15. Fatigue and Sleep Disorders Post ABI

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# Table of Contents

Introduction.................................................................................................................................................. 5

Sleep Disorders Post ABI ...................................................................................................................................6

15.1 Fatigue Post ABI ........................................................................................................................................7
   15.1.1 Self-Reports of Fatigue Post ABI ...........................................................................................................7
   15.1.2 Impact on Participation and Quality of Life (QOL) ................................................................................10
   15.1.3 Vigilance and Fatigue ..........................................................................................................................11
   15.1.4 Pacing .................................................................................................................................................12

15.2 Pharmacological Treatments for Fatigue Post ABI ....................................................................................13
   15.2.1 Modafinil ..............................................................................................................................................13

15.3 Sleep Disorders Post ABI ..........................................................................................................................15
   15.3.1 Cognitive Behavioural Therapy ............................................................................................................15

15.4 Pharmacological Treatments for Sleep Disorders Post ABI ........................................................................16
   15.4.1 Methylphenidate ................................................................................................................................17
   15.4.2 Lorazepam and Zopiclone .....................................................................................................................18

15.5 Summary ..................................................................................................................................................20

15.6 Conclusions .............................................................................................................................................21

15.7 Reference List ..........................................................................................................................................22
Table Directory

Table 15.1: Reports of Fatigue Post ABI
Table 15.2: Fatigue and its Impact on Participation and QOL
Table 15.3: Vigilance and Fatigue Post TBI
Table 15.4: Modafinil Treatment for Fatigue Post ABI
Table 15.5: Cognitive Behavioural Therapy for the Treatment of Insomnia
Table 15.6: Methylphenidate Treatment for Sleep Disorders
Table 15.7: Lorazepam and Zopiclone for Fatigue Post TBI
Key Findings

- **Fatigue symptoms appear to be increased in individuals who sustain an ABI.**

- **Higher levels of fatigue lead to a poorer quality of life.**

- **Fatigue experienced post ABI has been linked to a decrease in vigilance.**

- **Pacing may be an effective technique to use with those who have sustained an ABI.**

- **Modafinil has not been shown to be effective in treating fatigue or excessive daytime sleepiness post-ABI.**

- **Acupuncture therapy has been shown to improve perception of sleep and cognitive function; however due to the small sample further research is needed.**

- **Methylphenidate does not improve the sleep-wake cycle of those who have sustained a TBI.**

- **Both lorazepam and zopiclone are effective in assisting with insomnia symptoms post-ABI.**
15-Fatigue and Sleep Disorders Post ABI

Introduction

Fatigue has been and remains one of the more common symptoms associated with and reported on by those who have sustained a brain injury (Elovic et al., 2005). Over the years, researchers, physicians and psychologists have all tried to define fatigue: What is it? How do we measure it? How do we treat it? It is believed that fatigue is a subjective experience and thus not easily assessed by objective measures (Lewis and Wessely, 1992). It is also believed that because fatigue is common with all who sustain a brain injury, it is therefore not related to damage within a specific area of the brain (Lezak, 1978).

Individuals experiencing fatigue report it as a feeling of tiredness, weakness or exhaustion (Rao et al., 2006). Fatigue has been defined as the “unconscious decreased ability for physical and or mental activity due to an imbalance in availability, utilization or the retrieval of the physiological or psychological resources required to perform the activity” (Aaronson et al., 1999). Those studying or reporting on fatigue have attempted to distinguish between physiological vs psychological fatigue (Aaronson et al., 1999). Psychological fatigue has been defined “as a state of wariness related to reduced motivation, prolonged mental fatigue or boredom” (Jha et al., 2008; Lee et al., 1991). This type of fatigue has been associated with stress, anxiety and depression. Physical fatigue has been defined as “the result of excessive energy consumption, depleted hormones or neurotransmitters or diminished ability of muscle cells to contract” (Jha et al., 2008).

It has been hypothesized that individuals who sustain a brain injury, especially those with a closed head injury (CHI) complain of: tiring easily (even more so when engaging in activities that require a degree of mental stamina); an increase in the number of headaches they are experiencing; and irritability (Riese et al., 1999; van Zomeren and van den Burg, 1985). van Zomeren & van den Burg (1985) suggested that these complaints are the result of individuals trying to meet the demands of their life and their perceived responsibilities following a CHI.

In Ziino and Ponsford’s (2006a) study of 46 individuals with and without a traumatic brain injury (TBI), those without a TBI scored higher on the vigilance task test than those with a TBI. The number of misses recorded on the vigilance task was significantly higher for those with a TBI (p<0.001). Toda et al. (Toda et al., 2006) found that individuals, who had sustained a TBI, reported significantly higher levels of fatigue during their time in rehabilitation than they did at 6 or 12 months post injury (p=0.0092). It was hypothesized that perhaps rehabilitation itself played a role in the feeling of fatigue and once removed from these demands along with the individuals’ greater understanding of their deficits the feelings of fatigue lessened. Similarly in Keshavan’s et al. (1981) study, fatigue was reported by 29% to 47% of those with a TBI in the first month post-injury. Three months post injury this number had decreased to 22-37%. One year post-injury, approximately 20% of those with a mild TBI were still reporting fatigue to be a problem (Middelboe et al., 1992). In a study conducted by Olver et al. (1996), 68% of those surveyed (n=254) reported fatigue 2 years post ABI and of the 103 surveyed 5 years post injury,
73% reported fatigue. It has been noted that fatigue appears to be an issue with 20 to approximately 70% of those who have sustained a brain injury (BI) (Rao et al., 2006; Bay and de-Leon 2011) and it appears to be persistent often occurring 1 to 5 years post injury (Olver et al., 1996; Ouellet and Morin 2006).

For those recovering from an ABI/TBI fatigue has the ability to interfere with an individual’s ability to participate in recovery programs designed to assist them in performing their activities of daily living.

Fatigue post ABI can be treated using pharmacological or non-pharmacological measures. Non-pharmacological measures include educating both patients and their family members about the occurrence of fatigue post-TBI and expectations following an injury. Diet and lifestyle may play a role in combating fatigue; thus it is believed that eating a “balanced diet” and learning to balance exercise with rest may help to combat fatigue (Elovic et al., 2005; Rao et al., 2006). Those who are suffering from fatigue may benefit by performing important activities when they feel they are at their best (Lezak, 1978). Conserving energy and pacing are two ways an individual is encouraged to overcome or deal with his or her levels of fatigue (Fellus and Elovic 2007).

**Sleep Disorders Post ABI**

Although it would make sense to link disorder of sleep with fatigue (Clinchot et al., 1998), this relationship remains inconclusive (Fellus & Elovic, 2007). Sleep disturbances or disorders tend to be classified as insomnia, excessive sleep, or excessive daytime sleepiness (EDS) (Elovic et al., 2005). It is believed that in individuals with ABI, sleep complaints correlate with higher Glasgow Coma Scores (GCS), better immediate memory, pre-presence of fatigue, a history of substance abuse, age and gender (Thaxton and Patel 2007). There are few studies that have investigated sleep disorders and their effects on rehabilitation post ABI (Clinchot et al., 1998; Baumann et al., 2007). It has been suggested that those who sustain a more severe TBI may underreport poor sleep, while those with a mild injury may be more aware of the changes in their sleep patterns and over report any changes that have occurred as a result of the injury (Elovic et al., 2005). Castriotta et al. (2007) found that 47% (41/87) of study participants reported EDS. In a recent Canadian study, Ouellet et al. (2006) found that approximately 50% of the sample (total n=452), reported insomnia symptoms and those that did not report insomnia as a problem were sleeping more than before the injury. Individuals with insomnia reported having sleep difficulties 5.7 times per week (Ouellet et al., 2006). It was also noted that more than half of the individuals who reported having sleep difficulties were not treated for the condition (Ouellet et al. 2006).

This chapter explores the problems of fatigue and sleep disorders post ABI first by reviewing studies identifying the incidence and prevalence of these symptoms post TBI and ABI as well as summarizing and evaluating studies examining treatment interventions for each.
15.1 Fatigue Post ABI

15.1.1 Self-Reports of Fatigue Post ABI

Even though fatigue has been documented to be a problem post ABI it remains understudied. To gain information on the severity of the problem, data is often collected through surveys, interviews or questionnaires (Kempf et al., 2010; Ashman et al. 2008; Bushnik et al. 2008; Ziino and Ponsford 2005; Borgaro et al., 2005; Whiteneck et al. 2004b; LaChapelle and Finlayson 1998). Comparison groups are generally those without an ABI. Scales used in these surveys include: Fatigue Severity Scale (FSS), the Fatigue Impact Scale (FIS), the Visual Analogue Scale-F (VAS-F), the Global Fatigue Index (GFI), the Barroso Fatigue Scale (BFS), the Epworth Sleepiness Scale; however, none of these scales were designed especially for this population, but rather they were developed for HIV or MS populations (Fish et al., 2007; Armutlu et al., 2007).

Individual Studies

**Table 15.1: Reports of Fatigue Post ABI**

<table>
<thead>
<tr>
<th>Author/Year Country/Study Design</th>
<th>Methods</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>Ashman et al., (2008) USA Case-Control</td>
<td>N=275 For the following study, 202 individuals with a TBI and 73 non-injured individuals were selected to participate. Participants were given a series of tests from the computerized CANTAB test at 3 time points.</td>
<td>The test results indicated a significant difference between the two groups on the rating of day to day fatigue and situational fatigue (p&lt;0.001). Performance of the TBI group declined between the 2nd and 3rd testing periods but the control group remained the same.</td>
</tr>
<tr>
<td>Bushnik et al., (2008) USA Case series</td>
<td>N=51 Participants in the following study were asked to complete a survey at 3, 6, 12, 18 and 24 months post-injury. Only 46 of the respondents provided enough data for analysis. Surveys included the: Barroso Fatigue Scale (BFS), Global Fatigue Index (GFI), Beck Depression Inventory-II (BDI-II), Craig Handicap Assessment Reporting Technique (CHART), Neurobehavioral Functioning Inventory (NFI), Pittsburgh Sleep Quality Index (PSQI), Visual Analogue Scale (VAS) and others</td>
<td>Results from the GFI scores significantly changed from T1 to T2 (from 23 to 17, p&lt;0.01). A decrease from T2 to T3 was noted but not significant. Significant changes were not seen on the remaining subsections of the GFI or FSS scores. Decreases were noted when looking at the scores on the VAS (p&gt;0.0001), the PSQI &amp; NFI motor subscale (p&lt;0.01). Increases were noted from T1 to T3 on the CHART-cognitive independence (p&lt;0.0001) and the occupation (p&lt;0.001) sub scale.</td>
</tr>
<tr>
<td>Ziino and Ponsford (2006a) Australia Case-Control</td>
<td>N=92 Those with a TBI (n=46), those without (n=46) were asked to complete a survey including the following scales: Causes of Fatigue Questionnaire (COF), Visual Analogue Scale –F (VAS-F), Fatigue Severity Scale (FSS), Hospital Anxiety and Depression Scale (HADS) and others</td>
<td>Those with a TBI reported significantly greater levels of fatigue than those without an injury (p&lt;0.002). Results of the VAS-F showed no significant differences between the two groups. When looking at the results of the HADS, scale those with a TBI scored significantly higher than the non-injured group (p&lt;0.001). The higher depression scores in the TBI group were</td>
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### Evidence-Based Review of Moderate to Severe Acquired Brain Injury

#### Module 15 - Fatigue and Sleep Disorders Post ABI_V9_2013

Updated August 2013

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Methodology</th>
<th>Results</th>
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<tr>
<td>Borgaro et al., (2005) USA Case-Control</td>
<td>77</td>
<td>47 individuals with a brain injury and 30 without were administered the following scales: Barrow Neurological Institute Fatigue Scale (BNIS) and the BNI scale for higher cerebral functions.</td>
<td>Results from the BNI fatigue scale indicate that those with a TBI had higher levels of fatigue than those recruited from the normal population. Self-reports of fatigue did not appear to be influenced by cognitive performance, days since injury, injury severity and gender. Scores of the BNIS indicated that those with a severe injury had a significantly greater cognitive impairment (p&lt;0.004) than those with a moderate and mild brain injury.</td>
</tr>
<tr>
<td>Whiteneck et al., (2004a) USA Case series</td>
<td>1591</td>
<td>A chart audit was conducted, along with a series of interviews 8 to 12 months post-injury. Interviews were also conducted at 24, 36 and 48 months post-injury although not all were available for the follow-up interviews.</td>
<td>41% felt fatigue was more of a problem post-injury. Of those with a severe injury, 77% reported one or more difficulties and were more likely to need assistance compared to those with a mild or moderate injury. Of those employed at time of injury only 76% were employed one-year post injury. Those with severe injuries or those over 65 yrs of age were more likely to need assistance.</td>
</tr>
<tr>
<td>LaChapelle &amp; Finlayson (1998) Canada Case-control</td>
<td>60</td>
<td>30 individuals with a TBI and 30 without were asked to complete a survey and participate in a thumb press exercise. The thumb press exercise consisted of 4 trials. Participants were asked to complete the Visual Analogue Score for Fatigue (VAS-F), Fatigue Severity Scale (FSS), Fatigue Impact Scale (FIS), and an objects measurement of fatigue.</td>
<td>Results from the FIS indicated that individuals with a TBI did experience fatigue more often those without an injury. The thumb pressing exercises were correlated to the FSS (section 1) and the FIS (section 2). Results from the objective measure of fatigue indicate that TBI participants did fatigue more quickly the non-TBI participants. Scores on the VAS-F were not statistically different between the two groups.</td>
</tr>
<tr>
<td>Kempf et al., (2010) Switzerland Self-Reports (Survey)</td>
<td>51</td>
<td>Individuals who had previous sustained a TBI were asked to complete both telephone interviews and questionnaires regarding their sleep patterns (excessive daytime sleepiness) and fatigue.</td>
<td>Overall sleep times (amount of sleep received each day) was not associated with level of TBI, presence of depression or anxiety. Twenty-six, of those who responded, reported increased day time sleepiness, lack of energy and increased levels of exhaustion since their TBI. This was not associated with the level of injury, age, gender, or location of injury. A moderate correlation was found when looking at the scores on the Fatigue severity scale and the BDI (depression) and the HADS (anxiety).</td>
</tr>
<tr>
<td>Englander et al., (2010)</td>
<td>119</td>
<td>Patients were asked to complete a survey which included the</td>
<td>Although endocrine function was found to be abnormal in 65% of participants this was</td>
</tr>
</tbody>
</table>
Evidence-Based Review of Moderate to Severe Acquired Brain Injury  

<table>
<thead>
<tr>
<th>Country</th>
<th>Study Type</th>
<th>Sample Size</th>
<th>Methodology</th>
<th>Results/Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>Self-Reports</td>
<td>N=84</td>
<td>Survey looking at fatigue and its impact on their quality of life. A modified version of the Fatigue Impact Scale was used</td>
<td>For individuals living in the community results of the QOF-Fatigue were related perceived somatic symptoms and situational stress.</td>
</tr>
<tr>
<td>USA</td>
<td>Self-Reports</td>
<td>N=150</td>
<td>Sleep-wake survey included the Epworth Sleepiness Scale (ESS), the Hamilton Anxiety Scale (HAS) and the Beck Depression Inventory (BDI).</td>
<td>Excessive daytime somnolence presented itself in half of the study population, with over half of this group reported moderate to severe sleepiness throughout the day. A quarter of the group reported insomnia with 50% of this group having sleep onset insomnia with high HAS scores. The remaining 50% were found to have sleep maintenance insomnia with high BDI scores.</td>
</tr>
<tr>
<td>USA</td>
<td>Self-Reports</td>
<td>N=91</td>
<td>Survey included the Pittsburgh Sleep Quality Index (PSQI) and the Beck Depression Inventory (BDI).</td>
<td>In this study insomnia was associated with pain, the GCS (series of milder head injuries) and depression.</td>
</tr>
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</table>

**Discussion**

Results from Ashman et al. (2008), Ziino and Ponsford (2006a) and Borgaro et al. (2005), indicate that those who sustained a severe brain injury reported greater fatigue than those who had not. LaChapelle and Finlayson (1998) reported that those with an ABI did fatigue more easily on an objective measure of fatigue (thumb pressing). Results from subjective measures of fatigue (such as the VAS-F) did not show significant differences between the two groups. In the case study conducted by Whiteneck et al. (2004), they noted that 41% of those with a TBI...
felt that fatigue was a greater problem post-injury. Additionally those with a moderate or mild injury reported needing less assistance in performing various activities than those individuals with a more severe injury. Bushnik et al. (2008a) found that when looking at study results, fatigue levels were higher immediately post injury but leveled off after 6 months.

Several studies have looked at the sleep patterns and fatigue of those recovering from a mild to severe TBI (Verma et al., 2007; Bay & de-Leon, 2010; Englander et al., 2010; Fichtenberg et al., 2000; Kempf et al., 2010). All report difficulties with sleep, daytime sleepiness and elevated levels of fatigue. In each of these studies individuals completed various surveys which included tools such as the Beck Depression Inventory, the Hamilton Anxiety and Depression Scale, the Hamilton Anxiety Scale, or the Epworth Sleepiness Scale. In all studies almost 50% of the study populations reported elevated levels of fatigue and were found to have a variety of sleep disorders. Both of these increased levels of depression and anxiety. Englander et al. (2010) also assessed then neuroendocrine function of their study participants, but found that pituitary dysfunction did not correlate with sleep and fatigue symptoms.

Conclusions

*Results from various studies have found that those who sustain a TBI report greater levels of fatigue post injury.*

**Fatigue symptoms appear to be increased in individuals who sustain an ABI.**

### 15.1.2 Impact on Participation and Quality of Life (QOL)

There are many challenges to studying fatigue post TBI. One of the challenges is separating fatigue from pain, depression and any other health related issues. Several assessments, including the DSM-IV (the American Psychiatric Association) and the Beck Depression Inventory (Beck et al., 1996), assess fatigue as a symptom of depression. Few scales assess fatigue alone. To do so, one must reduce the overlap that exists between the various scales or tools that are used post-TBI (Cantor et al., 2008).

#### Individual Study

**Table 15.2: Fatigue and its Impact on Participation and QOL**

<table>
<thead>
<tr>
<th>Author/Year Country/Study Design</th>
<th>Methods</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cantor et al., (2008) USA Case-Control</td>
<td>N=308 223 individuals with an ABI and 85 individuals with no history of BI were recruited to participate in this survey. The survey included the: Global Fatigue Index (GFI), Beck</td>
<td>Those with a TBI had greater levels of fatigue, depression, pain, poorer sleep quality and health related quality of life than the control group. There was a significant difference on the scores of the GFI between the two groups</td>
</tr>
</tbody>
</table>
Evidence-Based Review of Moderate to Severe Acquired Brain Injury

Module 15 - Fatigue and Sleep Disorders Post ABI_V9_2013

Updated August 2013

<table>
<thead>
<tr>
<th>Methods</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression Inventory (BDI), McGill Pain Questionnaire (MPQ),</td>
<td>for those who scored over 21 (p&lt;0.001). A large portion of the fatigue</td>
</tr>
<tr>
<td>Pittsburgh Sleep Questionnaire (PSQ), Participation Objective</td>
<td>experienced in the TBI group was felt to be a consequence of the injury</td>
</tr>
<tr>
<td>Participation Subjective (POPS), the SF-36-Health Survey (SF-36), and the</td>
<td>(BI) and it was independent of pain, depression and sleep.</td>
</tr>
<tr>
<td>Life-3</td>
<td></td>
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Discussion

Cantor et al. (2008) found that those in the TBI group showed greater levels of fatigue, depression and pain and they reported poorer sleep quality and health related quality of life than those in the non-TBI group. When looking at the scores of the GFI for those who scored higher than 21, 75% of those with a TBI had significant fatigue compared to only 40% of those who did not (p<0.001). Fatigue was not related to participation in major life activities; it was however, related to overall QOL and health related QOL. It was also noted that fatigue scores on the GFI were significantly higher for women than men (p<0.05) regardless of the group these women were in. Study authors concluded that the fatigue felt by participants was in fact the result of the injury and not related to other co-morbid conditions alone (Cantor et al., 2008).

Conclusion

There is Level 3 evidence, from one study, to suggest that higher levels of fatigue may lead to a poorer quality of life.

Higher levels of fatigue lead to a poorer quality of life.

15.1.3 Vigilance and Fatigue

Vigilance has been defined as the ability to sustain a level of alertness over long periods of time (Parasuraman 1984). It has been noted that those who sustain a TBI do have a lower cognitive reserve and often are not able to maintain the same levels of vigilance or sustained attention as they did before the injury (Ziino and Ponsford 2006b). It has been suggested that this variability in performance maybe the result of fatigue (Cohen and Sparling-Cohen 1993).

Individual Study

Table 15.3: Vigilance and Fatigue Post TBI

<table>
<thead>
<tr>
<th>Author/Year Country/Study Design</th>
<th>Methods</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ziino and Ponsford (2006b)</td>
<td>N=92 Cases (n=46 (TBI)) and controls (n=46) were asked to complete a</td>
<td>Results of the study indicate: 1) decision time on the vigilance task</td>
</tr>
<tr>
<td>Australia Case-Control</td>
<td>survey (questionnaire). Approximately 64% of the cases had</td>
<td>performance test significantly slower (p&lt;0.001) for cases than controls;</td>
</tr>
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</table>
<pre><code>                                                                        |                                                                         | 2) task effect for controls was faster |
</code></pre>
sustained a moderate or severe TBI. Following the completion of the survey, all were asked to complete several attention measures as part of a larger study; the VAS-F, the complex selective attention task (C-SAT) and the vigilance task. The vigilance task lasted 45 minutes and was designed to increase the likelihood of loss of sensitivity to signals. Completing the tasks required mental effort. The task combined a fast rate of stimulus presentation, a low target frequency and a memory load. Reaction time (RT), decision time (DT) and movement time (MT) were all recorded.

than for cases (p<0.006); and 3) cases had a slower movement time (p<0.001) than controls. Cases had higher pre-vigilance VAS-F fatigue ratings and these were associated with more missed targets over the entire vigilance task (p<0.03).

Discussion
In the study conducted by Ziino and Ponsford (2006b), individuals with a TBI (n=46) were slower on the vigilance task performance test than those without a TBI (p<0.001); the time on task effect was faster for controls (p<0.006); and movement time was slower for those with a TBI than controls (p<0.001). Mean movement times indicated there were no significant differences between the two groups when looking at the Time on Task Effect (p=0.08) or Group x Time on Task Interaction (p=0.86). Results from the fatigue subscale indicate that both groups had increased fatigue levels following the completion of the vigilance tasks they were asked to complete. In TBI subjects higher previgilance VAS-F fatigue rating were associated with more missed targets over the entire vigilance task (p<0.03). Lower vigilance was linked to a greater number of missed targets in the TBI group (Ziino and Ponsford 2006b)

Conclusions

There is Level 3 evidence, based on one study that has noted individuals who sustain a TBI do experience greater fatigue and a decrease in vigilance than those without an injury.

Fatigue experienced post-TBI has been linked to a decrease in vigilance.

15.1.4 Pacing
Following a brain injury, regardless of the cause, an individual may be instructed to conserve energy or to “pace” oneself (Fellus & Elovic, 2007). Many may find that simple tasks require more concentration and effort and they tire more easily (Lezak 1978). As part of their rehabilitation, individuals may be taught or re-taught how to prioritize their commitments and are encouraged to recognize their abilities and limitations (Fellus and Elovic 2007). For some
this may come easily, but for others it may require more education or other intervention programs (Fellus and Elovic 2007). Although pacing is a concept that has been accepted with health care professionals and encouraged with the ABI/TBI population its benefits have not yet been studied with this group.

The effects of pacing strategies for those who have sustained an ABI are not known.

15.2 Pharmacological Treatments for Fatigue Post ABI
Despite the knowledge that fatigue and sleep disorders play a role in the recovery from an ABI very few interventions have been developed to help manage these issues. Many pharmacological interventions have been tested in other populations (narcolepsy, multiple sclerosis (MS), Parkinsons, etc.) (Rao et al., 2006), but few have been tested within the ABI population. There has been some discussion about the possible therapeutic benefits of using methylphenidate, dextroamphetamine, carbidopa, amantadine, and modafinil to treat fatigue post-TBI (Rao et al., 2006).

15.2.1 Modafinil
Modafinil, a wakefulness promoting agent, was initially approved for use with those who were having difficulty with excessive daytime sleepiness (EDS) (Jha et al., 2008). The drug was subsequently approved for use with those who suffer from narcolepsy and those who may experience sleeping difficulties associated with shift work (US Modafinil in Narcolepsy Multicenter Study Group 2000; US Modafinil in Narcolepsy Multicenter Study Group 1998). This medication has been found to enhance the quality of life for those with narcolepsy (Beusterien et al., 1999). Two studies were found which investigated the effectiveness of modafinil with the ABI population.

**Individual Study**

Table 15.4: Modafinil Treatment for Fatigue Post ABI

<table>
<thead>
<tr>
<th>Author/Year Country/Study Design/PEDro Score</th>
<th>Methods</th>
<th>Outcome</th>
</tr>
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<tbody>
<tr>
<td>Kaiser et al., (2010)</td>
<td>N=20 Patients were given either 100/200mg per day of modafinil or placebo for 6 weeks. The Epworth Sleepiness Scale the Fatigue Severity scale were completed by participants pre and post treatment.</td>
<td>At the end of the 6 weeks, those receiving modafinil had lower FSS scores than those in the placebo group but these were not significantly lower scores. A decrease in the ESS scores was also noted, with the modafinil group’s scores decreased significantly throughout the treatment period (p&lt;0.005) compared to the placebo group. Of note scores on the depression and anxiety scales did not differ between the two groups, either at the start of the study or at the end of the 6 weeks. Modafinil had no impact on post</td>
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Evidence - Based Review of Moderate to Severe Acquired Brain Injury

Module 15 - Fatigue and Sleep Disorders Post ABI_V9_2013

N=51 Participants were divided into 2 groups: one group (n=27) receiving modafinil and the other (n=24) receiving a placebo. At the end of phase 1 groups were "crossed-over''. While in the intervention group, modafinil was given 1 x daily 100mg for 3 days. This was increased to 100mg BID for 11 days. A maintenance dose of 200mg was given BID. Participants were monitored with the Fatigue Severity Scale (FSS), Modified Fatigue Impact Scale (MFI), Epworth Sleepiness Scale (EPS)

Glasgow Coma Scale revealed that 51% and 23.5% of participants had a severe or moderate head injury. By the 4th week of the study, FSS scores improved by 6.7 points on the placebo but only 5.8 points on the modafinil. A placebo effect was noted with improvements for a number of outcomes between baseline and other on both medications. Although there was a 10.9 (p<0.03) point difference between the two groups at week 4 on the MFI scale, this dropped to 8.1 (p=.14) at week 10. Similar results were noted for the EPS, on average 1.2 point decrease (p<0.02). At week 10 there was a .5 (p=.56) average decrease in scores. Overall the medication was well tolerated but not very effective in treating fatigue in this ABI population.

Discussion

Two randomized controlled trials were found looking at the effects of modafinil on fatigue and excessive daytime sleepiness (EDS) (Jha et al., 2008; Kaiser et al., 2010). Overall, study results did not find modafinil was very effective in treating fatigue and daytime sleepiness in individuals’ post ABI, although some changes could be seen. These changes were only significant at the 4 week test period and not at the 10 week retest period. At week 4 there was a 10.9 point difference between the two groups on the MFI scale (p<0.03) and on average 1.2 point difference on the EPS (p<0.02). By week 10 these changes had decreased to 8.1 (p=.14) on the MFI and .5 (p=.56) on the EPS. A placebo effect was noted when looking at the mean scores on the fatigue severity scale (FSS). Scores increased at week 4 by 5.8 points for those on the modafinil and 6.7 points for those on the placebo. Scores on the ImPACT Verbal Memory Compact Scale, decreased from 80.3 points at baseline to 77.4 points at week 10. For those in the placebo group, the scores increased from 78.1 to 87.1 points. As noted by the lack of statistically significant differences on the various subjective and objective measures of fatigue used in the study modafinil did not appear to be effective in treating fatigue in post ABI patients (Jha et al. 2008). These results appear to be similar to those found when using modafinil to treat fatigue in other populations such as Parkinson disease or multiple sclerosis (Jha et al. 2008).

In the study conducted by Kaiser et al. (2010) modafinil (100 to 200 mg daily) was administered to a treatment group of 10 patients who had been diagnosed with fatigue or excessive daytime sleepiness (EDS). The control groups was administered a placebo. Depression and anxiety were assessed using the Beck Depression and Anxiety Inventory (BDAI). Sleepiness and fatigue were assessed using the Epworth Sleepiness Scale (ESS) and the Fatigue Severity Scale (FSS). No significant changes were noted on the FSS between the two groups at the end of the 6 week period as a result of taking the modafinil. A significant reduction in the scores on the ESS post

PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al. 2002).
intervention was noted in the treatment group compared to the control group (p=0.005). Study results indicate that modafinil was effective in reducing ESS but not FSS.

Conclusion

*There is Level 1a evidence that Modafinil is not effective in treating fatigue but has shown to be effective in treating excessive daytime sleepiness post ABI.*

*Modafinil has not been shown to be effective in treating fatigue but in treating daytime sleepiness it have been shown to be effective.*

15.3 Treatment for Sleep Disorders Post ABI

15.3.1 Cognitive Behavioural Therapy

Although sleep disturbance is a frequently documented problem post ABI, there is little scientific research that has been conducted looking into this (Ouellet and Morin 2004). Sleep disorders, such as insomnia, can affect a person’s quality of life, family and social commitments, and their ability to return to work (Ouellet & Morin, 2004). In a case study conducted by Ouellet et al. (2004) sleep disturbances were alleviated through the implementation of cognitive behavioural therapy (CBT).

Individual Study

<table>
<thead>
<tr>
<th>Author/Year Country/Study Design</th>
<th>Methods</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ouellet and Morin (2007) Canada Pre/Post</td>
<td>N=11 Participants underwent cognitive behavioural therapy (CBT) for insomnia (8 or 10 weekly sessions lasing 1 hour). CBT included stimulus control, sleep restrictions, cognitive restructuring sleep hygiene education and fatigue management.</td>
<td>In the post-treatment phase a significant decline in the total wake time was noted compared to the pre-treatment phase (p&lt;0.001). Differences in these improvements were maintained for most participants at the 1 and 3 month follow-up time periods. All significantly increased sleep efficiency post-treatment (p&lt;0.01). Sleep time, during treatment did not change significantly, however at 3 months post discharge a significant increase was seen (p&lt;0.015).</td>
</tr>
</tbody>
</table>
Discussion
Quellet and Morin (2007) found that CBT, (a psychological intervention) was effective in dealing with insomnia. Participants (n=11) were assessed at baseline, during the treatment phase, post-treatment (1 month post-treatment) and at follow-up (3 months post-treatment). Baseline assessments confirmed that all were dealing with symptoms of insomnia. During the treatment phase, participants received 8 to 10 weeks (8 sessions in total) of CBT. For some, improvements in sleep were noted within the first 2 weeks of treatment; for others, improvement was more progressive. Following the treatment 8 of the 11 participants had improved their sleep and these improvements could be seen at follow-up for most of the participants. In four, inter-night variability was noted at the initial follow-up but this pattern seemed to “normalize” at the 3 month follow-up (Ouellet and Morin 2007).

Conclusion

*There is Level 4 evidence, based on one study, to suggest that cognitive behavioural therapy may assist in treating insomnia and help in the management of fatigue post ABI.*

15.3.2 Acupuncture
Following a TBI or ABI it is very common for survivors to have their sleep patterns disrupted. In fact 36 to 73% of those who sustain a head injury will experience sleep disruptions (Cohen et al., 1992). Although acupuncture has been found to be an effective tool for treating insomnia in other populations, they have only just begun to study it with individuals who have sustained a TBI.

Table 15.6 Acupuncture as a Treatment for Insomnia  Post ABI

<table>
<thead>
<tr>
<th>Author/Year Country/Study Design</th>
<th>Methods</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zollman et al., (2012) USA RCT PEDro=5</td>
<td>N=24 Individuals who had sustained a TBI were randomly assigned to either the acupuncture group or the control group. Those in the Control group met with study physicians and were given information about what to avoid and new sleep related medication. Previous medications were not altered. Those in the acupuncture group had all sleep related medications prescribed by the study doctor, and were provided with acupuncture treatments. Treatments</td>
<td>A total of 20 individuals completed the study. Results from the ISI indicated no significant difference between the groups at baseline. At one month follow-up again no differences were noted. Significant differences were noted when looking at the changes within the groups. Those in the acupuncture group showed significant improvement from pre to post treatment (p&lt;0.01). Those in the control group showed no improvement.</td>
</tr>
</tbody>
</table>
lasted 20 minutes. Points included the kidney, heart bladder, liver. Large intestine and pericardium, governor vessel and ear points. The Insomnia Severity Index (ISI) was used to assess degree of insomnia.

PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002)

Discussion
Zollman et al. (2012) randomly assigned 24 individuals to either the acupuncture group or the control group to treat insomnia post TBI. The degree of insomnia was rated using the Insomnia Severity Index (ISI). Sleep was also measured using the actigraphy which was attached to the individuals arm. Depression and cognitive impairments were also assessed pre and post treatment. A between group comparison showed no significant improvement when looking at the results of the ISI. Within group comparison showed the treatment group’s scores were significantly decreased following treatment (p<0.01). This was not seen in the control group. Those in the treatment groups also showed significant improvement on overall cognitive functioning and divided attention. Despite no differences being noted between the two group when assessing sleep time, those in the treatment groups did show improvement in cognitive function.

Conclusions

There is Level 2 evidence to suggest acupuncture is effective in improving perception of sleep and cognitive function in those who sustain a TBI.

Acupuncture therapy has been shown to improve perception of sleep and cognitive function; however due to the small sample further research is needed.

15.4 Pharmacological Treatments for Sleep Disorders Post ABI
Individuals, who have sustained a brain injury, often have cognitive disabilities as a result of the injury. Insomnia and sleep disorders have been known to compound the neurocognitive difficulties resulting from the injury. Treatments have included the administration of various non-pharmaceutical medications (Sleep-Eze, Nytol etc.) and pharmaceutical medications (sedative/hypnotic drugs, antihistamines, antidepressants etc.) (Thaxton and Patel 2007). This section focuses on three medications used to treat sleep disorders post ABI.

15.4.1 Methylphenidate
Of the neurostimulatints used in the post-acute care of those with a TBI, methylphenidate is one of the most common, assisting with memory, attention, verbal fluency, and improving processing speed; however, little has been written on the effects of methylphenidate on the sleep-wake cycles of those with a BI (Al-Adawi et al., 2006). In one double-blind, placebo-
controlled study looking at the effects of methylphenidate, sertraline or placebo on individuals with a mild or moderate TBI, Lee et al. (2005) noted that those on methylphenidate, along with those in the placebo group reported significantly less day-time sleepiness than those in the sertraline group. In this study all medications were given during the day for a total of four weeks which may have impacted on the effectiveness of sertraline (Lee et al. 2005).

**Individual Study**

<table>
<thead>
<tr>
<th>Author/Year Country/Study Design</th>
<th>Methods</th>
<th>Outcome</th>
</tr>
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<tbody>
<tr>
<td>Al-Adawi et al., (2006) Oman/USA Non-RCT</td>
<td>N=30 Those in the methylphenidate group (n=17) were given the medication at 8 am and 2 pm. The remaining individuals (n=13) received no medication.</td>
<td>No significant differences were noted when looking at the scores from the activities of daily living, mobility and cognition scales. FIM scores were lower for those in the methylphenidate group 30.0 than for those not in the methylphenidate group their FIM scores were 34.9. No significant differences were noted when looking at the total sleep time between the two groups.</td>
</tr>
</tbody>
</table>

**Discussion**

In the current study by Al-Adawi et al. (2006) no significant differences were found between the two groups (those receiving methylphenidate and those not receiving the medication) when looking at the scores on various assessment scales (activities of daily living, mobility and cognition, FIM). Sleep times for the two groups also showed no significant differences between the two groups.

**Conclusion**

*There is Level 2 evidence, based on one cohort study, that methylphenidate does not improve the sleep-wake cycle of those who have sustained a TBI.*

**Methylphenidate does not improve the sleep-wake cycle of those who have sustained a TBI.**

**15.4.2 Lorazepam and Zopiclone**

Individuals who survive a TBI, for 27 to 56% of the population, insomnia is a common complaint (Thaxton and Patel 2007). Lorazepam, a benzodiazepine (also known as Ativan or Temesta), is primarily an anti-anxiety medication; however, due to its side effects it also has been used for
the treatment of sleep disorders (Thaxton and Patel 2007). Zopiclone, a nonbenzodiazepine working at the same receptor sites as benzodiazepines, has been used in the treatment of insomnia in individuals who have identified one of the following problems: sleep onset is delayed, they are having difficulties maintaining sleep or they wake early (Thaxton and Patel 2007; Hair et al. 2008).

**Individual Study**

Table 15.7: Lorazepam and Zopiclone for Fatigue Post TBI

<table>
<thead>
<tr>
<th>Author/Year Country/Study Design/ PEDro Score</th>
<th>Methods</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>Li Pi Shan and Ashworth (2004) RCT Canada PEDro = 10</td>
<td>N=18 Individuals who had either a stroke or had sustained a brain injury were recruited to participate in the following study. Individuals were divided into one of two groups: lorazepam group (n=9); zopiclone group (n=9). Those in the lorazepam group were given 0 to 1 mg/day PRN. Those in the zopiclone were given 3.75 to 7.5 mg PRN. Participants decided how much medication they would receive. Each medication was given for one week. The order in which medication was given was reversed for week two. The Mini Mental Status Exam (MMSE) was completed at the end of each time period.</td>
<td>No significant differences were noted between the two groups or between the two medications when looking at length of time asleep, alertness, feelings of being refreshed, quality of sleep, depth of sleep, feelings of tiredness or the results of the MMSE.</td>
</tr>
</tbody>
</table>

PEDro = Physiotherapy Evidence Database rating scale score (Moseley et al., 2002)

**Discussion**

In a randomized, crossover, double-blind trial conducted by Li Pi Shan and Ashworth (2004) a group of stroke and TBI patients were divided into one of two groups. To assist with sleep, one group received lorazepam orally (0 to 1mg/daily PRN) in the evenings while the second group received zopiclone orally (3.75 to 7.5 mg/daily PRN) in the evening. At the end of the two week period, Li Pi Shan and Ashworth (2004) found little differences between the two groups. Differences in the length of sleep each group received were not found. Subjects found no differences on quality of sleep, depth of sleep, feelings of being refreshed or alertness between the two treatments. Cognition scores on the Mini Mental Status Exam were not significantly different between the two time periods.

**Conclusion**

*There is Level 1b evidence, from one RCT, that lorazepam and zopiclone work equally well in assisting with insomnia symptoms post ABI.*
Both lorazepam and zopiclone are effective in assisting with insomnia symptoms post ABI.

15.5 Summary
The results of this review provide little guidance to clinicians in the management of the common problems of fatigue and sleep disorder post ABI. The significance of the symptom of fatigue remains important since the high prevalence can influence not only the rehabilitation process early on in the course of recovery, but can also affect quality of life in the long run where many survivors have persisting symptoms. Cognitive behavioural strategies such as energy conservation and pacing that are commonly encouraged by health professionals have no published research evidence to support their effectiveness. Pharmacological interventions for management of fatigue also appear to be under studied leading clinicians to rely on their individual clinical experiences or research based on other medical conditions. Sleep disorders post ABI can encompass problems with insomnia, disturbed sleep cycles as well as hypersomnolence. Again, current research has focused on exploring and identifying sleep related issues post ABI and has not as of yet significantly addressed treatment interventions. Clearly, there is a need for further research into the management of fatigue and sleep disorder symptoms post ABI.
15.6 Conclusions

1. Results from 4 case-control studies and 2 case series have found that individuals who sustain a TBI feel greater levels of fatigue post injury.

2. There is evidence, from one study, to suggest that higher levels of fatigue may lead to a poorer quality of life.

3. Based on the finding of one study, individuals who sustain a TBI do experience greater fatigue and a decrease in vigilance than those without an injury.

4. There is Level 4 evidence, based on one study, to suggest that cognitive behavioural therapy may assist in treating insomnia and help in the management of fatigue post ABI.

5. There is Level 1a evidence, based on one RCT, that Modafinil is not effective in treating fatigue or excessive daytime sleepiness post ABI.

6. There is Level 2 evidence to suggest acupuncture is effective in improving perception of sleep and cognitive function in those who sustain a TBI.

7. There is Level 2 evidence, based on one cohort study, that methylphenidate does not improve the sleep-wake cycle of those who have sustained a TBI.

8. There is Level 1b evidence, from one RCT, that lopezapam and zopiclone work equally well in assisting with insomnia symptoms fatigue post ABI.
15.7 Reference List


