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Evaluation of the Mental Fatigue Scale and its relation to Cognitive and Emotional Functioning after Traumatic Brain Injury or Stroke

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Abstract

Objective: After traumatic brain injury (TBI) or stroke, long-term mental fatigue may occur with significant impact on work and social interactions. With the intention to measure mental fatigue irrespective of neurological illness, we developed the Mental Fatigue Scale (MFS). The scale incorporates affective, cognitive and sensory symptoms, duration of sleep and daytime variation in symptom severity. In this study, we evaluated the MFS and its relationship to cognitive and emotional functions.

Participants: Healthy controls and well-rehabilitated subjects suffering from mental fatigue after mild TBI, TBI or stroke (age 19-69) were included in the study.

Results: The results showed MFS to be invariant to age, gender and education. A cutoff score at 10.5 is suggested. Of the cognitive functions measured, information processing speed was found to be a significant predictor for the rating on MFS. We found that a significant effect on depression between controls and brain injured subjects can be a misleading conclusion if the effect of mental fatigue is not considered.

Conclusions: We suggest MFS to be linked to mental impairment after brain injury. This study also demonstrated that mental fatigue must be treated as a separate construct and should not be mixed up with depression or anxiety.

Keywords: Mental fatigue; Cognition; Depression; Stroke; Traumatic brain injury

Introduction

Mental fatigue is a common symptom following Traumatic Brain Injury (TBI), or stroke. In the case of long-lasting mental fatigue, the mental fatigue could be one important factor that keeps people from returning to the full range of activities they pursued prior to their injury with work, studies and social activities. Mental fatigue is no illness, rather it represents a mental sequel probably due to disturbance of higher brain functions, either physical or psychological in origin. It is included in, and defined within the diagnoses Mild cognitive impairment (F06.7), Neurasthenia (F48.0) and Posttraumatic brain syndrome (F07.2) [1].

Annually, about 100-300/100 000 sustain a TBI and most of the injuries are mild [2]. Fatigue is one of the most important long-lasting symptoms, but it is difficult to arrive at any clear figure as to how common fatigue or especially mental fatigue is, since different results have been obtained due to differences in definitions and methodological differences between the studies. A majority of patients recover within one to three months after a mild TBI [3,4]. Improvement from fatigue has been reported during the first year following TBI, after which time the improvement has been limited [5]. In follow-up studies, the frequency of prolonged fatigue varies between 16 and 73% [6-9]. Fatigue is also commonly reported after stroke, irrespective of severity [10-16]. However, there is great variation in the level of suffering between individuals. Furthermore, there is no correlation between persistent fatigue and severity of the primary injury [17]. Fatigue is also commonly reported in other neurological diseases, e.g. Multiple Sclerosis, meningitis, encephalitis, and Parkinson´s disease [18-20]. Levin and Greenwald stated that fatigue should always be suspected and inquired about in patients with neurological illnesses [21].

Mental Fatigue and Cognitive Functioning

A typical feature of pathological mental fatigue after TBI or stroke is that the mental exhaustion becomes pronounced during sensory stimulation or when cognitive tasks are performed for extended periods without breaks. Another typical feature is a disproportionally long recovery time needed to restore mental energy levels after the individual has become mentally exhausted. Mental fatigue is also dependent on the total activity level as well as the demands of daily activities, and fatigue often fluctuates during the day depending on the activity. Thus, this fatigue seems to be a dynamic process with ups and downs in mental energy levels. The fatigue can appear very rapidly and, when it does, it is not possible for the affected person to continue the ongoing activity. Other common associated symptoms include: memory and concentrations problems, slowness of thinking, irritability, tearfulness, sound and light sensitivity, sensitivity to stress, sleep problems and headache [20,22].

Assessment of fatigue

There is an abundance of different scales for assessing fatigue in general and several of these scales are designed for different diseases [23,24]. Scales are developed from questions which depend on the target of the study or its focus, and may also measure different aspects of fatigue [24], for example for brain injuries [17,25,26].

We have developed the self-reporting Mental Fatigue Scale (MFS) since we were not able to find an assessment scale adapted to mental fatigue irrespective of neurological illness [27]. The MFS is based on symptoms commonly reported after TBI, tumours, infections, vascular diseases, and other brain disorders [22,28,29]. Among the symptoms we suggest mental fatigability or mental exhaustion to be the most significant symptom having considerable consequences for all aspects of life. Typical symptoms included in the mental fatigue construct suggested by us include: rapid drain of mental energy upon mental activity, impaired attention and concentration capacity over time following over-exertion, long recovery time disproportionate to the exertion level, diurnal variation of the fatigue symptom with the fatigue often being better in the mornings and worse in the afternoons and evenings; variations from one day to the next. Usually one or several associated symptoms are common: mood swings, irritability and stress intolerance, trouble with memory, sleep problems, sensitivity to, or intolerance of light and loud noise following over-exertion. Typical, associated symptoms are included in MFS and we have previously shown that the included items in MFS have a high internal consistency and are closely connected [27].

Since 2008 we have used the MFS in research and we have been able to assimilate and collect significant amounts of information which has supported our target of extending our knowledge of the scale. With the use of these data, the purpose here has been to evaluate the MFS and its connection to cognitive and emotional functioning.

Methods

This evaluation of the MFS is based on data collected in our research group. The data are taken from previously published studies and also from unpublished studies [27,30-33]. In these studies we have used the same assessments with rating scales and cognitive tests, and in this study, we have only used the baseline data taken from these studies. The studies were approved by the regional Ethics Committee in Gothenburg. The participants gave their written informed consent before the assessments.

Inclusion of subjects

The inclusion criteria were mild TBI, TBI or stroke with no other neurological or psychiatric illnesses, and having sustained the injury more than 6 months prior to inclusion. Subjects were healthy before the injury. The participants had recovered from neurological symptoms, but were suffering from pathological mental fatigue. All mild TBI participants had been diagnosed with commotion cerebri/concussion (ICD-10 S06.0). Control participants with no history of head injury, no neurological disturbance or psychiatric illness, no limitation in working capacity and of similar age, education and gender were recruited from the general community. In total, 161 brain injured patients and 121 controls were included in the study (Table 1). All participants had answered the MFS, but not all had completed the cognitive tests and the Comprehensive Psychopathological Rating Scale (CPRS) (the exact number is reported along with the results). Age differed significantly between the groups (F=6.6, p<0.001), with

the control group being slightly younger than the mild TBI and stroke group. The control group also had more years of education compared to the TBI and stroke groups (F=13.9, p<0.001) (Table 1).

Group	No	No females/ males	Age	Years since injury/stroke	Education, years
Mild TBI	106	67/39	46.4 ± 10.6	7.2 ± 6.4	14.2 ± 2.8
TBI	21	11/10	41.8 ± 12.9	11.1 ± 8.7	14.0 ± 2.7
Stroke	34	17/17	49.6 ± 9.5	7.8 ± 6.1	14.2 ± 2.5
Total brain injured	161	95/66	46.5 ± 10.8	7.8 ± 6.7	14.1 ± 2.7
Healthy controls	121	63/58	42.4 ± 16.6		16.4 ± 2.3

Table 1: Demographic data, mean and standard deviation

Self-assessment scales

The mental fatigue scale (MFS) is a multidimensional questionnaire containing 15 questions. It incorporates affective, cognitive and sensory symptoms, duration of sleep and daytime variation in symptom severity. The questions concern fatigue in general, lack of initiative, mental fatigue, mental recovery, concentration difficulties, memory problems, slowness of thinking, sensitivity to stress, increased tendency to become emotional, irritability, sensitivity to light and noise, decreased or increased sleep as well as 24-hour symptom variations [27]. Each item comprises examples of common activities to be related to four response alternatives. A rating of 0 corresponds to normal function, 1 indicates a problem, 2 a pronounced symptom and 3 a maximal symptom. The construction of the questionnaire resembles the questionnaire for the Comprehensive Psychopathological Rating Scale (CPRS) which was used in this study for depression and anxiety [34,35]. The items included are shown in Table 2.

The CPRS depression scale is also called the Montgomery-Asberg Depression Rating Scale (MADRS) [36].

Neuropsychological tests

The neuropsychological tests measured information processing speed, attention and working memory. The tests included were digit symbol coding from the WAIS-III [37], measuring information processing speed; the digit span [37], measuring working memory; the Trail Making Test (TMT) A and B measuring visual scanning, divided attention and motor speed [38]. Also a series of new trail making tests were constructed to evaluate higher demands such as dual tasks. The tests were constructed with three and four factors, respectively [30]. Months were added in part C, and both months and days of the week in chronological order in part D. In the latter, the order of letters and digits was switched.

Statistics

Analysis of variance (ANOVA), analysis of covariance (ANCOVA) and t-test were used for comparisons between the groups. The MFS, digit coding and Trail Making Test did not fulfill the criterion relating to homogenous variances when all groups were included. Non-parametric tests, namely the Kruskal-Wallis and Mann Whitney were

used for these comparisons. Bonferroni was used for post-hoc analysis and for correction of multiple comparisons. Chi-square analysis was used for nominal data. Pearson's and Spearman's were used for correlation analyses. Multiple regression analysis was used to evaluate the relationship between MFS and cognitive tests. The analysis of MFS cutoff scores was done with the computer program Singlims.exe [39]. This implements classical methods for comparison between the scores obtained in a single case and the scores obtained in a control sample. The interval estimate of the effect size for the difference between case and controls is obtained using classical methods [39,40]. Since there were four items which overlapped between MFS and CPRS, the items from the MFS and CPRS scales were analyzed by means of a principal component analysis, with varimax rotation. The intention was thus to examine the internal structure of the scales. SPSS 21.0 for Windows was used for data analysis.

Results

Mental Fatigue Scale

No significant differences were detected between females and males in any of the brain injured and control groups in relation to the rating on the MFS. No correlations between age and rating on MFS (Figure 1) and between MFS and education were found.

The cutoff score is based on the data from the control group. The analysis of MFS cutoff scores was carried out using the computer program Singlims.exe [39]. A score of 10.5 for MFS case was found to deviate significantly from the control sample (one-tailed, $p < 0.05$). A MFS score of 10.5 is also above the 99th percentile of the control group. It has been suggested that a cutoff score should be set at a MFS score of 10.5.
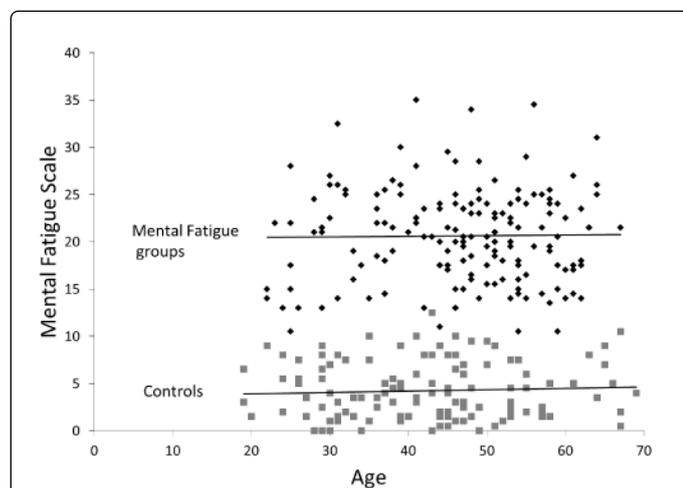
Figure 1: No significant correlation was detected between age and rating on Mental Fatigue Scale (MFS) for healthy controls and for subject suffering from long term mental fatigue after a TBI or stroke (Controls n=121; mental fatigue n=161).

The control group rated MFS significantly lower than mild TBI, TBI and stroke (Mann-Whitney, $p < 0.001$, Figure 2). When analyzing separate items of the MFS, all items were rated significantly lower by the control group compared to the brain injured groups (Kruskal-Wallis, all items $p < 0.001$, Figure 3). Figure 3 also shows how the items

are closely connected. A higher rating on one item resulted in a higher rating on the other items. The rating on 24-hour variation differed significantly between controls and brain injured groups (Chi-square, $p < 0.001$). Among the brain injured, 73% reported a clear 24-hour variation while 14% among the controls reported a clear variation during the day.
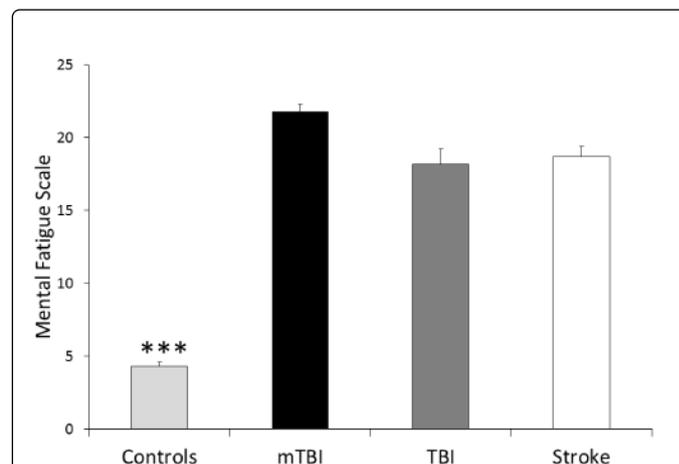
Figure 2: The control group rated the Mental Fatigue Scale (MFS) significantly lower than the mild TBI, TBI and stroke groups (*** $p < 0.001$).
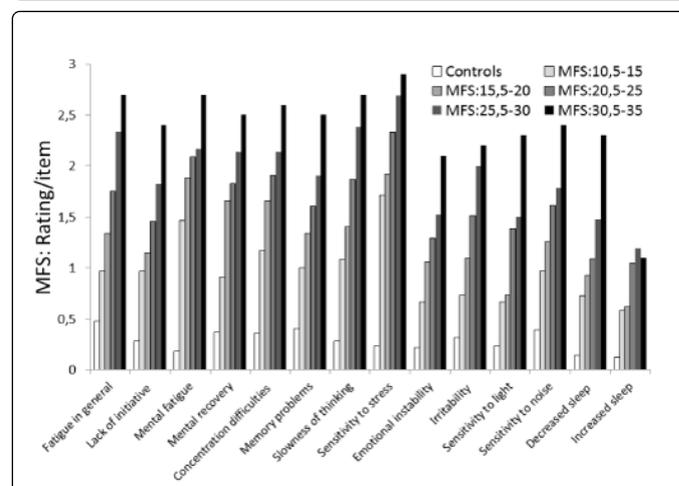
Figure 3: The figure shows ratings on all items included in Mental Fatigue Scale (MFS). The subjects are divided into six groups based on their total sum of score from MFS. A low total score on MFS also results in low rating on the other items and vice versa, indicating a close connection between the items

Depression and anxiety in relation to MFS

In total 46 controls and 113 brain injured subjects had answered both the self-rating of MFS and CPRS (mild TBI n=72, TBI n=7, stroke n=34). CPRS depression and anxiety scales were rated significantly higher for the brain injured groups compared to the controls (Log transformed, $p < 0.001$). The MFS and CPRS are constructed in the same way, making it easy to compare the ratings from both scales.

However, four items from the MFS and CPRS overlap and are exactly the same (concentration difficulties, lack of initiative, irritability and decreased sleep) and these may have confounding effects if the scales are interpreted according to sum of scores only. With the intention to examine the internal structure of the scales, a principal component analysis, with varimax rotation was done. The various indicators of factorability were good. Five components with an eigenvalue of greater than 1.0 were found. The components and the variables loaded on them are shown in Table 2. The MFS items loaded mainly on component 1, including the overlapping items, lack of initiative and concentration difficulties. Items from CPRS loaded mainly on component 2 including the overlapping item, irritability. The overlapping item, decreased sleep loaded on component 5. Pain from the CPRS anxiety scale was in this sample included in component 1. Four of the CPRS items loaded on component 3 and 4. CPRS is divided into a depression and an anxiety scale, but this division was not detected in this analysis.

Component 1	Component 2	Component 3	Component 4	Component 5
Mental fatigue	Sadness/gloominess (D)	Phobias (A)	Reduced appetite (D)	Decreased sleep (O, D, A)
Concentration difficulties (O, D)	Anxiety/feelings of inner tension (D, A)	Autonomic disturbances (A)	Concern for health (A)	Increased sleep
Slowness of thinking	Zest for life (D)			
Mental recovery	Pessimistic thoughts (D)			
Memory problems	Emotional involvement (D)			
Sensitivity to stress	Dread or anguish over trivial matters (A)			
Fatigue in general	Panic attacks (A)			
Lack of initiative (O,D)	Irritability (O, A)			
Emotional instability				
Pain (A)				
Sensitivity to noise				
Sensitivity to light				

Table 2: The items from the MFS and CPRS scales were analyzed by mean of a principal component analysis, with varimax rotation. The components and variables that load on them are shown in the figure. (D=depression, A=anxiety, O=overlapping items between MFS and CPRS)

A further comparison between controls and brain injured groups was done, and now with the sum of scores from component 1 (mental fatigue items) and component 2 (depression and anxiety items). The overlapping items no longer had any effect on both scales. Both components differed significantly between the groups, with the controls rating component 1 and component 2 lower than the brain injured groups (ANOVA, log transformed data, both components p<0.001). However, when controlling for component 1, ANCOVA and comparing the groups for component 2, there was no significant difference sustained between the controls and the brain injured groups. When doing the opposite analysis, the effect on component 1 persisted after controlling for component 2 (p<0.001). This means that removing the effect of mental fatigue, also removed the difference in depression-anxiety rating between controls and brain injured subjects, while removing the depression-anxiety effect did not have an effect on mental fatigue and the effect sustained.

Cognitive tests and relation to MFS

For the cognitive tests, 161 brain injured subjects and 86 control subjects were included in the analysis. The symbol digit coding and Trail Making Test did not fulfill the criterion relating to homogenous variances. Non-parametric tests (Kruskal-Wallis and Mann-Whitney) were used for these comparisons. The control group showed a significantly better result on all tests compared to the brain injured groups. Significant differences were found for digit symbol coding, Trail Making Test A, B, C and D, errors made in TMT C and D, digit span total score and also digit span forward and backward (Table 3).

No significant differences between the brain injured groups were detected. A multiple regression with the dependent variable MFS and the tests; TMT A, B, C, D, symbol digit coding and digit span total as predictors, using the enter method, detected a significant model (F=21.38, p<0.001). The model explained 34% of the variance (adjusted R^2=0.340). The only significant predictor among the cognitive tests was symbol digit coding (p<0.001). Symbol digit coding correlated significantly with MFS (r=-0.591, Figure 4).

Discussion

MFS

MFS was not sensitive to age, education and gender among subjects of working age. This finding was valid in Sweden both for healthy controls and subjects complaining of fatigue a long time after a TBI or stroke. A cutoff score for MFS at 10.5 is suggested. A score above 10 implicates problems, not always serious but the person should consider the current situation with work or social life. The MFS items were rated significantly higher among brain injured subjects compared

with healthy subjects. An increased rating on one item was also followed by an increase on the other items.

	MTBI (n=106)	TBI (n=21)	Stroke (n=34)	Controls (n=86)	p-value
Digit symbol coding	60.2 ± 17.3	59.9 ± 13.7	58.7 ± 12.9	81.4 ± 12.8	>0.001
TMT A, sec	44.2 ± 22.3	43.8 ± 21.8	43.9 ± 16.2	28.8 ± 9.1	>0.001
TMT B, sec	93.2 ± 47.9	85.1 ± 27.3	97.8 ± 49.6	61.0 ± 17.1	>0.001
TMT C, sec	100.4 ± 61.8	94.8 ± 33.0	95.3 ± 39.2	61.5 ± 24.5	>0.001
TMT D, sec	155.0 ± 69.6	163.9 ± 69.2	163.6 ± 53.8	102.9 ± 36.9	>0.001
TMT A errors	0.03 ± 0.17	0.00 ± 0.00	0.26 ± 0.16	0.00 ± 0.00	0.370
TMT B errors	0.28 ± 0.71	0.05 ± 0.22	0.34 ± 0.75	0.14 ± 0.38	0.123
TMT C errors	0.58 ± 0.94	0.80 ± 1.06	0.46 ± 1.126	0.28 ± 0.61	0.028
TMT D errors	1.12 ± 1.33	1.35 ± 1.50	1.30 ± 1.31	0.66 ± 0.88	0.025
Digit span	14.1 ± 4.0	14.8 ± 3.4	14.1 ± 3.4	16.4 ± 3.5	>0.001
Digit span forward	8.4 ± 2.3	8.8 ± 1.9	8.4 ± 1.7	9.6 ± 2.1	>0.001
Digit span backwards	5.7 ± 2.1	6.0 ± 1.7	5.9 ± 2.2	6.9 ± 2.2	0.001

Table 3: Cognitive tests included in the study (mean and standard deviation) and the p-value from the comparisons between groups (Kruscal-Wallis)

Figure 4: Correlation between Mental Fatigue Scale and information processing speed (symbol digit coding, r=-0.591, p<0.001)
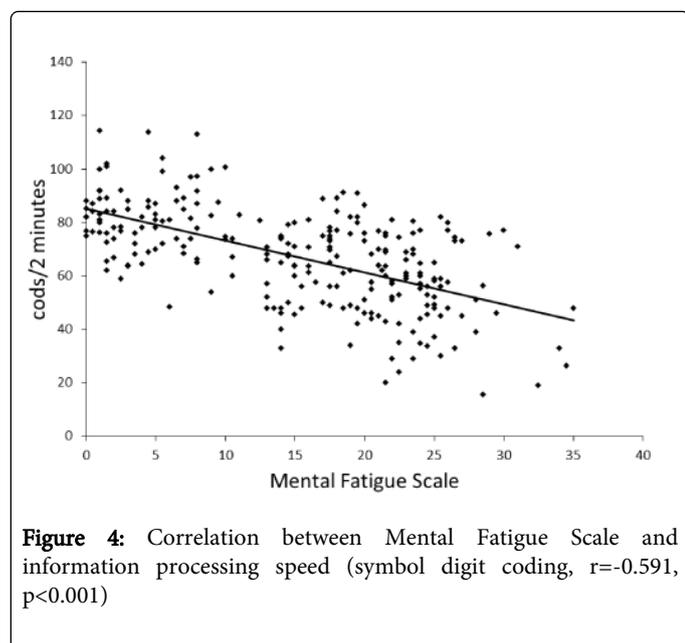
MFS and cognitive functioning

Information processing speed, attention and working memory were significantly reduced for the brain injured groups compared to controls. The more demanding TMT C and D also resulted in more errors being made by brain injured subjects compared to controls. Processing speed was also found to be a significant predictor for the rating on MFS. Impaired processing speed and attention in subjects suffering from long-term cognitive deficits after brain injury may result in an overload of the present brain capacity, with subsequent mental fatigue. Mental activities with demand on concentration appear for many persons after TBI or stroke to need more energy and brain capacity, than is usually expected [41].

It has been proposed that increased subjective mental fatigue after TBI or mild TBI correlates to poor performance in attention tests and reduced processing speed. Both slower speed and less accuracy in a selective attention task were recorded after severe TBI and a correlation was found between attention performance, subjective fatigue and subjective mental effort [42]. Azouvi and co-authors proposed that mentally-tiring activities after brain injury are related to reduced resources and that patients with brain injury also describe mental activity as more energy-demanding than healthy subjects [43]. TBI subjects also performed slower on a complex attention test, made more errors and reported a higher level of subjective fatigue [44]. Their performance was slower, but remained on the same level during a vigilance test, and a higher fatigue rating was attributed to more errors [45]. Furthermore, practice increased the response speed over time for controls, while this was not the case for subjects with mental fatigue after TBI [46]. Moreover, a simultaneous load on working memory that demands total control of the situation was more tiring for TBI subjects than an automatic activity [47]. In a study by Ponsford and co-authors, 37% of well-rehabilitated mild TBI victims performed less well than controls on a visual memory test and also reported problems with fatigue three months after the TBI [48]. In addition, we have previously reported a correlation with mental fatigue to impairments in processing speed, both after mild and moderate TBI [30]. Leegard reported frequent problems with fatigue after stroke, but did not find impaired cognitive functions [49], while Van Zandvoort and co-authors reported frequent problems with fatigue, and a subtle decrease in cognitive performance [50]. We found physically well-recovered stroke subjects to have a decreased information processing speed, and they made more errors in demanding cognitive tasks compared to the control subjects [51].

MFS and connection to depression and anxiety

We have included participants who complained of mental fatigue and who had no major depression. However, in the population of TBI or stroke subjects, depression was elevated, although there was a wide variation in frequency, depending on the methodological differences [52-56]. An elevation in the rating of depression for the brain injured compared to the controls was also detected in this study. However, there were overlapping items connected to both mental fatigue and depression in the scales used. With a factor analysis, the overlapping items were separated into a mental fatigue component and a depression and anxiety component. A new analysis, this time with the new components used, showed that an adjustment of mental fatigue (component 1) removed the difference in depression and anxiety rating (component 2) between controls and brain injured subjects. However, by removing depression and anxiety rating (component 2) this did not have an effect on mental fatigue. On the whole, in this sample we can demonstrate that a significant effect on depression between controls and brain injured subjects can be a misleading conclusion if the effect of mental fatigue is not considered. This indicates that fatigue and depression must be treated as separate constructs.

Limitations

The study is based on volunteers suffering from mental fatigue after a brain injury and healthy controls, and it is not based on a population with varying degrees of health problems. The reason for this was that it was our intention to find out how healthy people rated the MFS scale. Furthermore, the assembly of subjects originates from different studies, but as the assessments used have been the same, we decided that we could pool the data and thus gain more information relating to the MFS. The homogeneity of the controls and the brain injured subjects was not perfect, with the controls being slightly younger and having more years of education. This evaluation is being carried out in Sweden. However, the MFS needs to be evaluated in other countries and in other languages.

Conclusion

Fatigue in general is multidimensional, and is connected to physical, cognitive, emotional and social factors. All aspects of fatigue must be considered and need to be carefully examined in the clinic. Fatigue is a normal condition, but it can also be pathological. It is currently generally-accepted that fatigue can originate from peripheral or central causes, thus being physical or mental in nature. The overriding problem, however, is that in-depth analyses of the different types of fatigue have yet to be performed. It is obvious that we need to explore mental fatigue more thoroughly and to increase our knowledge of factors which are relevant to mental fatigue. Mental fatigue must also be considered when exploring treatments after a traumatic brain injury or stroke. We have shown in this study that the MFS is linked to cognitive functioning and that depression and mental fatigue must be treated as separate constructs.

Acknowledgement

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