



VISION-RELATED SYMPTOMS AFTER ACQUIRED BRAIN INJURY AND THE ASSOCIATION WITH MENTAL FATIGUE, ANXIETY AND DEPRESSION*

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Background: Brain injury causes multiple symptoms. Among these, visual disturbances are common; 50–70% of patients experience some change in vision after injury/illness. Other very common and disabling symptoms are fatigue, anxiety and depression. This study examines whether levels of fatigue, anxiety and depression are increased if the patients also experience vision disorders.

Materials and Methods: A total of 123 patients enrolled in day care rehabilitation unit for medium-to-severe brain injury completed questionnaires about self-experienced fatigue, anxiety, depression and self-experienced level and type of visual disturbances. Symptoms of fatigue, anxiety and depression were compared with the occurrence of visual disturbances. Analyses were performed using binary logistic regression.

Results: An association was found between visual symptoms and fatigue, but not between visual symptoms and anxiety/depression. However, some visual symptoms, such as glare, blurred vision and reading difficulties, showed great differences between patients with or without anxiety/depression.

Conclusion: Vision rehabilitation may be a tool for mitigating fatigue after acquired brain injury.

Key words: vision disorder; mental fatigue; anxiety; depression; traumatic brain injury; stroke.

Accepted May 17, 2019; Epub ahead of print Jun 5, 2019

J Rehabil Med 2019; 51: 499–505

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Acquired brain injury (ABI) is known to give rise to a diversity of symptoms that interact with everyday life and reduce abilities for social communication and work. Among these, mental fatigue, depression and anxiety stand out as both common and important, causing poor functional outcome (1, 2). The prevalence of fatigue, anxiety and depression after ABI differ in different studies but are always high; a range of 21–71% for fatigue (1, 3, 4), 17–29% for anxiety (5), and 23–50% for depression (6, 7). Many reports have also shown associations between these symptoms

LAY ABSTRACT

Brain injury causes multiple symptoms. Among these, visual disturbances are common; 50–70% of patients experience some change in their vision after injury/illness. Other very common and disabling symptoms are fatigue, anxiety and depression. This study discusses whether the levels of fatigue, anxiety and depression are increased if the patients also experience vision disorders. A total of 123 patients enrolled in a day care rehabilitation unit for medium-to-severe brain injury completed questionnaires about self-experienced fatigue, anxiety, depression and self-experienced level and type of vision disturbances. Symptoms of fatigue, anxiety and depression were compared with the occurrence of visual disturbances. There was an association between visual disturbances and fatigue, but not between visual disturbances and anxiety/depression. However, some visual symptoms, such as glare, blurred vision and reading difficulties, showed great differences between patients with or without anxiety/depression. In conclusion, vision rehabilitation may be a tool for mitigating fatigue after acquired brain injury.

(8, 9) and the treatment of these symptoms plays an important role in neuro-rehabilitation.

A neuro-rehabilitation assessment describes the patient's functional deficits after ABI, but there is no common knowledge of how different symptoms interact. Considering the importance of managing mental fatigue, depression and anxiety in the rehabilitation process, a relevant question is: are there co-existing factors that untreated could potentially worsen these symptoms?

Vision is a key sensory-motor modality for activities such as reading, mobility and social interaction. The visual system is complex and widely distributed in the brain (10) and is therefore susceptible to injury after ABI. Studies show that 50–75% of patients experience visual dysfunction after ABI (11–13). The visual disturbances may manifest as a loss of visual field, photophobia, double vision, different types of ocular motor disturbances and visual vertigo (12, 14). The basic visual functions are the foundation for higher visual cognitive abilities, social interactions and motor skills and may influence mental fatigue, depression and anxiety (15).

Mental fatigue is a multi-factorial symptom and vision deficits may be one of the causes. The interference of reduced ocular motor control may affect reading and

*This article has been handled and decided upon by Chief-Editor Henk Stam

visual scanning, making them more demanding (16). An inability to exert visual accommodation for longer periods or to shift accommodation consumes more energy and increases the effort required as supported by experimental studies (17, 18). In these studies the subjects were still able to read normally; however, with greater strain, manifesting as increased visual symptoms.

The visual system is highly integrated in the processes of cognition and emotion and it is possible that interference with the visual system may lead to increased levels of depression and anxiety (19, 20). Goodrich et al. described differences in visual symptoms in patients with traumatic brain injury (TBI) or both TBI and post-traumatic stress disorder (PTSD). The groups were rather similar regarding visual symptoms, although the TBI-PTSD patients reported more light sensitivity and more reading problems (21). Another treatment relating the vision and emotion is Eye Movement Desensitization and Reprocessing (EMDR), which is a method used for PTSD, in which horizontal eye movements are used as a tool for the treatment (22).

With this background, the aim of this study was to explore whether visual-related symptoms in ABI are associated with self-perceived mental fatigue, anxiety or depression and, if there is an association, whether this supports further investigations and the development of potential interventions.

MATERIALS AND METHODS

Participants

A total of 165 consecutive patients, admitted to the outpatient neuro-rehabilitation clinic at Danderyd University Hospital, Stockholm, Sweden, during the period September 2011 to June 2013, were recruited to the study. The clinic offers a team-based neurorehabilitation, both assessments and day-care rehabilitation, for moderate-to-severe brain-injured patients, including visual assessment with the Vision Interview (VI). Seventeen patients were excluded due to severe aphasia ($n=5$), incomplete admission ($n=7$) or another diagnosis showing similar symptoms as after brain injury, but not caused by brain injury ($n=5$). Of the 148 remaining patients, 123 had answered all 3 questionnaires and were included in the analysis. A total of 145 answered the Vision Interview (VI), 123 answered the Mental Fatigue Scale (MFS), and 132 answered the Hospital Anxiety and Depression Scale (HADS). The severity of the brain injury was measured with the Glasgow Outcome Scale Extended

(GOSE) a well-documented and valid scale (23). The severity of injury ranged between grade 4 and grade 7 (GOSE 4: 4.1%, GOSE 5: 49.6%, GOSE 6: 42.3%, GOSE 7: 4.1%).

The brain injuries included diagnoses such as stroke, traumatic brain injury (TBI), subarachnoid haemorrhage (SAH), infection, tumour and other diagnoses. The concept, Other diagnoses, included sinus thromboses, dissection of the vertebral artery, NMDA-receptor encephalitis, severe epilepsy, surgery of a foramen of Monroe cyst, cognitive dysfunction after cytostatic treatment, deterioration after previous stroke, and 2 patients with anoxic brain injury (Table I). SAH, infection, and tumour (mainly meningioma) were treated as a single group due to a small number of patients with each diagnosis, but also due to their similarities in clinical characteristics.

The patients were divided into 3 age groups, considering the different demands in life; age 18–34 years (start up your own life, starting a family), age 35–54 years (active working period, active family time with great responsibilities and different demands), and age 55–65 years (children move away, work is established, higher risk of other diseases). Demographic data are shown in Table I.

This article is the third report from a cross-sectional study of patients with ABI admitted for neuro-rehabilitation (13, 24).

Assessment methods

Visual-related symptoms were assessed with the Vision Interview (VI), which is an adapted and translated version of “Die Anamnese Zerebral betingter Sehestörungen” (25), intended to pick up visual disturbances after ABI and described in detail previously (13). The VI has 18 questions, 16 of which cover the most common visual symptoms and their influence on visual-based activities. The remaining 2 questions are more general; one concerns whether the patient has experienced visual changes and the other whether a previous visual examination has been performed after injury/illness. The interview was conducted by the physician during admission and the answers are dichotomous; yes/no. The outcome of the VI was calculated to a score, between 0 and 17. The question concerning whether an examination had been performed was not included in the score. The responses to the other questions, 1–17, were assigned a value of 0 if answered No (symptom not experienced) and 1 if answered Yes (symptom experienced).

During the assessment, standard validated self-assessment instruments were used routinely. The MFS and HADS (26–28) evaluate the patients’ perceived levels of fatigue, depression and anxiety. MFS is used mainly in patients after stroke and TBI. MFS includes 15 questions, one of which is analysed separately (26). The other 14 questions are graded between 0 and 3, and the maximum sum of the test is 42. The sum is valued as no problems (0–10), mild mental fatigue (10.5–14.5), moderate mental fatigue (15–20), and severe mental fatigue (20.5–42) (25). In this study a cut-off value of 15 points was applied, corresponding to moderate–severe fatigue.

Table I. Patient demographics

Diagnosis	Total <i>n</i>	Male/Female <i>n</i>	Age, years		Time range post-injury, months	
			Mean (SD)	Range	Mean (SD)	Range
Stroke	57	40/17	51.5 (10.3)	21–65	6.1 (5.3)	1–30
TBI	33	19/14	39.0 (13.6)	19–65	10.3 (4.7)	1–62
SAH, Infection, Tumour	24	5/19	47.4 (11.7)	19–65	7.1 (4.5)	3–18
Other	9	3/6	41.7 (15.7)	20–62	7.9 (6.4)	2–18
Total	123	67/56	46.6 (13.0)	19–65	7.6 (8.9)	1–62

TBI: traumatic brain injury; SAH: subarachnoid haemorrhage; SD: standard deviation.

The HADS includes 14 items; 7 items are depression grades and 7 are anxiety grades (27). Each item is graded 0–3; the maximum sum for anxiety is 21 and the same for depression. A total score of 0–7 indicates no problems, 8–10 indicates possible anxiety or depression, and 11–21 indicates depression or anxiety. In this study a cut-off value of 8 points was applied, corresponding to possible symptoms of depression and anxiety.

Statistical analysis

All analysis was performed using SPSS 23. Mann–Whitney *U* test and Kruskal–Wallis test were used to compare outcome values between sex and diagnosis groups, respectively. Pearson χ^2 or Fisher’s exact tests were used for analysis of cross-tabulations of frequencies. Binary logistic regression was performed with the purpose of exploring factors affecting the likelihood that the patients had clinically significant mental fatigue (MFS \geq score 15), anxiety (HADS-A \geq score 8) or depression (HADS-D \geq score 8). The dependent variables (MFS, HADS-A, HADS-D) were treated as dichotomous values based on the cut-off scores. The binary logistic regression was conducted in 2 model blocks; the null model with no predictors and the model with all independent variables added according to the Enter method. The Nagelkerke R^2 method was applied to calculate the explained variation.

Ethical considerations

The study was approved by the Regional Ethic Board of Stockholm, Sweden, (Dnr. 2013/157-31/3), were performed according to the principles of the Declaration of Helsinki 1978.

RESULTS

The analysis and reporting of the results is based on the patients who had complete data for VI, MFS, HADS-A and HADS-D ($n=123$). Of the 123 patients 100 patients (81.3%) had experienced some visual-related symptoms according to the VI (median VI score 4, range 1–15 while the rest of the patients (18.7%) did not report any symptoms). Men scored median 3 (range 0–15) while women scored median 4 (range 0–10) (Mann–Whitney *U* test, $p=0.026$). No statistically significant associations were found between age group or diagnosis group and VI score (Kruskal–Wallis).

Sixty-four patients (52.1%) scored 15 or higher on the MFS, indicating the presence of moderate (28.5%) to severe (23.6%) mental fatigue. A total of 52 patients (42.3%) scored 8 or more on HADS-A, indicating “possible anxiety” (18.7%) or “anxiety” (23.6%). A total of 42 patients (34.1%) scored 8 or more on HADS-D, indicating “possible depression” (18.7%) or “depression” (15.4%).

Analysis of the different diagnoses’ groups showed MFS scores of 15 or higher in 66.7% of patients with TBI, 66.7% of patients with SAH/infection/tumour, and 55.6% of other, but only 36.8% of stroke patients.

Anxiety (HADS-A ≥ 8) was found in 40.4% of stroke patients, 36.4% of TBI patients, 50.0% of SAH/

infection/tumour patients, and 55.6% of patients with other diagnoses. A corresponding score for HADS-D was found in 28.1% of stroke patients, 42.4% of TBI patients, 33.3% of SAH/infection/tumour patients, and 44.4% of patients with other diagnoses.

Some of the questions in the VI showed a marked difference between those who had or had not experienced symptoms of mental fatigue, anxiety or depression. (Fig. 1) The questions that differed the most concerned reading disturbances, blurred vision, light sensitivity, needing more light while reading, and a generally higher need for light to see well, or an increased tendency to bump into objects (Fig. 1)

Univariate analyses of the VI score showed significant associations with MFS and HADS. There were also statistically significant associations between demographics factors (sex, age-group, diagnosis) and MFS and between HADS-A and HADS-D. It was therefore decided to include demographics in addition to VI score as independent variables in the logistic regression models.

Mental fatigue

The logistic regression model was statistically significant ($\chi^2 71.138$, $df=8$, $p=0.000$). The model explained 58.6% of the variance (Nagelkerke R^2) and correctly classified 82.9% of the cases. Increasing VI score and HADS-D exceeding cut-off (≥ 8) were associated with an increased likelihood of exhibiting mental fatigue (Table II).

Anxiety

The logistic regression model was statistically significant ($\chi^2 53.092$, $df=8$, $p=0.000$). The model explained 47.1% of the variance (Nagelkerke R^2) and correctly classified 79.7% of cases. Diagnosis TBI, and HADS-D

Table II. Logistic regression predicting the likelihood of mental fatigue (MFS ≥ 15) based on sex, age group, diagnosis group, Visual Interview score, HADS-A and HADS-D. Sex is for females compared with males, diagnosis group is compared with stroke

Variable	Wald	Df	Odds ratio	Significance
Sex, 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

TBI: traumatic brain injury; SAH: subarachnoid haemorrhage; HADS-A: Hospital Anxiety and Depression Scale anxiety; HADS-D: Hospital Anxiety and Depression Scale depression; VI: Visual Interview; MFS: Mental Fatigue Scale; Inf./Tum.: Infection/Tumour.

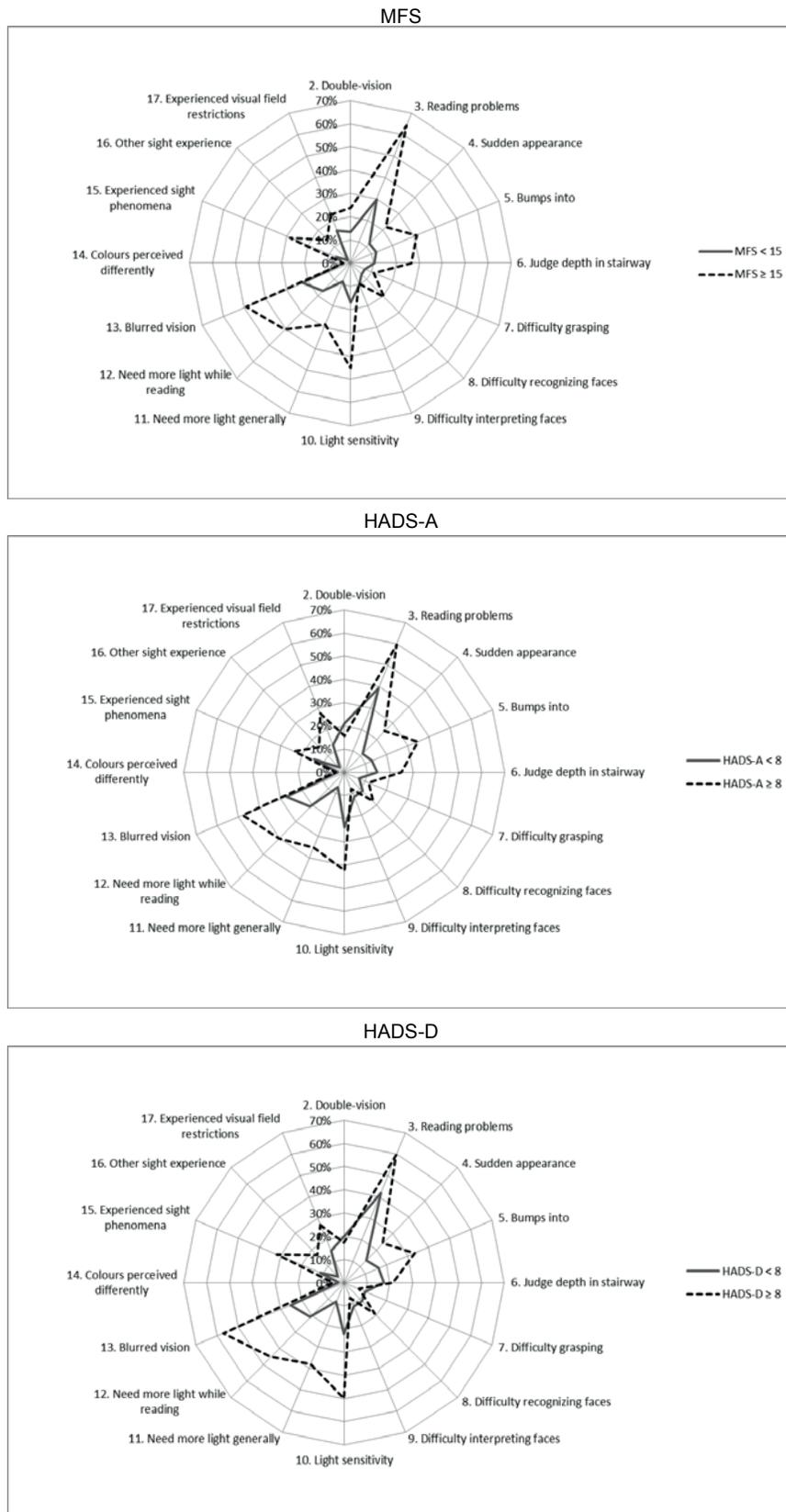


Fig. 1. Share of patients responding “yes” to each symptom in the Visual Interview (VI) depending on whether exhibiting mental fatigue (top), anxiety (middle), or depression (bottom). MFS: Mental Fatigue Scale; HADS-A: Hospital Anxiety and Depression Scale-anxiety; HADS-D: Hospital Anxiety and Depression Scale-depression.

Table III. Logistic regression predicting likelihood of anxiety (HADS-A ≥ 8) based on sex, age group, diagnosis group, visual interview score, mental fatigue (MFS ≥ 15) and depression (HADS-D ≥ 8). Sex is for females compared with males, diagnosis group is compared with stroke

Variable	Wald	Df	Odds ratio	Significance
Sex, female	0.021	1	1.076	0.885
Age group	0.598	1	0.762	0.439
Diagnosis, stroke	4.907	3		0.179
Diagnosis, TBI	4.117	1	0.233	0.042
Diagnosis SAH/Inf./Tum.	0.034	1	0.884	0.853
Diagnosis, other	0.036	1	1.209	0.849
VI score	1.487	1	1.105	0.223
HADS-D	16.201	1	9.749	0.000
MFS	3.781	1	3.071	0.052
Constant	1.626	1	0.302	0.202

TBI: traumatic brain injury; SAH: subarachnoid haemorrhage. HADS-A: Hospital Anxiety and Depression Scale anxiety; HADS-D: Hospital Anxiety and Depression Scale depression; VI: Visual Interview; MFS: Mental Fatigue Scale; Inf./Tum.: Infection/Tumour.

exceeding cut-off (≥ 8), was associated with an increased likelihood of exhibiting anxiety (Table III).

Depression

The logistic regression model was statistically significant ($\chi^2 64.394$, $df=8$, $p=0.000$). The model explained 56.4% of the variance (Nagelkerke R^2) and correctly classified 82.1% of the cases. MFS and HADS-A exceeding cut-off (≥ 8) was associated with an increased likelihood of exhibiting depression (Table IV).

DISCUSSION

The aim of this study was to determine whether there is an association between increased levels of self-reported visual deficits in patients with ABI and increased levels of self-reported mental fatigue, depression and anxiety. The study was observational and performed at a neurorehabilitation centre. The patients had mixed diagnoses dominated by stroke. As a rule, studies are

Table IV. Logistic regression predicting likelihood of depression (HADS-D ≥ 8) based on sex, age group, diagnosis group, Visual Interview score, mental fatigue, and anxiety. Sex is for females compared with males, diagnosis group is compared with stroke

Variable	Wald	Df	Odds ratio	Significance
Sex, female	0.248	1	0.749	0.618
Age group	0.216	1	1.201	0.642
Diagnosis, stroke	1.551	3		0.671
Diagnosis, TBI	0.647	1	1.830	0.421
Diagnosis SAH/Inf./Tum.	0.291	1	0.665	0.589
Diagnosis, other	0.024	1	1.196	0.878
VI score	0.861	1	1.081	0.354
HADS-A	15.936	1	9.702	0.000
MFS	12.285	1	10.971	0.000
Constant	10.440	1	0.016	0.001

TBI: traumatic brain injury; SAH: subarachnoid haemorrhage. HADS-A: Hospital Anxiety and Depression Scale anxiety; HADS-D: Hospital Anxiety and Depression Scale depression; VI: Visual Interview; MFS: Mental Fatigue Scale; Inf./Tum.: Infection/Tumour.

directed towards a single diagnosis, mostly stroke or TBI. Our starting point was that vision processing is so widely spread in the brain that it should be susceptible to injury in most of the diagnoses of ABI that present at a neurorehabilitation centre.

The prevalence of mental fatigue, (52%), anxiety, (42%) and depression, (34%) were in line with other studies (1, 3, 5, 6), and in conformity with other studies (8, 9), we found an association between mental fatigue and depression and between depression and anxiety.

Visual deficits

Eight out of 10 of the patients experienced visual-related symptoms. The most frequent symptoms were reading difficulties, blurred vision, light sensitivity, increased need for light and an increased tendency to bump into objects or persons. These symptoms may be related to reduction in visual acuity, visual field defects, reduced contrast vision, ocular health issues and ocular motor problems, including eye alignment and accommodation. Thus, a more thorough examination is necessary to determine the background to the symptoms. This also highlights the need to have a care plan that incorporates an optometrist/ophthalmologist/orthoptist for further assessment to avoid basic visual function issues being overlooked. Rowe et al. (29) point out that integration of a vision specialist in the neurorehabilitation team is a key factor to obtain successful rehabilitation. This is also highlighted in patients with combat injuries, as described in an article by Brahm et al. (30), and in the conceptual model of vision rehabilitation formed by American Congress of Rehabilitation Medicine (ACRM) (31).

Visual deficits and fatigue

Mental fatigue after ABI is a multifactorial symptom with no general definition. Staub et al. (32) define mental fatigue as: “a feeling of early exhaustion developing during mental activity, with weariness, lack of energy, and aversion to effort”. Mental fatigue is a subjective experience and difficult to define in research, although it is a huge problem for patients with ABI. A statistically significant association between increased levels of self-reported visual deficits and self-reported moderate-to-severe mental fatigue was, however, found in this study. There are few earlier studies available with which to compare the present findings, but the result is in line with the follow-up study by Sand et al. (33) and the study by Schow et al. (34). In these studies, an association between fatigue and visual dysfunctions was described. It is also known that ocular motor deficits and the efforts associated with attempts to overcome these, may lead

to asthenopic symptoms and visual fatigue (17). Another aspect is the reduced accuracy and automaticity in eye movements. Clear and single vision, which is normally maintained subconsciously, tends to be less perseverant and more variable in patients with ABI and to require conscious mental effort to compensate. Thus, this may have a negative impact on mental capacity and endurance. This is further supported by the results of the study by Show et al. (35), showing reduced fatigue following a rehabilitation programme including visual rehabilitation of ocular motor dysfunctions.

Whether ocular motor disorder is a consequence of mental fatigue or an isolated aspect that contributes to the level of mental fatigue needs to be further elaborated. However, the findings of the present study open opportunities for further research into the role of visual function as a component in mental fatigue.

Visual deficits and anxiety/depression

There was no significant association between increased visual deficits and high levels of depression and anxiety in the present study. Univariate analysis showed a significant association between VI score and HADS, but this significance disappeared on adjustment with the factors in the logistic regression model. However, Gall et al. (36) examined 122 patients with visual field defects after stroke. The level of distress was increased and increased further if other sensory systems were injured. In the study by Sand et al. (33) an association between vision dysfunction and both depression and anxiety was described.

The characteristics of the visual symptoms differed between those with or without anxiety/depression, particularly regarding reading difficulties, blurred vision, light sensitivity, light-dependent issues, and an increased tendency to bump into objects or persons. Goodrich et al. (21) found that the TBI-PTSD group experienced more problems, especially regarding light sensitivity and reading difficulties. These symptoms are among those with the highest diversity in our study, and one may speculate that there might be an association between certain visual symptoms and anxiety/depression.

Limitations

Fifteen percent of the patients did not return the MFS questionnaire and 10% did not return the HADS. Completing and returning a questionnaire may be too demanding for patients with cognitive and/or emotional deficits, and this may conceal that there was a selection of more active patients with less mental fatigue, depression and anxiety.

As pointed out above, patients with different diagnoses and a diversity of visual symptoms and

dysfunctions were included in the present study. The diagnoses differ in number. This may have influenced the result; however, we believe that the main results are valid for the 2 main diagnoses, i.e. TBI and stroke.

Conclusion

Finally, both visual disturbances and mental fatigue are common after ABI. The current study found an association between increased number of visual symptoms and increasing mental fatigue. Thus, visual-related symptoms should be considered in the management of mental fatigue. These findings warrant further elaboration, and it is possible that vision rehabilitation is a tool to mitigate mental fatigue.

ACKNOWLEDGEMENTS

The authors would like to thank the team at Huddinge for help and support. This study was founded by Stiftelsen Torsnspiran, Strokeförbundet and the community of Stockholm.

The authors have no conflicts of interest to declare.

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