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### Mental Fatigue; A Common Long Term Consequence After a Brain Injury

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#### 1. Introduction

The aim of this chapter is to describe mental fatigue, and emphasize the need to consider its importance when discussing rehabilitation and return to work. It will include suggestions how mental fatigue can be assessed, both objectively and subjectively and how mental fatigue and cognitive functions may be related.

#### 1.1 Why care about mental fatigue?

The less visible consequences such as cognitive, emotional and behavioural problems after a traumatic brain injury (TBI) are often not recognized immediately after an incident. In the beginning, the focus will be on the apparent problems as motor and language impairment, if the brain injury is more severe. After rehabilitation or when it is time to leave the hospital, which could occur pretty soon after a mild TBI, the person may feel rather well, although not recovered, but well enough to go home and rest, with the hope of returning to a productive everyday life after a while. This is the case for most people after a mild TBI. Patients will recover within days to weeks, but a significant minority develop persistent mental fatigue, and it will take a long time before they can accept the situation and find ways to lead their "new life". Until then, life can be very mentally tiring and for many it can be a great strain.

In the case of a slow recover, things might turn out not to work as smooth and easily as they used to. It is possible for patients to take walks in the forest, but reading, talking on the telephone or attending a meeting could be mentally very tiring and may require a prolonged rest afterwards. It is no longer a pleasure to go to parties, as they can't take part in conversations, and they soon become extremely tired and want to go home. It might also be shameful for the person to admit that the brain does not work properly. They also tend to experience difficulties concentrating, and it could be difficult to filter what they hear and see. Every unimportant detail is registered. Sensitivity to stress is also very common, even in minor situations which they are normally able to handle.

Many studies also report increased susceptibility to depression after brain injury (Ashman et al., 2004; Silver, Mc Allister, & Arciniegas, 2009; Whelan-Goodinson, Ponsfold, & Schönberger, 2008). Depression and mental fatigue can occur alone, but they sometimes occur simultaneously. Many symptoms overlap, but the core symptoms of the two states are different. For people with mental fatigue there is a clear picture of fatigue which is related to

concentration and attention, and in particular the degree of mental load. The fatigue fluctuates over the day, and the recovery period can be long. Persons suffering from depression present low-spiritedness and a decreased interest in their surroundings. Many also find it difficult to feel pleasure, experiencing fatigue throughout the day. In most cases, the long-term post TBI problems relate to mental fatigue. It is also one of the most limiting, long-term consequences after TBI.

It can be very difficult for the person with mental fatigue, but also for relatives and fellow employees to understand the limitations caused by a brain injury. However, mental fatigue will become central to their lives and will have a significant impact on everyday life. They cannot continue with work or studies as they used to. There is a high risk that they will continue to work and pursue daily activities at an unsustainable level. Most people are eager to do what they are used to, but it takes a long time to change habits.

In case of mental fatigue there are often claims for incapacity benefit after a brain disorder, and the number of claims will increase significantly in our high-technology society, with the increasing demands on our mental capacity. Upon returning to work patients may need to seek renewed acceptance from fellow employees and colleagues who will need to be willing to change strategies and demands. In the beginning, this might be possible. After a while the injured brain is expected to become "normal" again. When this does not happen it can be a heavy burden involving stress and demands over and above tolerable levels. There is a risk to be totally exhausted or even of becoming losing one's job. However, people with mental fatigue is competent and can be well-educated and many have long-term experiences which are valuable in the work-place. With the high demands placed on efficiency and economical limitations of modern living, how can the skilled person's qualifications be used to maximum advantage when energy levels are not sufficient?

The long-term effects suffered by patients after a mild TBI can be illustrated by the example of a person who tried, for many years, to find explanations and treatments, but failed.

"After my summer holiday, I started to work again. I struggled for three weeks. I was sitting on the floor in my office crying, and I was extremely fatigued and I had a severe headache. My workload increased, as I could not do my work as efficiently as before. I was sent off for sick leave and I started to feel that I might never be able to continue with my work as before. This was a great disappointment and I became depressed. Life was not worth living and I didn't manage to take care of my children. My brain was not working properly.

After six long and difficult years, I finally met a doctor who understood my problems and who could explain to me why I was feeling this way. It helped a lot when I was given some useful information about my problems, and I started to understand things. I was no longer an awkward patient. This was a relief for me. From that moment on, I was able to lead my new life and I could do the things I found pleasurable and enjoyable, despite not being able to work".

#### 2. What is mental fatigue?

#### 2.1 Mental fatigue

Mental fatigue is common and it occurs after both a mild TBI as well as moderate to severe TBI. Mental fatigue is suggested to be a diffuse or a multifocal brain disorder (Chaudhuri & Behan, 2004; Hansson & L, 2004). The degree of the fatigue appears to have no relation to the severity of the trauma or time since injury and the extent of the fatigue seems to have no relation to the area of the brain that is primarily affected (Belmont, Agara, Hugeron, Gallais, & Azouvia, 2006).

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Mental fatigue is characterized by pronounced mental fatigue after mental activity.

People suffering from this kind of mental fatigue may also experience rapid mental exhaustion which is disproportionate to the expected level following mental activity. Some people can continue to be productive in their jobs, but for others, problems connected to work and everyday activities are common. There are some people who are unable to work, who have obvious difficulties in everyday activities such as shopping, reading the newspaper as well as spending time with their family and friends. In today's society, we have to take in, process and handle a lot of information, which may be too taxing for those suffering from mental fatigue. This particular kind of fatigue can easily be mistaken for laziness or unwillingness. This is unfortunate as, in most cases people want to be able to accomplish more than they are actually capable of. Sometimes mental fatigue can also be mistaken for apathy, but a careful examination will show that most patients will be shown to have levels of high motivation, but the energy is missing.

#### Mental fatigue

- Mental exhaustion already after ordinary activities.
- Long mental recovery.
- Distinct 24h variation.

#### 2.2 Mental recovery

A common symptom of mental fatigue is an extended time for recovering one's mental energy. If there is not enough time for rest, mental fatigue may increase over time and it is very common to experience/see an increase during the course of the day. Most people also have a clear 24-hour variation with the morning being the most productive time of the day and also the best time for taking on important tasks (figure 1).

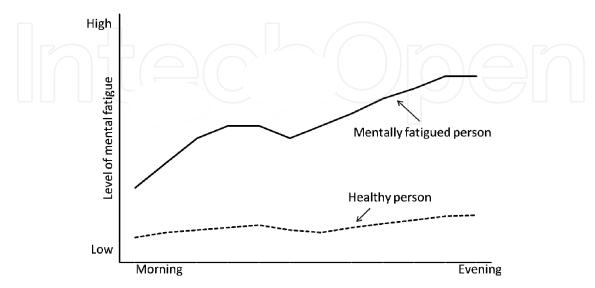


Fig. 1. The figure illustrates how fatigue can typically change over the day.

It is essential for the person to reserve extra time for rest, and most importantly, to avoid too many activities. It is crucial to consider the extended recovery time needed and this should be looked at in conjunction with working capacity. People suffering from mental fatigue are usually able to perform most tasks, but their patience is often limited. It is therefore sometimes difficult to understand that a person, who is normally able to perform tasks like any other person, is unable to accomplish tasks persistently long over a period of time.

#### 2.3 Common associated symptoms

Other common associated symptoms often accompany mental fatigue. These symptoms include sensitivity to stress, even in situations where they previously had no problems. The symptoms can be very hard to handle. Memory problems are also common. However, in most cases the attention is decreased, with the result that the person is not being able to record activities being carried out by other people. Irritability and tearfulness are also common and could be embarrassing and difficult to manage. Sensitivity to light, and most frequently, noise is also common. Many also complain of decreased sleep, or disturbed sleep, while others sleep more than normal. Fatigue also impairs the ability to take initiative and make decisions. They also commonly report slowness of thinking. Many people suffer from headaches after activities involving deep concentration.

#### Common symptoms which often accompany mental fatigue

- Poor concentration
- Slowness of thinking and slow information processing speed
- Impaired memory
- Stress
- Emotional lability and irritability
- Sleeping problems
- Noise and light sensitivity
- Impaired ability to take initiative
- Headaches

#### 3. Mental fatigue and cognitive functions

Mental fatigue also affects cognitive abilities. Increased subjective mental fatigue after TBI or mild TBI correlates to poor performance in attention tests and reduced processing speed (Belmont, Agar, & Azouvi, 2009). During a dual-task condition, reduced performance was also found with an increase in reaction time with a reported increase in subjective mental effort (Azouvi et al., 2004). TBI subjects also performed more slowly on a complex attention test, made more errors and reported a higher level of subjective fatigue (Ziino & Ponsfold, 2006a). Their performance was slower, but remained on the same level during a vigilance test, and a higher fatigue rating was associated with an increase in the number of errors made (Ziino & Ponsford, 2006b). Furthermore, practice increased the response speed for controls across time, while a lack of effect was found for subjects with mental fatigue after TBI (Ashman et al., 2008). Moreover, a simultaneous load on working memory that demands total control of the situation was more tiring than an automatic activity for TBI subjects (Park, Moscovich, & Robertson, 1999). Thumb pressing was used as an objective test of processing speed and the findings correlated with subjective fatigue (D. L. Lachapelle &

Finlayson, 1998). Mental fatigue has also been reported to correlate to decreases in processing speed and attention, both after mild and moderate TBI and processing speed was found to be the primary predictor for mental fatigue (Johansson, Berglund, & Rönnbäck, 2009).

An increased mental effort may be needed to compensate for a decreased cognitive capacity, or impaired neural network, resulting in an increase in mental fatigue. This has been explained by the "coping hypothesis", suggesting that the brain needs to work harder in order to compensate for impairments to cognitive functions such as attention and processing speed (Zomeren & van den Burg, 1985). This hypothesis has been supported by several authors (Belmont, et al., 2009; Ziino & Ponsfold, 2006a; Ziino & Ponsford, 2006b). This compensation after mild TBI or TBI has been measured during a memory and attention task and was suggested to be related to an increase in brain activity (Turner & Levine, 2008), and recruitment of brain areas outside the working memory network (Smits et al., 2009). This increased brain activity was measured using functional Magnetic Resonance Imaging (fMRI). Mental fatigue after TBI was also suggested to be related to an increased brain activity measured by fMRI for processing speed over time (Kohl, Wylie, Genova, Hillary, & Deluca, 2009). The neural network associated with diminished processing speed after a TBI was similar to the network used by healthy individuals and the network used was suggested to be partially related to reaction time. This indicates, according to the authors, that the neural network is the same as for healthy subjects, but the processing speed is slower. The prefrontal cortex plays a more important role in performing a cognitive task relating to the assessment of processing speed (Hillary et al., 2010). Reduced anisotropy in white matter after mild TBI was also detected by analysis using diffusion tensor imaging. At the same time abnormally slow functional connectivity patterns were detected in cortical grey matter using magnetoencephalography (Huang et al., 2009). Deficits in scores for complex visual information processing after mild TBI were found to be attributable to a reduced amplitude of event-related potential (J. Lachapelle, Bolduc-Teasdale, Ptito, & McKerral, 2008).

#### 4. How common is mental fatigue after TBI?

It is difficult to have any clear figure as to how common mental fatigue is since it varies significantly in accordance with the methodological differences between studies and also how mental fatigue is defined. A majority of patients recover after a mild TBI within 1 to 3 months (Carroll, Cassidy, & Peloso, 2004; Lundin, de Boussard, Edman, & Borg, 2006), but for many individuals mental fatigue persists for a longer period. In follow-up studies, the frequency of prolonged fatigue varies from 30 to 73 %. One third of the patients who suffered from mild TBI complained of severe fatigue at 6 months as well as a decrease in physical and social activities (Naalt, Zomeren, Sluiter, & Minderhoud, 1999; Stulemeijer et al., 2006). After 5 years, 73 % reported still having a problem with fatigue, which affected their everyday life (Olver, 1996). Even after ten years, fatigue was still present, irrespective of injury severity (O'Connor, Colantonio, & Polatajko, 2005). Improvement was reported during the first year, after which time it was limited (Bushnik, Englander, & Wright, 2008).

Many participants were suffering from persistent mental fatigue, with mean time since injury of 6 years after mild TBI and 11 years after moderate TBI (Johansson, et al., 2009). The problem varied from those who could manage a position in full-time employment, to

those who were extremely exhausted even after a short conversation or reading the newspaper. Mental fatigue is also dependent on the total activity as well as the demands of daily activities. We found a significantly increased subjectively reported mental fatigue among participants who had suffered a mild TBI but were working full-time compared to healthy controls. Their subjective report did not differ greatly from that given by the participants on sick leave. The differences reported between those on sick leave and those working full-time were found to be related to cognitive performance. Those subjects in full-time employment performed on similar level as the controls on cognitive tests, while those on sick-leave had primarily a decreased processing speed. Furthermore, no differences in relation to the prolonged cognitive effects as well as mental fatigue scores were found between mild TBI on sick leave and moderate TBI. According to a study carried out by Reitan and Wolfson some subjects with mild TBI may suffer a more severe injury, although this has not been diagnosed as such (Reitan & Wolfson, 1999). A study revealed that 30-year post-TBI follow-up, most patients presented a mild cognitive decline, but this was attributable to gender and age differences, with women and younger patients maintaining their cognitive level, and some younger subjects even improving their cognitive level, while older men showed a decline. It was suggested that there was a qualitative difference from the early sign of dementia of the Alzheimer type (Himanen et al., 2006).

The long-term effects after brain injury is today an area which is not covered in the research and one in which it has been difficult to produce concrete findings. Recent studies report long-term effects after recurring concussion among athletes actively engaged in their sport with a high incidence of head injuries. Whether or not this is similar to persistent postconcussion syndrome is unknown, but long-term or even deteriorating problems can occur after repeated head traumas (Gavett, Stern, & McKee, 2011). We also found a high frequency (44 %) among the mild TBI participants who had sustained more than one injury and had been on sick leave for several years, and were complaining of long-term mental fatigue and cognitive problems (Johansson, et al., 2009).

#### 5. Assessment of mental fatigue

In clinical practice, fatigue is noticed, but not always as important and central as it could be. Mental fatigue has also been difficult to assess. Therefore, the problem has so far not generated any extensive research. It is treated by many professionals as an issue of secondary importance, one which has a specific diagnosis. The focus is on other problems, depending on the professional approach. Researchers report on incidences of depression, apathy, emotional problem, fatigue and impaired executive functions after mild TBI and TBI with a combination of these diagnosis/symptoms. A psychiatrist might focus on depression and anxiety, while a neuropsychologist will focus on executive functions and problems. It is possible to analyse all these symptoms with use of different scales or questionnaires, and all these symptoms could be significant.

As mental fatigue has such a great impact on many functions, it is important to consider the problem from a wide perspective and to look at the issue with an open mind, in order to develop an understanding of the cause of the problem. Mental fatigue is something specific, but it is easy to misunderstand symptoms if there is a limited amount of knowledge available. It could be mistaken for apathy if the person has difficulties with getting things done during the day, is not interested in learning new things and is not doing things that

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interest him or her. However, these problems could be the result if the energy levels are low. It might be too exhaustive to carry out activities that demand a high degree of concentration, as talking to friends, reading and learning new things. A good strategy is actually to be careful with the existing energy levels and to use it on fewer important activities.

#### 5.1 Self-assessment of mental fatigue

Fatigue is usually assessed as a subjective problem with self-report questionnaires. It has been difficult to relate to objective assessment as a means of measuring it. There is, however, a dual problem as both the subjective scale and the objective test used must be sensitive and specific for mental fatigue.

A new self-assessment scale, the mental fatigue scale (MFS) was adapted from Rödholm et al. (Rödholm, Starmark, Svensson, & von Essen, 2001). The MFS contains 15 questions and these cover the most common symptoms occurring after brain injury (King, Crawford, Wenden, Moss, & Wade, 1995; Zomeren & van den Burg, 1985). The selection of items is based on many years of clinical experience and reports (Lindqvist & Malmgren, 1993). The questions include symptoms reported early on, as well as a long time after a brain injury or other neurological diseases. The questions relate to 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 variations.

The items are based on common activities and the estimation relates to intensity, frequency and duration with exemplified alternatives. The intention was to make the scale more consistent between individuals and also between ratings for the same individual. Each item comprises examples of common activities to be related to four response alternatives. A higher score reflects more severe symptoms. A rating of 0 corresponds to normal function, 1 indicates a problem, 2 a pronounced symptom and 3 a maximal symptom. It is also possible to provide an answer which falls in between two scores (see example below).

The self-assessment scale for mental fatigue and related items was evaluated. Significant correlations were found between all the 14 questions (24-hour variation was not included as only 'yes' and 'no' responses were measured). The 14 questions had adequate internal consistency. The Cronbach's alpha scale was used, giving a reliability coefficient of 0.944 (Johansson, et al., 2009). This indicates that the core problem with mental fatigue comprises a broader spectrum of relevant items with either primary or secondary symptoms. The response alternatives are refined in such a way as to make the self reports more consistent. This might have resulted in a more definite deviation from the healthy controls (the scale can be downloaded at www.mf.gu.se).

The question relating to 24-hour variation was analysed separately as it was constructed differently. A majority of the participants with brain injury (about 70 %) stated that the morning time was best time and afternoon and evening was the worst. This shows the increase in fatigue due to mental load during the daytime, while this was not clearly noticed among healthy controls (10 % had a clear 24h variation, see also figure 1).

Individuals with mild TBI who were working full-time did not change their leisure and social activities, although they rated their mental fatigue and related items on the same level as the participants with mild TBI and TBI who were on sick leave and had decreased their

Example of a question from the self-assessment scale of mental fatigue.

#### Mental fatigue

Does your brain become fatigued quickly when you have to think hard? Do you become mentally fatigued from things such as reading, watching TV or taking part in a conversation with several people? Do you have to take breaks or change to another activity?

0 I can manage in the same way as usual. My ability for sustained mental effort is not reduced.

0.5

- I become fatigued quickly but am still able to make the same mental effort as before.
   1.5
- 2 I become fatigued quickly and have to take a break or do something else more often than before.

2.5

3 I become fatigued so quickly that I can do nothing or have to abandon everything after a short period (approx. five minutes).

leisure and social activities. Depending on their mental load during the day, subjects working full-time might need to devote more attention to mental load and use more energy than is normal. However, the scores for subjects in full-time employment did not reveal any significant differences compared to controls on cognitive tests, which indicates a difference in severity compared to mild TBI on sick leave.

Many participants gave spontaneous comments on the scale as it included important, key items which have been confusing for them. From a clinical viewpoint, the self-assessment scale can be a valuable therapeutic tool for the patient as it can clearly describe mental fatigue and common symptoms which co-occur. A better understanding of the problem is a very good starting point for further treatment.

#### 5.2 Cognitive tests

With the intention of finding sensitive neuropsychological tests to assess mental fatigue, tests were chosen according to common problems after mild TBI. Tests included measured information processing speed (the time required to execute a cognitive task within a finite time period) (DeLuca & Kalmar, 2007), attention, working memory, verbal fluency and reading speed. The tests were digit symbol-coding from the WAIS-III NI (Wechsler, 2004), measuring information processing speed. Attention and working memory, both auditory and visual, were measured by means of the digit span and spatial span (Wechsler, 2004). Both tests included repetition of forward series of random numbers or blocks in order as well as in reverse. The verbal fluency test (FAS) measures the ability to generate as many words as possible beginning with a specific letter within one minute (Ellis, Kaplan, & Kramer, 2001). Parts A and B of the Trail Making Test (TMT), (Reitan & Wolfson, 1985)

were used to measure visual scanning, divided attention and motor speed (Lezak, Howieson, & Loring, 2004). The test consists of a series of connect-the-circle tasks. The tasks in part A is to connect the circles in a sequence with a numerical order of 1 to 25. Part B comprise letters and digits in alternating numerical and alphabetical order, which have to be completed as quickly as possible. In order to evaluate higher demands such as dual tasks, a series of new tests was constructed with three and four factors, respectively. The same number of circles (25) was used in all parts. The alternation between factors was similar to part B but months was 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 changed. The reading speed was measured using the DLS reading speed test used for the screening of dyslexia (Madison, 2003).

Information processing speed and attention tasks were found to be most sensitive and were significantly decreased compared to healthy control, while no such effect was found for both visual and auditory working memory. The subjective rating of the mental fatigue scale was primarily linked to processing speed and attention and processing speed was found to be the primary predictor for mental fatigue. The total sum of scores also correlated significantly with percentages for sick leave (Johansson, et al., 2009). Information processing speed is also the cognitive function most likely to be affected after a brain injury (Frencham, Fox, & Maybery, 2005; Madigan, DeLuca, Diamond, Tramontano, & Averill, 2000; Martin, Donders, & Thompson, 2000).

The self-assessment scale in combination with tests that primarily measure information processing speed and a high cognitive load on attention might make it possible to evaluate problems described by patients with mental fatigue, as subjective mental fatigue after mild TBI and TBI are suggested to primarily correlate with objectively measured information processing speed. If cognitive decline within these neuropsychological regions are evident, the mental loading can be even higher. In addition, other cognitive impairments may also occur, which will also affect and interfere with a person's daily functioning.

#### 6. Treatment

There is no known effective treatment for mental fatigue. When it persists, it can be very frustrating, leading to an increased risk of a depression. However, the situation can improve if the proper treatment and support are offered.

Rehabilitation should include information and advice on how to handle symptoms, offering counselling immediately after the trauma or illness. However, as the mental fatigue can be long-term, many years of support and rehabilitation may be needed.

A thorough examination will ensure that the patient has the necessary information about the problems concerning fatigue and the accompanying symptoms he or she is experiencing. With a better understanding of the situation, it is possible to find a balance between activities and rest, and this is essential. Time for rest during the day is necessary, as well as good strategies which conserve the energy levels. It is sensible to use the available energy for important tasks. It is also important to try to avoid stress as much as possible. For example, it is advisable to do one thing at a time, take more time for each activity, to avoid planning too many activities in a short period and to ensure that rest is included when

planning the day's activities. Activities in everyday life and work can be managed more efficiently by keeping the total mental load under control.

It is recommended to avoid taking on more activities over longer periods in an attempt to improve mental endurance as this does not work. When the limits of mental activity are pushed, mental fatigue increases and there is a decrease in performance. Poor concentration and more mistakes can be the consequence if one's mental activities are not adapted to one's mental fatigue.

It is essential to stress that the individual's activity level in the majority of cases has to be profoundly reduced following the injury/disease. For some individuals affected by persistent mental fatigue, it can take a long time, sometimes several years, to find the right balance between rest and activity in daily life. It can also take time to find appropriate working strategies and to accept that the activity level must be greatly reduced compared to before the mental fatigue developed. However, once the person realizes the need for a more calm and stress-free way of living, he/she can start finding a new way of handling everyday activities, including a job.

Persons suffering from mental fatigue often feel better in an environment where it is possible to rest and keep the tempo low, although resting and sleeping do not resolve the problem. Going for walks in natural environments as well as doing calm and relaxing activities can provide mental rest.

Several substances have been tested, but no pharmacological therapy has been successful in treating mental fatigue in the acute phase nor for the alleviation of long-term cognitive and emotional problems (Arcinegas, Anderson, Topkoff, & McAllister, 2005; Beauchamp, Mutlak, Smith, Shohami, & Stahel, 2008). However, symptomatic treatments can be administered. Depression can be treated in various ways, for instance by administering selective serotonin reuptake inhibitors (SSRI) drugs and with psychotherapy. A low dose of an anti-depressant may also reduce the emotional lability and irritability in persons suffering from mental fatigue, but anti-depressants are not effective in treating the mental fatigue itself. If a pharmacological treatment is used, it is however, important to start on a low dose and increase gradually as people with TBI are particularly susceptible to adverse effects (Arcinegas, et al., 2005).

#### 7. Future research

Mental fatigue is an extensive problem, and both mild TBI as well as TBI may have similar persistent problems with mental fatigue and long-term absence from work due to illness. About 2 % of the U.S. population is living with long-term consequences after TBI (Prevention, 2003). Accordingly, research on different aspects of mental fatigue is necessary. We need to increase our knowledge of the pathophysiological mechanisms underlying mental fatigue, and also our knowledge of the risk factors. It is also important to develop more specific and sensitive diagnostic tools. There is also an urgent need to find therapeutic methods for this group of people.

In our work we focus on different aspects of mental fatigue and we have recently started treatment studies. These include both non-pharmacological and pharmacological treatment. At present we are concentrating on exploring whether altered dopamine levels in the brain affect fatigue, as dopamine is to have an improved effect on attention. In addition, we have studied the effect of mindfulness-based stress reduction (MBSR) on

persons who suffer from mental fatigue after traumatic brain injury and stroke. The intention is to assess whether the adaptation of a person's activity levels and improved stress management can lead to a reduction in mental fatigue. Promising results have been found in both studies and we will continue with further studies using these methods (unpublished data, in preparation).

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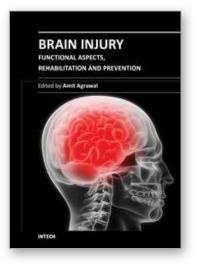
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