Q9)	Fisher Exact p = 0.026, Phi = 0.29				
Frequently bumping into people or objects (Q13)					Fisher Exact p = 0.027, Phi = 0.302

Twenty-five patients reported no visual concerns, however abnormal findings were made in the objective examination, see table 16.

**Table 16.** Clinical findings in patients who reported or who deny general vision concerns. Published with permission of Brain and Behavior.

	General vision concern	
	No of patients reporting (n = 45)	No of patients denying (n = 25)
<b>Subnormal visual acuity</b>	13 (28.9 %)	6 (24.0 %)
<b>Visual field defect</b>	12 (26.7 %)	3 (12.0 %)
<b>Convergence issues</b>	25 (55.6 %)	14 (56.0 %)
<b>Fusional vergence issues</b>	39 (86.7 %)	18 (72.0 %)
<b>Accommodation issues</b>	2 (4.4 %)	3 (12.0 %)

#### 4.3.1 Study IV

The study included 89 patients, 48 patients in the intervention group and 41 in the control group. The study evaluated the rehabilitation of vergence issues. The intervention group contained 5 patients who did not have binocular function and the control group 8. Thus, for rehabilitation of vergence issues, 43 patients in the intervention group and 33 patients in the control group were analyzed. The results of the objective measurement at admission are presented in table 17.

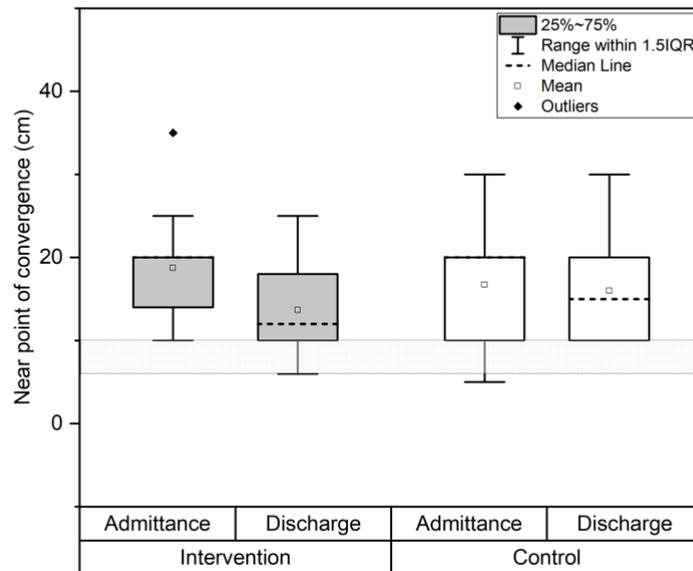
**Table 17.** Clinical findings in the vision examination, paper IV. Published with permission of Taylor & Francis in Journal of Brain Injury.

Visual issues		Intervention group n = 48	Control group n = 41
<b>Suboptimal spectacle correction (visual acuity)</b>		9 (18.7%)	13 (31.7%)
<b>Suboptimal near correction (near visual acuity)</b>		9 (18.7%)	10 (24.4%)
<b>Visual field defects</b>		2 (4.2%)	5 (12.2%)
<b>Strabismus, eye motility disorder</b>		2 (4.2%)	2 (4.9%)
<b>Eye teaming issue (only patients with binocular vision)</b>		n = 43	n = 33
	Convergence	15 (34.9%)	7 (21.2%)
	Vergence facility	24 (55.8%)	20 (60.6%)
	Fusional vergence (distance), width	12 (27.9%)	18 (54.5%)
	Fusional vergence (near), width	16 (37.2%)	12 (36.4%)

The intervention group received visual rehabilitation focusing on individual visual dysfunctions, this article presents the results from VT aimed at convergence, vergence facility and fusion vergence both near and far. For convergence; 15 patients received VT and 7 patients were controls. For vergence facility; 24 patients received VT and 20 patients were controls. For fusion vergence at distance; 12 patients received VT and 18 patients were controls. For fusion vergence close up; 16 patients received VT and 12 patients were controls. Comparison was made between admission and discharge for each group.

#### *Convergence insufficiency*

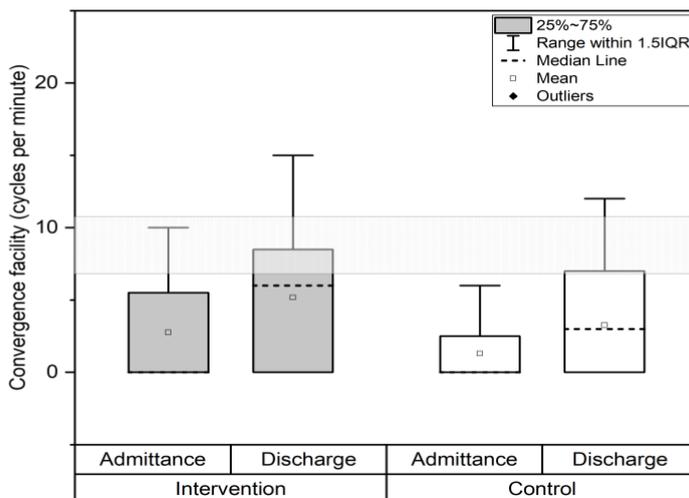
The intervention group (n=15) improved significantly in near point convergence (NPC) ( $Z=2.26$ ,  $p=0.02$ ), the control group (n=7) improved as well, but not significantly. The grey area shows the normal range. The normal NPC is 6-10 cm, see figure 4.



**Figure 4.** NPC, result of the rehabilitation. Published with permission of Taylor & Francis in Journal of Brain Injury.

### *Vergence facility*

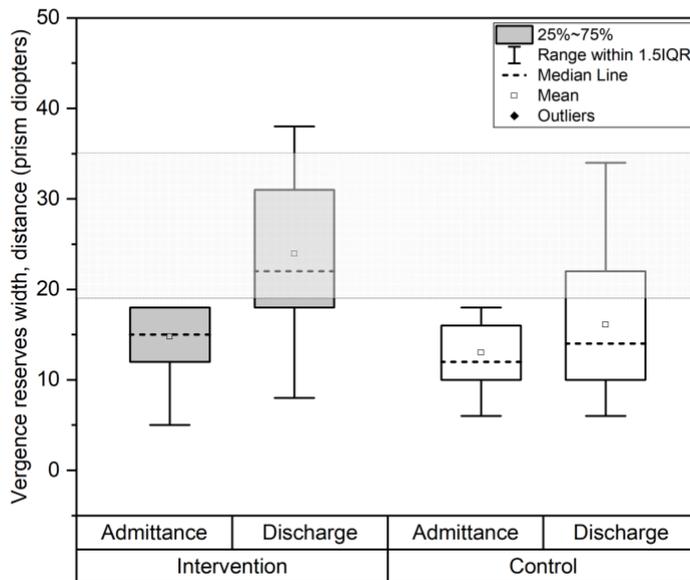
The improvement in the intervention group (n=24) was statistically significant in vergence facility ( $Z=-2.16$ ,  $p=0.03$ ). The control group (n=20) improved as well, but the change was not statistically significant as seen in figure 5. A higher value indicates an improved vergence facility, the normal zone of 7–11 cpm (cycles per minute) is indicated by the greyed area.



**Figure 5.** Vergence facility, result of the rehabilitation. Published with permission of Taylor & Francis in Journal of Brain Injury.

*Fusion vergence at distance*

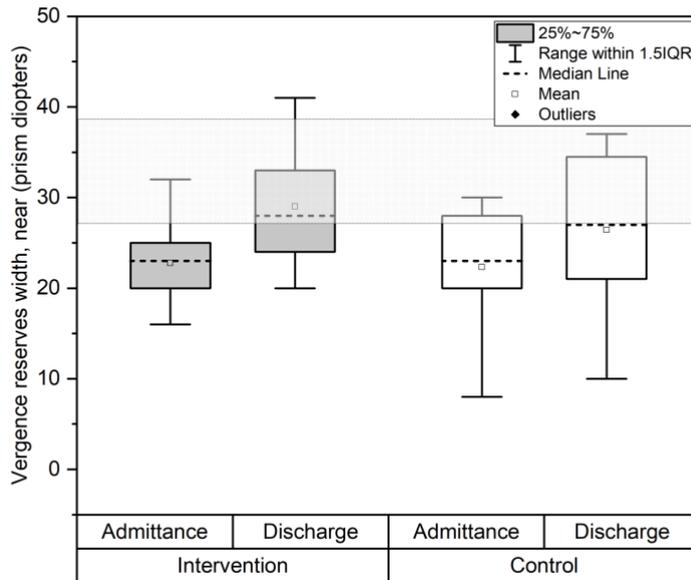
The intervention group (n =12) showed a statistically significant improvement in fusion vergence at distance ( $Z=-2.44$ ,  $p<0.01$  and  $t = -4.47$ ,  $dF = 15$ ,  $p<0.01$ ) after VT. There was also a statistically significant improvement in the control group (n =18) ( $Z=-1.99$ ,  $p=0.04$ ). The median of the intervention group reached the target interval, the greyed area seen in figure 6.



**Figure 6.** Result of the rehabilitation for fusion vergence at distance viewing. A higher value indicates an improvement, the normal zone of 19 prism diopters or more is indicated by the greyed area. Published with permission of Taylor & Francis in Journal of Brain Injury.

*Fusion at near*

The increase in fusion vergence at near in the intervention group (n=16) was statistically significant ( $t=4.47$ ,  $dF=15$ ,  $p<0.01$ ). The control group (n=12) increased but not to a statistically significant level. The median of both groups reached the target interval as seen in figure 7.



**Figure 7.** Result of rehabilitation of fusion vergence at near. A higher value indicates an improvement, the normal zone of 27 prism diopters or more is indicated by the greyed area. Published with permission of Taylor & Francis in Journal of Brain Injury.

The CISS survey was used on admission and at discharge to capture visual symptoms in connection with near activity. The change in CISS-score was analyzed for those who had at least one visual dysfunction: 38 in the intervention group and 31 in the control group (figure 8). The intervention group showed an elevated level of symptoms at admission (mean 24), while the control group did not (mean 15). Improvement in the intervention group was statistically significant ( $Z = 2.97$ ,  $p < 0.01$ ), but no statistically significant change was found in the control group. There was a difference between the groups at baseline ( $U = 932$ ,  $Z = 3.51$ ,  $p < 0.01$ ) which may impact on the interpretation of the outcome.



## 5 DISCUSSION

The general aim of this thesis was to identify and investigate the impact of visual dysfunctions on patients with medium to severe ABI and to evaluate different assessment models that could be used in neurorehabilitation. The different studies in the thesis have demonstrated a high occurrence of visual dysfunctions. More than half of the ABI patients experienced visual changes and the results are in line with earlier reports (28, 33, 34, 75–79). These studies are often restricted to one type of diagnosis. In our thesis we have dealt with a mix of diagnoses, to reflect reality in clinical practice. This has been a deliberate choice and our findings showed that visual dysfunctions were common across the diagnosis groups. The symptom characteristics and specific dysfunctions may however differ, which is why assessment of symptoms as well as visual functions will help to identify needs for intervention.

The visual dysfunctions had a common pattern in all studies, reading disorders in more than half of the patients, followed by light hypersensitivity and blurred vision in about a third of the patients. These findings are also in line with earlier reports (28, 33, 34, 37). Reading is a complex ability, as it involves a combination of oculomotor functions, cognition, endurance and motivation (67, 78), thus, rehabilitation of reading difficulties should take all these aspects into account. The pathophysiology of light hypersensitivity is also complex and partly unknown. Theories span from injury to retinal ganglion cells (79, 80) to injuries of the meninges through nociceptive information to the thalamic light sensitive neurons (81). The treatment of light hypersensitivity is to use colored lenses and different strategies for reducing light (79, 82, 83). The connection with reduced reading capacity found in study I and the effect of a tendency of increased avoidance behavior (83) make it important to attend to this symptom in a neurorehabilitation setting. Blurred vision is the result of a variety of causes: decreased acuity, refractive error, vergence facility, fusional vergence, or may even be a symptom of cataract (30). Thus, blurred vision is an important symptom to note and assess further.

The most evident visual dysfunctions, VFD and double vision, were found in between 20–25 % of the patients in the current studies. Previous studies have reported even higher levels (84). In a study by Rowe et al. (85) it was reported that 50 % of VFD patients also suffered from other visual dysfunctions. In the VFD group in study I, a comorbidity with oculomotor dysfunctions was found in 15–30 % of the patients, see table 10. This is important for the design of vision rehabilitation. The eyes' unconscious pattern of automatic bilateral movement is disturbed by VFD (86, 87). This indicates that if there is a combination of VFD and ocular motor dysfunctions, one may speculate that it would be better to start vision rehabilitation with training of the ocular motor dysfunctions and then continue with compensatory training targeting VFD. This is based on the assumption that achieving a stable gaze control increases the ability of using the compensatory method.

In study I, 20 % of all patients who did not report visual dysfunction, answered “yes” to four up to nine questions concerning specific visual symptoms in the VI. In study III 18 of the 25 patients who did not report visual problems had at least one oculomotor dysfunction. It appears that there are patients who are unaware of their visual dysfunctions or are unable to define them. However, when you ask the patients more specific questions about their vision, or perform a vision examination, the problems emerge. Visual problems may therefore be concealed, which indicates that a structured assessment is required to discover them.

In study I, half of the patients had been examined by a vision specialist before they were admitted to the rehabilitation day-care unit. Among the patients experiencing visual dysfunctions, a third were not examined. Even among patients with evident visual symptoms, such as VFD and double vision, more than 25% of the VFD patients and nearly 40% of the patients with double vision reported that they had not been examined. These reports should be treated with some caution as they are based on the patients’ own responses. It is possible that a patient in the acute phase after an ABI is unable to remember an examination. Even so, there appears to be a disparity between rehabilitation medicine and vision specialists. The best way to minimize this gap would be to include a vision specialist in the neurorehabilitation team (41, 42).

A link between fatigue and oculomotor dysfunction was discussed in a study by Möller et al (88) suggesting an association between saccades and fatigue. This is in line with the link found in study II between medium to severe fatigue and increasing visual dysfunctions. From another point of view this also suggests a need to assess vision dysfunctions. Fatigue is one of the most serious sequelae after an ABI (89, 90) and all the different ways to mitigate its effect are very important. Combining the link between medium to severe fatigue and increasing visual dysfunctions found in study II with the high levels of refractive errors and vergence dysfunctions found in study III, it may be speculated that these oculomotor dysfunctions are the cause. Eyes with an unstable gaze, have to redirect frequently in a tiresome way and the image becomes blurred (12). Blurred acuity is tiresome in itself as anyone who has left their glasses at home can confirm. Shifting gaze is an action that occurs constantly and if each move is somewhat more demanding than usual, it ought to increase fatigue.

The link between increased vision dysfunctions and mental fatigue, as found in study II, did not explain whether it also functioned in the other direction: fatigue causing visual dysfunctions. There are treatment models using other known associations between eye movements and other factors. A well-established psychiatric method directed to Post-Traumatic Stress Disorder ( PTSD) is Eye-Movement Desensitization and Reprocessing (EMDR) (91). This method uses horizontal eye movements as an important part of the treatment and is based on the brain’s cooperative complex networks, where eye movements are able to play a part in reprocessing emotional networks. This aspect of communicating networks was also discussed in a study by Meadmore et al. (92) concerning visuo-motor disorders after stroke. A disturbed ocular motor function was demonstrated when the affected upper limb was required to perform movements. This disturbance was not found when a

movement was made by the unaffected arm and it decreased if the affected limb was supported during the movement. This illustrates the communication networks of visuo-motor function. The movement of the upper limb is related to the direction of the gaze, and if the association is strengthened by support of the defective limb, the visuo-motor function improves. Thus, the next step according to the result of study II is to examine if vision therapy is able to mitigate fatigue. Schow et al. (63) described a group of stroke patients who received vision rehabilitation. One of the effects of the rehabilitation was decreased levels of fatigue. The improvement remained stable in a six-month follow-up.

A profile of oculomotor dysfunctions after ABI appears in the results from the objective measurements in study III and IV, in line with earlier studies: convergence insufficiency (33, 34), vergence facility (93-95), fusion vergence (33, 96) and the dysfunctions are often combined (97). There are different methods for vision rehabilitation of these disturbances. In study IV vision rehabilitation was evaluated. The patients examined were few, but the results are in line with earlier reports (29, 98, 99). The intervention group improved statistically in all components of vergence, and the control group improved statistically in fusion at distance. An interesting fact was that the control group also improved, although not statistically, in the other vergence parameters. One may speculate that near work activities, which are common in neurorehabilitation, have an effect on vergence dysfunction, even if the effect is smaller, compared with targeted VT.

Dysfunctional pursuit- (66, 100) and saccadic movements (32-34, 66) are also common after ABI. Saccades were measured in study III and IV, although the results have not yet been analyzed. Saccade and pursuit movements are of great importance after ABI in many different ways, see table 1. The signs of defective saccades in a medical examination are prolonged latencies, hypo metric movements, and reduced velocity (37). Defective saccades have, because of their widespread cortical networks (11), also been described as markers for cognitive impairment (88, 101).

In study III a comparison between objective and subjective assessments of visual deficits was made. The conclusion, that both types of assessments are necessary and complement each other for a thorough picture, is consistent with earlier reports (42, 102). A neurorehabilitation assessment has to be broad and sometimes requires another assessment from a different medical specialty. Vision is integrated in a huge number of processes in the brain, and a dysfunction is able to distort results from the neuropsychological, occupational, speech therapy, or physiotherapy examinations. Although the VI is able to define visual symptoms, takes 5-10 minutes to perform and has proved its usefulness as a screening instrument, some common visual dysfunctions, such as for example vergence facility and fusion vergence, are difficult to identify using a visual screening and ordinary medical examination. Thus, it is important to get rapid access to a vision specialist assessment for further rehabilitation plans. The easiest way to plan this care chain is to attach a vision specialist to the rehabilitation team. This has also been pointed out by Rowe et al and ACRM (41, 42).

The impact of vision dysfunctions on activities and social interaction is complex. To get a better understanding, a learning process is needed, which the ACRM describes in the article (42) “A conceptual model for vision rehabilitation”. A learning process that takes time is something worth fighting for in the slimmed down reality of everyday practice. To incorporate vision aspects in the team assessment into the routine of neurorehabilitation medicine would be a start. The model we have applied in our research is easy to use in everyday practice. If this model is to be able to identify visual dysfunctions at an activity and participation level it has to be extended and include the effects of visual dysfunction found in the assessments of occupational-, speech- and physiotherapists.

Rehabilitation research focuses on outcomes for activities and participation. Many authors who describe the state of vision rehabilitation research, identify its difficulties due to lack of consensus regarding definitions, treatment intensity, treatment duration and weak follow-up at the activity level (49, 103, 104). Today, however, a readiness to coordinate evaluation instruments and to structure common research models has begun to develop (44, 46, 105).

## 6 CONCLUSIONS

More than half of ABI patients suffer from visual dysfunctions. The most common ones are reading difficulties, glare and blurred vision. A group of patients are unaware of visual problems or are not able to define them. More detailed questions concerning specific visual symptom will reveal their difficulties. The extent of these symptoms indicates a need for visual screening as a routine after ABI.

Increased visual dysfunctions are linked to medium to severe fatigue after ABI.

Both subjectively reported visual symptoms and objective measurements show high levels of visual dysfunctions. At a functional level there are links between the different types of measurement and the VI covers more of the activity level.

Vision rehabilitation improved vergence function in patients with ABI. Common neurorehabilitation with focus on near work also leads to improvement, although to a lesser extent than targeted visual rehabilitation.

## 7. POINTS OF PERSPECTIVE

The field of visual dysfunctions and rehabilitation after ABI is relatively new. The increased number of studies in the last years indicates a growing interest. Most of the research has been undertaken by vision specialists. So, as Simpson-Jones and Hunt point out (60), in this field there is a need of research from the neurorehabilitation perspective.

In 2020 Grasso et al.(106) summarized the knowledge about the visual system's great ability to build new combinations in interaction with the environment. They stated that this ability also applies to the damaged brain and therefore justifies rehabilitation.

For evaluating vision rehabilitation at the activity level, there are technical methods that promise to be helpful. The fMRI technique, which has been used in several studies (107), is able to verify the nature of the injury as well as the impact on networks after VT. Eye tracking technology (108) can record a chosen activity before and after treatment, and is able to verify if VT has mitigated the patient's oculomotor dysfunctions.

The research concerning visual dysfunctions has mainly been directed to either stroke or TBI. There are other diagnoses of specific interest such as patients with sequelae after encephalitis. In our clinical experience these patients often suffer from vision-related deficits, frequently a mix of glare, ocular motor dysfunctions and hypersensitivity for vision impressions. In rehabilitation research this diagnosis group is often too small to allow any conclusions to be drawn. COVID-19 is an infectious disease which can attack the brain and cause neurological symptoms. Clinical experience from follow-up after COVID-19 has revealed that vision dysfunctions occur as one of the remaining symptoms. In the aftermath of COVID-19 and the ensuing research, deeper knowledge of visual dysfunctions after encephalitis may be acquired.

Oculomotor assessment has been suggested as a tool to provide evidence of brain injury after mTBI (109-111). Several studies have examined this and recommend an eye examination directly in connection with trauma. Here, it has been proposed that eye tracker technology could be useful (112).

This thesis has concentrated on visual dysfunctions, but there are other important sensory deficits after ABI such as for example noise sensitivity. Dual sensory impairment (DSI) is a term used for both visual and auditory hypersensitivity and a few studies have shown that DSI affects the quality of life negatively (113). The combined distortion of sensory information after ABI is almost a virgin research area. There is no shortage of future opportunities.

## 8 SVENSK SAMMANFATTNING

Hjärnan får sin information om yttrevärlden från våra sinnen; syn, hörsel, lukt, smak och känsel. Synen är det dominerande sinnet hos människan. Både att förmedla syninformationen, och ställa in blicken på det man vill se, är komplicerade processer och styrs via vitt spridda nätverk i hjärnan, vilket medför att de lätt kan skadas i samband med en förvärvad hjärnskada. Synen är basen för så viktiga funktioner som rörelser, läsning, avvärja hinder och upptäcka faror, kunna köra bil eller cykla. En påverkan efter förvärvad hjärnskada kan delas upp i skador direkt på syninformationsflödet, som synfältsbortfall eller bländning, eller skador på ögonmotoriken, vilket ger svårigheter att styra blicken.

Denna avhandling har varit inriktad på att upptäcka och definiera olika typer av synstörningar efter en förvärvad hjärnskada samt att utreda effekterna av synrehabilitering. Alla patienter som har deltagit i studierna hade en medel- till svår hjärnskada, i de flesta fall orsakade av stroke, och var i åldern 18–67 år.

I den första studien svarade 170 patienter på en strukturerad intervju vars syfte var att definiera om det fanns en synpåverkan och, i så fall, vilken typ av förändring. Hälften upplevde en synförändring. Det vanligaste var påverkan på läsförmågan, 53%, bländning, 35%, eller suddigt seende, 35%. Resultatet överensstämde med resultatet från tidigare studier. Två femtedelar av de patienter som inte upplevde någon synförändring, svarade ja på 4–9 av frågorna i Synanamnesen. Således kan det vara svårt för patienterna att definiera en synstörning, men om de får mer konkreta frågor så kommer svårigheterna fram.

Den andra studien, som inkluderade 123 patienter, undersökte om ökade synproblem hade ett samband med andra vanliga och svåra symtom efter en förvärvad hjärnskada som trötthet, ångest och depression. Resultatet från studien visade ett samband mellan medel till svår mental trötthet och ökande synproblem, men inte mellan ökande synproblem och ångest eller depression.

I den tredje studien intervjuades 73 patienter om synbesvär och genomgick även en synundersökning utförd av en synspecialist. Båda typerna av undersökning visade på samma höga nivåer av synstörningar som i den första studien. De vanligaste ögonmotoriska problemen var svårigheter att ställa in och hålla kvar blicken, eller att byta skärpedjup mellan nära och långt borta. Dessa nedsättningar är svåra att diagnostisera i ett vanligt läkarstatus och slutsatsen var att både subjektiva och objektiva undersökning behövs för en adekvat bedömning av synförmågan.

I den fjärde studien fick en patientgrupp bestående av 48 patienter synrehabilitering riktad mot deras individuella svårigheter. Resultatet jämfördes med 41 patienter i en kontrollgrupp. Alla patienter var inskrivna på klinikens dagvårdsenheter och fick sedvanlig rehabilitering. De som fick synträning förbättrades signifikant, men även kontrollgruppen förbättrades, men inte signifikant. Sammanfattningsvis ger den sedvanliga rehabiliteringen, som ofta är inriktad på närarbete, en viss förbättring i sig, men att förbättringen blir mer uttalad med specifikt riktad synrehabilitering.



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## 10 REFERENCES

1. Lekander I, Willers C, Ekstrand E, von Euler M, Fagervall-Ytting B, Henricson L, et al. Hospital comparison of stroke care in Sweden: a register-based study. *BMJ Open*. 2017;7(9):e015244.
2. Lexell J. Rehabilitation of traumatic brain injuries in Sweden. *The Journal of head trauma rehabilitation*. 2007;22(4):229-33.
3. Khoshnam SE, Winlow W, Farzaneh M, Farbood Y, Moghaddam HF. Pathogenic mechanisms following ischemic stroke. *Neurological sciences : official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*. 2017;38(7):1167-86.
4. Andriessen TM, Jacobs B, Vos PE. Clinical characteristics and pathophysiological mechanisms of focal and diffuse traumatic brain injury. *Journal of cellular and molecular medicine*. 2010;14(10):2381-92.
5. Sen N. An insight into the vision impairment following traumatic brain injury. *Neurochemistry international*. 2017;111:103-7.
6. Hayes JP, Bigler ED, Verfaellie M. Traumatic Brain Injury as a Disorder of Brain Connectivity. *Journal of the International Neuropsychological Society : JINS*. 2016;22(2):120-37.
7. Xiong Y, Mahmood A, Chopp M. Current understanding of neuroinflammation after traumatic brain injury and cell-based therapeutic opportunities. *Chinese journal of traumatology = Zhonghua chuang shang za zhi*. 2018;21(3):137-51.
8. Corrigan F, Mander KA, Leonard AV, Vink R. Neurogenic inflammation after traumatic brain injury and its potentiation of classical inflammation. *Journal of neuroinflammation*. 2016;13(1):264.
9. Kolb B, Whishaw IQ. *Fundamentals of Human Neuropsychology*: Macmillan Learning; 2015.
10. Gazzaniga MS, Ivry RB, Mangun GR. *Cognitive Neuroscience: The Biology of the Mind*: W.W. Norton; 2009.
11. Kennard C. Disorders of higher gaze control. *Handbook of clinical neurology*. 2011;102:379-402.
12. Suter PS, Harvey LH. *Vision Rehabilitation: Multidisciplinary Care of the Patient Following Brain Injury*: CRC Press; 2016.
13. Ygge J. *Ögat och synen* 2011.
14. Departments of Neurology R. John Leigh Professor NOBECWRUHVAMCCO, Departments of Neurology David S. Zee Professor OOHNSN, Ocular Motor-Visual Testing Lab Johns Hopkins University rector BM. *The Neurology of Eye Movements : Text and CD-ROM: Text and CD-ROM*: Oxford University Press, USA; 1999.
15. Mani R, Asper L, Khuu SK. Deficits in saccades and smooth-pursuit eye movements in adults with traumatic brain injury: a systematic review and meta-analysis. *Brain injury*. 2018;32(11):1315-36.
16. Bryan Kolb IQW. *Fundamentals of neuroscience*2015.

17. Stone JV. *Vision and Brain: How We Perceive the World*: MIT Press; 2012.
18. Krebs C, Weinberg J, Akesson E, Dilli E. *Neuroscience*. Second edition. ed. Philadelphia: Wolters Kluwer; 2018. vii, 468 pages p.
19. Goodale MA, Milner AD. Separate visual pathways for perception and action. *Trends in neurosciences*. 1992;15(1):20-5.
20. Van Essen DC, Drury HA. Structural and functional analyses of human cerebral cortex using a surface-based atlas. *The Journal of neuroscience : the official journal of the Society for Neuroscience*. 1997;17(18):7079-102.
21. Milner AD, Goodale MA. Two visual systems re-viewed. *Neuropsychologia*. 2008;46(3):774-85.
22. Lauwereyns J. *Brain and the Gaze: On the Active Boundaries of Vision*: MIT Press; 2012.
23. Padula WV, Capo-Aponte JE, Padula WV, Singman EL, Jenness J. The consequence of spatial visual processing dysfunction caused by traumatic brain injury (TBI). *Brain injury*. 2017;31(5):589-600.
24. Sohlberg MM, Mateer CA. Effectiveness of an attention-training program. *Journal of clinical and experimental neuropsychology*. 1987;9(2):117-30.
25. Rosenberg MD, Finn ES, Scheinost D, Constable RT, Chun MM. Characterizing Attention with Predictive Network Models. *Trends in cognitive sciences*. 2017;21(4):290-302.
26. Spaccavento S, Marinelli CV, Nardulli R, Macchitella L, Bivona U, Piccardi L, et al. Attention Deficits in Stroke Patients: The Role of Lesion Characteristics, Time from Stroke, and Concomitant Neuropsychological Deficits. *Behavioural neurology*. 2019;2019:7835710.
27. Ponsford JL, Downing MG, Olver J, Ponsford M, Acher R, Carty M, et al. Longitudinal follow-up of patients with traumatic brain injury: outcome at two, five, and ten years post-injury. *Journal of neurotrauma*. 2014;31(1):64-77.
28. Bulson R, Jun W, Hayes J. Visual symptomatology and referral patterns for Operation Iraqi Freedom and Operation Enduring Freedom veterans with traumatic brain injury. *Journal of rehabilitation research and development*. 2012;49(7):1075-82.
29. Greenwald BD, Kapoor N, Singh AD. Visual impairments in the first year after traumatic brain injury. *Brain injury*. 2012;26(11):1338-59.
30. Rowe F. Symptoms of stroke-related visual impairment. *Strabismus*. 2013;21(2):150-4.
31. Berthold-Lindstedt M, Ygge J, Borg K. Visual dysfunction is underestimated in patients with acquired brain injury. *Journal of rehabilitation medicine*. 2017;49(4):327-32.
32. Stelmack JA, Frith T, Van Koeveering D, Rinne S, Stelmack TR. Visual function in patients followed at a Veterans Affairs polytrauma network site: an electronic medical record review. *Optometry (St Louis, Mo)*. 2009;80(8):419-24.
33. Capo-Aponte JE, Jorgensen-Wagers KL, Sosa JA, Walsh DV, Goodrich GL, Temme LA, et al. Visual Dysfunctions at Different Stages after Blast and Non-blast Mild Traumatic Brain Injury. *Optometry and vision science : official publication of the American Academy of Optometry*. 2017;94(1):7-15.

34. Brahm KD, Wilgenburg HM, Kirby J, Ingalla S, Chang CY, Goodrich GL. Visual impairment and dysfunction in combat-injured servicemembers with traumatic brain injury. *Optometry and vision science : official publication of the American Academy of Optometry*. 2009;86(7):817-25.
35. Warren M. Pilot study on activities of daily living limitations in adults with hemianopsia. *The American journal of occupational therapy : official publication of the American Occupational Therapy Association*. 2009;63(5):626-33.
36. Wolter M, Preda S. Visual deficits following stroke: maximizing participation in rehabilitation. *Topics in stroke rehabilitation*. 2006;13(3):12-21.
37. Armstrong RA. Visual problems associated with traumatic brain injury. *Clinical & experimental optometry*. 2018;101(6):716-26.
38. Rowe FJ. Stroke survivors' views and experiences on impact of visual impairment. *Brain and behavior*. 2017;7(9):e00778.
39. Smith TM, Pappadis MR, Krishnan S, Reistetter TA. Stroke Survivor and Caregiver Perspectives on Post-Stroke Visual Concerns and Long-Term Consequences. *Behavioural neurology*. 2018;2018:1463429.
40. Gall C, Brosel D, Franke GH. Mental distress in patients with cerebral visual injury assessed with the german brief symptom inventory. *Frontiers in aging neuroscience*. 2015;7:51.
41. Rowe F, Walker M, Rockliffe J, Pollock A, Noonan C, Howard C, et al. Delivery of high quality stroke and vision care: experiences of UK services. *Disability and rehabilitation*. 2015:1-5.
42. Roberts PS, Rizzo JR, Hreha K, Wertheimer J, Kaldenberg J, Hironaka D, et al. A conceptual model for vision rehabilitation. *Journal of rehabilitation research and development*. 2016;53(6):693-704.
43. Neumann G, Schaadt AK, Reinhart S, Kerkhoff G. Clinical and Psychometric Evaluations of the Cerebral Vision Screening Questionnaire in 461 Nonaphasic Individuals Poststroke. *Neurorehabilitation and neural repair*. 2016;30(3):187-98.
44. Laukkanen H, Scheiman M, Hayes JR. Brain Injury Vision Symptom Survey (BIVSS) Questionnaire. *Optometry and vision science : official publication of the American Academy of Optometry*. 2017;94(1):43-50.
45. Hepworth LR, Rowe FJ, Burnside G. Development of a patient reported outcome measures for measuring the impact of visual impairment following stroke. *BMC health services research*. 2019;19(1):348.
46. Rowe FJ, Hepworth LR, Kirkham JJ. Development of core outcome sets for vision screening and assessment in stroke: a Delphi and consensus study. *BMJ Open*. 2019;9(9):e029578.
47. Rauch A, Cieza A, Stucki G. How to apply the International Classification of Functioning, Disability and Health (ICF) for rehabilitation management in clinical practice. *European journal of physical and rehabilitation medicine*. 2008;44(3):329-42.
48. Scheiman M, Wick B, Steinman BA. *Clinical Management of Binocular Vision: Heterophoric, Accommodative, and Eye Movement Disorders*: Lippincott Williams & Wilkins; 2002.

49. Pollock A, Hazelton C, Henderson CA, Angilley J, Dhillon B, Langhorne P, et al. Interventions for disorders of eye movement in patients with stroke. The Cochrane database of systematic reviews. 2011(10):Cd008389.
50. Bulboaca AE, Bulboaca A, Stanescu I, Boarescu PM, Chirila I, Bulboaca A, et al. Homonymous hemianopsia versus unilateral spatial neglect rehabilitation strategies in stroke patients. *Balneo Res J.* 2019;10(2):67-73.
51. Pollock A, Hazelton C, Henderson CA, Angilley J, Dhillon B, Langhorne P, et al. Interventions for visual field defects in patients with stroke. The Cochrane database of systematic reviews. 2011(10):Cd008388.
52. Pollock A, Hazelton C, Rowe FJ, Jonuscheit S, Kernohan A, Angilley J, et al. Interventions for visual field defects in people with stroke. The Cochrane database of systematic reviews. 2019;5:Cd008388.
53. Rowe FJ, Hepworth LR, Conroy EJ, Rainford NEA, Bedson E, Drummond A, et al. Visual Function Questionnaire as an outcome measure for homonymous hemianopia: subscales and supplementary questions, analysis from the VISION trial. *Eye (London, England).* 2019.
54. Berger S, Kaldenberg J, Selmane R, Carlo S. Effectiveness of Interventions to Address Visual and Visual-Perceptual Impairments to Improve Occupational Performance in Adults With Traumatic Brain Injury: A Systematic Review. *The American journal of occupational therapy : official publication of the American Occupational Therapy Association.* 2016;70(3):7003180010p1-7.
55. Hanna KL, Rowe FJ. Clinical versus Evidence-based Rehabilitation Options for Post-stroke Visual Impairment. *Neuro-ophthalmology (Aeolus Press).* 2017;41(6):297-305.
56. Bolognini N, Rasi F, Coccia M, Làdavos E. Visual search improvement in hemianopic patients after audio-visual stimulation. *Brain : a journal of neurology.* 2005;128(Pt 12):2830-42.
57. Passamonti C, Bertini C, Làdavos E. Audio-visual stimulation improves oculomotor patterns in patients with hemianopia. *Neuropsychologia.* 2009;47(2):546-55.
58. Rowe FJ, Hanna K, Evans JR, Noonan CP, Garcia-Finana M, Dodridge CS, et al. Interventions for eye movement disorders due to acquired brain injury. The Cochrane database of systematic reviews. 2018;3:Cd011290.
59. Thiagarajan P, Ciuffreda KJ. Effect of oculomotor rehabilitation on accommodative responsivity in mild traumatic brain injury. *Journal of rehabilitation research and development.* 2014;51(2):175-91.
60. Simpson-Jones ME, Hunt AW. Vision rehabilitation interventions following mild traumatic brain injury: a scoping review. *Disability and rehabilitation.* 2018:1-17.
61. Ciuffreda KJ, Rutner D, Kapoor N, Suchoff IB, Craig S, Han ME. Vision therapy for oculomotor dysfunctions in acquired brain injury: a retrospective analysis. *Optometry (St Louis, Mo).* 2008;79(1):18-22.
62. Mucha A, Fedor S, DeMarco D. Vestibular dysfunction and concussion. *Handbook of clinical neurology.* 2018;158:135-44.
63. Schow T, Harris P, Teasdale TW, Rasmussen MA. Evaluation of a four month rehabilitation program for stroke patients with balance problems and binocular visual dysfunction. *NeuroRehabilitation.* 2016;38(4):331-41.

64. Thiagarajan P, Ciuffreda KJ, Capo-Aponte JE, Ludlam DP, Kapoor N. Oculomotor neurorehabilitation for reading in mild traumatic brain injury (mTBI): an integrative approach. *NeuroRehabilitation*. 2014;34(1):129-46.
65. Rowe F, Wright D, Brand D, Jackson C, Price A, Walker L, et al. Reading difficulty after stroke: ocular and non ocular causes. *International journal of stroke : official journal of the International Stroke Society*. 2011;6(5):404-11.
66. Goodrich GL, Flyg HM, Kirby JE, Chang CY, Martinsen GL. Mechanisms of TBI and visual consequences in military and veteran populations. *Optometry and vision science : official publication of the American Academy of Optometry*. 2013;90(2):105-12.
67. Schuett S, Heywood CA, Kentridge RW, Dauner R, Zihl J. Rehabilitation of reading and visual exploration in visual field disorders: transfer or specificity? *Brain : a journal of neurology*. 2012;135(Pt 3):912-21.
68. Magone MT, Kwon E, Shin SY. Chronic visual dysfunction after blast-induced mild traumatic brain injury. *Journal of rehabilitation research and development*. 2014;51(1):71-80.
69. Schuett S. The rehabilitation of hemianopic dyslexia. *Nature reviews Neurology*. 2009;5(8):427-37.
70. Griffiths GG, Sohlberg MM, Kirk C, Fickas S, Biancarosa G. Evaluation of use of reading comprehension strategies to improve reading comprehension of adult college students with acquired brain injury. *Neuropsychological rehabilitation*. 2016;26(2):161-90.
71. Teasdale GM, Pettigrew LE, Wilson JT, Murray G, Jennett B. Analyzing outcome of treatment of severe head injury: a review and update on advancing the use of the Glasgow Outcome Scale. *Journal of neurotrauma*. 1998;15(8):587-97.
72. Kerkhoff G, Schaub J, Zihl J. [Anamnesis of brain-originated vision disorders]. *Der Nervenarzt*. 1990;61(12):711-8.
73. Wilhelmsen GB. Å se er ikke alltid nok: synsforstyrrelser etter hjerneskader og mulige tiltak: Unipub; 2003.
74. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta psychiatrica Scandinavica*. 1983;67(6):361-70.
75. Johansson B, Starmark A, Berglund P, Rodholm M, Ronnback L. A self-assessment questionnaire for mental fatigue and related symptoms after neurological disorders and injuries. *Brain injury*. 2010;24(1):2-12.
76. Rouse MW, Borsting EJ, Mitchell GL, Scheiman M, Cotter SA, Cooper J, et al. Validity and reliability of the revised convergence insufficiency symptom survey in adults. *Ophthalmic & physiological optics : the journal of the British College of Ophthalmic Opticians (Optometrists)*. 2004;24(5):384-90.
77. Rowe FJ, Hepworth LR, Howard C, Hanna KL, Cheyne CP, Currie J. High incidence and prevalence of visual problems after acute stroke: An epidemiology study with implications for service delivery. *PloS one*. 2019;14(3):e0213035.
78. Reddy AVC, Mani R, Selvakumar A, Hussaindeen JR. Reading eye movements in traumatic brain injury. *Journal of optometry*. 2020;13(3):155-62.
79. Katz BJ, Digre KB. Diagnosis, pathophysiology, and treatment of photophobia. *Survey of ophthalmology*. 2016;61(4):466-77.

80. Nosedá R, Copenhágen D, Burstein R. Current understanding of photophobia, visual networks and headaches. *Cephalalgia : an international journal of headache*. 2019;39(13):1623-34.
81. Nosedá R, Kainz V, Jakubowski M, Gooley JJ, Saper CB, Digre K, et al. A neural mechanism for exacerbation of headache by light. *Nature neuroscience*. 2010;13(2):239-45.
82. Clark J, Hasselfeld K, Bigsby K, Divine J. Colored Glasses to Mitigate Photophobia Symptoms Posttraumatic Brain Injury. *Journal of athletic training*. 2017;52(8):725-9.
83. Albilali A, Dilli E. Photophobia: When Light Hurts, a Review. *Current neurology and neuroscience reports*. 2018;18(9):62.
84. Ambika S, Atiya A, Ravi A, Mani R, Bhattacharya B, Praveen S, et al. Visual profile of acquired brain injury in Indian cohort: a retrospective study. *Brain injury*. 2020:1-7.
85. Rowe FJ, Wright D, Brand D, Jackson C, Harrison S, Maan T, et al. A prospective profile of visual field loss following stroke: prevalence, type, rehabilitation, and outcome. *BioMed research international*. 2013;2013:719096.
86. Pouget MC, Levy-Bencheton D, Prost M, Tilikete C, Husain M, Jacquin-Courtois S. Acquired visual field defects rehabilitation: critical review and perspectives. *Annals of physical and rehabilitation medicine*. 2012;55(1):53-74.
87. Zangemeister WH, Oechsner U, Freksa C. Short-term adaptation of eye movements in patients with visual hemifield defects indicates high level control of human scanpath. *Optometry and vision science : official publication of the American Academy of Optometry*. 1995;72(7):467-77.
88. Moller MC, Nordin LE, Bartfai A, Julin P, Li TQ. Fatigue and Cognitive Fatigability in Mild Traumatic Brain Injury are Correlated with Altered Neural Activity during Vigilance Test Performance. *Frontiers in neurology*. 2017;8:496.
89. Staub F, Bogousslavsky J. Fatigue after stroke: a major but neglected issue. *Cerebrovascular diseases (Basel, Switzerland)*. 2001;12(2):75-81.
90. Beaulieu-Bonneau S, Ouellet MC. Fatigue in the first year after traumatic brain injury: course, relationship with injury severity, and correlates. *Neuropsychological rehabilitation*. 2016:1-19.
91. Coubard OA. Eye Movement Desensitization and Reprocessing (EMDR) re-examined as cognitive and emotional neuroentrainment. *Frontiers in human neuroscience*. 2014;8:1035.
92. Meadmore KL, Exell TA, Burridge JH, Hughes AM, Freeman CT, Benson V. Upper limb and eye movement coordination during reaching tasks in people with stroke. *Disability and rehabilitation*. 2018;40(20):2424-32.
93. Schaadt AK, Schmidt L, Reinhart S, Adams M, Garbacenkaite R, Leonhardt E, et al. Perceptual Relearning of Binocular Fusion and Stereoacuity After Brain Injury. *Neurorehabilitation and neural repair*. 2014;28(5):462-71.
94. Berthold-Lindstedt M, Johansson J, Ygge J, Borg K. How to assess visual function in acquired brain injury-Asking is not enough. *Brain and behavior*. 2020:e01958.

95. Johansson J, Berthold Lindstedt M, Borg K. Vision therapy as part of neurorehabilitation after acquired brain injury - a clinical study in an outpatient setting. *Brain injury*. 2020;1-8.
96. Schaadt AK, Schmidt L, Reinhart S, Adams M, Garbacenkaite R, Leonhardt E, et al. Perceptual Relearning of Binocular Fusion and Stereoacuity After Brain Injury. *Neurorehabilitation and neural repair*. 2014;28(5):462-71.
97. Alvarez TL, Kim EH, Vicci VR, Dhar SK, Biswal BB, Barrett AM. Concurrent vision dysfunctions in convergence insufficiency with traumatic brain injury. *Optometry and vision science : official publication of the American Academy of Optometry*. 2012;89(12):1740-51.
98. Ciuffreda KJ, Kapoor N, Rutner D, Suchoff IB, Han ME, Craig S. Occurrence of oculomotor dysfunctions in acquired brain injury: a retrospective analysis. *Optometry (St Louis, Mo)*. 2007;78(4):155-61.
99. Conrad JS, Mitchell GL, Kulp MT. Vision Therapy for Binocular Dysfunction Post Brain Injury. *Optometry and vision science : official publication of the American Academy of Optometry*. 2017;94(1):101-7.
100. Capó-Aponte JE, Urosevich TG, Temme LA, Tarbett AK, Sanghera NK. Visual dysfunctions and symptoms during the subacute stage of blast-induced mild traumatic brain injury. *Military medicine*. 2012;177(7):804-13.
101. Ettenhofer ML, Hershaw JN, Engle JR, Hungerford LD. Saccadic impairment in chronic traumatic brain injury: examining the influence of cognitive load and injury severity. *Brain injury*. 2018;32(13-14):1740-8.
102. Rowe FJ, Hepworth LR, Hanna KL, Howard C. Visual Impairment Screening Assessment (VISA) tool: pilot validation. *BMJ Open*. 2018;8(3):e020562.
103. Pollock A, Hazelton C, Rowe FJ, Jonuscheit S, Kernohan A, Angilley J, et al. Interventions for visual field defects in people with stroke. *The Cochrane database of systematic reviews*. 2019;5(5):Cd008388.
104. Hanna KL, Hepworth LR, Rowe FJ. The treatment methods for post-stroke visual impairment: A systematic review. *Brain and behavior*. 2017;7(5):e00682.
105. Hanna KL, Hepworth LR, Rowe F. Screening methods for post-stroke visual impairment: a systematic review. *Disability and rehabilitation*. 2017;39(25):2531-43.
106. Grasso PA, Gallina J, Bertini C. Shaping the visual system: Cortical and subcortical plasticity in the intact and the lesioned brain. *Neuropsychologia*. 2020:107464.
107. Nordin LE, Moller MC, Julin P, Bartfai A, Hashim F, Li TQ. Post mTBI fatigue is associated with abnormal brain functional connectivity. *Scientific reports*. 2016;6:21183.
108. Delazer M, Sojer M, Ellmerer P, Boehme C, Benke T. Eye-Tracking Provides a Sensitive Measure of Exploration Deficits After Acute Right MCA Stroke. *Frontiers in neurology*. 2018;9:359.
109. Debacker J, Ventura R, Galetta SL, Balcer LJ, Rucker JC. Neuro-ophthalmologic disorders following concussion. *Handbook of clinical neurology*. 2018;158:145-52.
110. Urosevich TG, Boscarino JJ, Hoffman SN, Kirchner HL, Figley CR, Adams RE, et al. Visual Dysfunction and Associated Co-morbidities as Predictors of Mild Traumatic

Brain Injury Seen Among Veterans in Non-VA Facilities: Implications for Clinical Practice. *Military medicine*. 2018;183(11-12):e564-e70.

111. Nowak MK, Bevilacqua ZW, Ejima K, Huibregtse ME, Chen Z, Mickleborough TD, et al. Neuro-Ophthalmologic Response to Repetitive Subconcussive Head Impacts: A Randomized Clinical Trial. *JAMA ophthalmology*. 2020;138(4):350-7.

112. Ventura RE, Jancuska JM, Balcer LJ, Galetta SL. Diagnostic tests for concussion: is vision part of the puzzle? *Journal of neuro-ophthalmology : the official journal of the North American Neuro-Ophthalmology Society*. 2015;35(1):73-81.

113. Shepherd D, Landon J, Kalloor M, Barker-Collo S, Starkey N, Jones K, et al. The association between health-related quality of life and noise or light sensitivity in survivors of a mild traumatic brain injury. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation*. 2020;29(3):665-72.

## **SUPPLEMENT:**

1. Vision Interview (VI), used in study I and II.
2. Vision interview (VI) used in study III and IV.