The Impact of Treatment for Sleep-Wake Disorders on Recovery and Outcomes Following Traumatic Brain Injury

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Overview of Presentation

1. Introduction to sleep/wake disorders following traumatic brain injury (TBI)
2. Epidemiology
3. Role of sleep in recovery and rehabilitation
4. Cognitive and behavioral consequences of TBI
5. The interaction between sleep & other symptoms/consequences of TBI
6. Presentation of research
Introduction to Sleep and TBI

- The primary acceleration-deceleration mechanism of traumatic brain injury (TBI) leaves the brain structures that regulate sleep, wakefulness and arousal vulnerable to mechanical injury.

- In addition to the TBI, there are external secondary post-injury factors that may contribute to development of disturbed sleep over time. May include changes in/ or reductions in activity, mobility, and lifestyle;

- Can result in alterations to the sleep schedule, depressed mood and/or changes in weight due to reduced mobility and activity development or sleep problems or exacerbation of pre-existing sleep problems.

- Patients with TBI have been found to be at high risk for developing chronic sleep-wake disturbances (SWDs) (Gosselin & Tellier 2010)
Impairments in sleep patterns and excessive day-time sleepiness, also known as sleep wake disorders (SWD), are among the most commonly reported neuropsychiatric sequelae following TBI. This holds true across all levels of severity and continuum of recovery (from acute to community reintegration), yet their impact on recovery and outcomes has received limited scientific attention.

Sleep is assessed objectively by polysomnography, actigraphy, and self report measures including questionnaires and sleep diaries.
Introduction to Sleep and TBI

- In severe TBI, disturbed sleep begins in acute stage with altered rest-activity circadian rhythms, followed by sleep duration with fragmentation.
- Resolution of day-night circadian cycle (i.e. clear periods of uninterrupted wakefulness during the day and clear periods of sleep at night) correlated with cognitive outcomes at discharge from acute care. (Duclos et al 2013)
- For mild TBI/concussion, we see an increase in sleep need and duration within the first 24 hours (Wiseman-Hakes et al 2014 in progress)
- Thus, we know that in the acute stage, sleep changes in response to the injured brain....
Epidemiology of Sleep Wake Disorders

According to the literature: More than 50% of those with TBI report SWD’s. In terms of diagnosis:

- 35% Insomnia - Sleep Initiation and Maintenance
- 23% Obstructive Sleep Apnea
- 20% Excessive Daytime Sleepiness
- 11% Post-Traumatic Hypersomnia (most common in severe)
- 6% Periodic Leg Movements in Sleep
- 5% Narcolepsy

Comparisons of SWD vs non-SWD subjects disclosed no clear relationship between presence of a sleep disorder and injury severity, cause of injury, or presence of positive CT scan findings.

(Duclos, Dumont et al 2014, Mathias & Alvaro 2012)
Why is this important? Role of Sleep in Recovery and Rehabilitation

- Examination of sleep after TBI is critical from the perspective of recovery.

- Sleep, particularly slow wave sleep, which predominates during the first part of the night, plays a crucial role in neuroplasticity and neurogenesis.

- Chronically restricted or fragmented sleep can impact the generation and maturation of new neurons in the adult human brain, particularly in the hippocampus.

- Disturbed sleep negatively impacts rehabilitation
Cognitive and Communication Consequences of TBI

Cognitive changes are the most salient features after TBI, and these impact directly onto communication.

| Cognition: | Attention, memory, information processing, reasoning, problem solving, executive functions |
| Communication: | Listening, speaking, reading, writing, thinking, social communication |

Cognition impacts directly onto communication.
Cognitive/Behavioral Sequelae

- Cognition
  - Impaired Attention & Working Memory
  - Memory and Executive Functions
  - Reduced Speed & Efficiency of Processing

- Emotion & Affect
  - Anxiety & Depression
  - Irritability
  - Emotional Lability

- Physical
  - Pain
  - Weakness
  - Reduced Mobility
  - Impaired Coordination

- Behaviour
  - Impulse Control
  - Agitation
  - Reduced Affect
Interaction Between Sleep and TBI Sequelae

- Sleep
- Headache & Pain
- Cognition & Communication
- Emotion & Behaviour

The diagram illustrates the interplay between sleep and the described sequelae, showing bidirectional relationships among these factors.
Neuropsychological Consequences of SWD & TBI: Current Literature

Sleep, wake and arousal disturbances post-TBI are associated with greater impairments in:

- Attention
- Concentration
- Executive functions
- Information and language processing
- Verbal and visual memory

Sleep and Depression in TBI

- SWD exacerbate trauma-related neuro-cognitive impairments, and are associated with depression as well as anxiety.

- Insomnia, in particular, is often associated with depression and the link may be bi-directional.

- The incidence of depression in the ‘normal population is 6-7% in the USA and Canada.

- For those with TBI incidence of depression is reported as 14% - 77%.

(Ashman et al., 2004; Baumann et al., 2005; Holsinger et al., 2002; Kennedy, Lumpkin, & Grissom, 2006; Koponen et al., 2011; Kreutzer et al. 2001; Mollayeva et al., 2013; Wiseman-Hakes et al., 2011)
Statement of the Problem:

- Sleep disorders are not routinely screened for or addressed in the TBI population.

- Many remain undiagnosed - Therefore, untreated.

- This compromises outcomes and increases the risk of developing disturbed or restricted sleep-related co-morbidities including depression.
Study Objective

To longitudinally examine the impact of post-traumatic sleep and wake disturbances prior to and after treatment on recovery of aspects of cognition, communication and mood in adults with moderate-severe TBI

NOTE: These were adults who all complained of sleep disturbances but had never been assessed or treated for their sleep.
Hypotheses

1. Abnormal sleep and wake patterns post TBI exacerbate cognitive impairments in auditory verbal attention, speed and capacity of information processing, and verbal memory.

2. These cognitive domains underlie communication, thus impairments in these domains exacerbate communication impairments.

3. Abnormal sleep also exacerbates or contributes to mood disorders post TBI.

4. Treatment of SWD will facilitate recovery and outcomes for cognition, communication and mood, even in those many years post-injury.
Study Design

- Prospective, longitudinal, single blind multi-site cohort study

- Recruited from the community by clinician referral and Brain Injury Association of Canada website

- Evaluation at baseline and after consistent sleep/wake treatment had optimized sleep and wake patterns
**N=13 community-residing adults with TBI; consecutive sample**

**Intake Interview - Baseline**
- Insomnia Severity Index (ISI)
- Diagnostic Interview for Insomnia
- Latrobe Communication Questionnaire
- Beck Depression and Anxiety Inventories
- Begin D-CCASP

**Clinical Sleep Assessment** with Neurologist, including BMI and blood work (where indicated)
- Baseline Neuropsych Testing

**Follow-Up**
- Medical follow-up to review Sleep Study Findings and Initiate Treatment

**Overnight Polysomnography; Multiple Wake Test** next day

**Follow-Up**
- With sleep intervention, follow-up clinical evaluation and repeat neuropsych, communication and mood measures, and ISI

**Follow-Up**
- 6-month clinical follow-up to review sleep status
## Data Collection Measures

<table>
<thead>
<tr>
<th>Sleep</th>
<th>Cognitive-Communication</th>
<th>Mood</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Subjective</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Session 1:</td>
<td>Baseline &amp; Follow-Up:</td>
<td>Session 1 &amp; 3:</td>
</tr>
<tr>
<td>• Diagnostic Interview for Insomnia* (DII)</td>
<td>• Latrobe Communication Questionnaire (LCQ)</td>
<td>• Beck Depression Inventory (BDI)</td>
</tr>
<tr>
<td>Session 1 &amp; 3:</td>
<td>• Daily Cognitive-Communication and Sleep Profile (D-CCASP)</td>
<td>• Beck Anxiety Inventory (BAI)</td>
</tr>
<tr>
<td>• Insomnia Severity Index (ISI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Daily Cognitive-Communication and Sleep Profile (D-CCASP)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Objective</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Session 2:</td>
<td>Baseline &amp; Follow-Up:</td>
<td></td>
</tr>
<tr>
<td>• Polysomnography (PSG)</td>
<td>• Speed and Capacity of Language Processing (SCOLP)</td>
<td></td>
</tr>
<tr>
<td>• Multiple Wake Test (MWT)</td>
<td>• Test of Everyday Attention (TEA)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)</td>
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</table>
Inclusion/Exclusion

What We Proposed: Ideal Criteria

- Formal diagnosis of moderate-severe TBI; Age 18-55; min 1 yr post
- Formal documentation of cognitive-communication deficits secondary to TBI including difficulties with attention, memory, language processing and new learning
- Report of post-traumatic sleep disturbance and/or excessive day-time sleepiness
- No primary diagnosis of depression and/or anxiety disorder
- No modafinil or ritalin (or other stimulants) 72 hours prior to polysomnography
A mixed bag of sleep and wake complaints, including ‘vague insomnias’ as well as hypersomnia and excessive day-time sleepiness

Almost all had some symptoms of depression and/or anxiety, and 8 were on medication for treatment of depression

2 with complicated mTBI; mild by objective diagnosis, severe by impact

10/12 were on a variety of prescriptions at onset of the study

2 on modafinil at study onset; 1 attempted wash-out prior to polysomnography
Breakdown of Primary Sleep Diagnosis: Based on Polysomnography/MWT

N=13*

*One participant had two primary diagnoses of CRSD and PLMD, and One participant had two primary diagnoses of Apnea and Insomnia
<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>TBI Severity</th>
<th>Time Post-inj</th>
<th>Employment Status (Baseline)</th>
<th>ISI (Baseline)</th>
<th>Sleep Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>F</td>
<td>Severe</td>
<td>2 yrs</td>
<td>School with FT 1-1 Support In TBI rehab</td>
<td>Severe</td>
<td>Insomnia, EDS</td>
</tr>
<tr>
<td>19</td>
<td>M</td>
<td>Severe</td>
<td>1 yr</td>
<td>School with PT Support In TBI rehab</td>
<td>Severe</td>
<td>Insomnia, EDS, fatigue</td>
</tr>
<tr>
<td>27</td>
<td>F</td>
<td>Severe</td>
<td>2 yrs</td>
<td>Not working In TBI rehab</td>
<td>Severe</td>
<td>Insomnia, day time sleepiness, fatigue</td>
</tr>
<tr>
<td>28</td>
<td>M</td>
<td>Severe</td>
<td>1 yr</td>
<td>Attempting RTW</td>
<td>Moderate</td>
<td>EDS, extreme fatigue</td>
</tr>
<tr>
<td>31</td>
<td>M</td>
<td>Comp mTBI</td>
<td>2 yrs</td>
<td>Not working PT student with Support TBI rehab</td>
<td>Moderate</td>
<td>Sleep maintenance insomnia, EDS, fatigue</td>
</tr>
<tr>
<td>32</td>
<td>F</td>
<td>Severe</td>
<td>2 yrs</td>
<td>Not working In TBI Rehab</td>
<td>Moderate</td>
<td>CRSD</td>
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<tr>
<td>37</td>
<td>M</td>
<td>Severe</td>
<td>22 yrs</td>
<td>Employed FT and working on GED</td>
<td>Sub threshold</td>
<td>PLM Disorder, Insomnia</td>
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<tr>
<td>47</td>
<td>M</td>
<td>Comp mTBI</td>
<td>2 yrs</td>
<td>Working</td>
<td>Severe</td>
<td>OSA, CSA, Insomnia</td>
</tr>
<tr>
<td>49</td>
<td>M</td>
<td>Severe</td>
<td>1 yr</td>
<td>Not working In TBI rehab</td>
<td>Severe</td>
<td>PLM Disorder, Mild apnea</td>
</tr>
<tr>
<td>53</td>
<td>F</td>
<td>Severe</td>
<td>3 yrs</td>
<td>Not working</td>
<td>Moderate</td>
<td>Insomnia, day-time sleepiness, fatigue</td>
</tr>
<tr>
<td>55</td>
<td>F</td>
<td>Severe</td>
<td>18 yrs</td>
<td>Working</td>
<td>Moderate</td>
<td>OSA</td>
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<tr>
<td>58</td>
<td>F</td>
<td>Severe</td>
<td>1.5 yrs</td>
<td>Not working</td>
<td>Moderate</td>
<td>OSA</td>
</tr>
<tr>
<td>ID</td>
<td>Sleep Diagnosis</td>
<td>Sleep Latency (mins)</td>
<td>Wake After Sleep Onset (mins)</td>
<td>Sleep Efficiency</td>
<td>Total Sleep Time</td>
<td>Total # of Awakenings</td>
</tr>
<tr>
<td>----</td>
<td>-----------------------------------------</td>
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<td>-------------------------------</td>
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<tr>
<td>1</td>
<td>CRSD &amp; PLM</td>
<td>73.5</td>
<td>63</td>
<td>65.5%</td>
<td>4h20m</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>Obstructive Apnea</td>
<td>27</td>
<td>127.5</td>
<td>60.5%</td>
<td>3h57m</td>
<td>24</td>
</tr>
<tr>
<td>3</td>
<td>Hypersomnia</td>
<td>14.5</td>
<td>30</td>
<td>91.6%</td>
<td>8h25m</td>
<td>21</td>
</tr>
<tr>
<td>4</td>
<td>Obstructive Apnea</td>
<td>28.5</td>
<td>114</td>
<td>70.3%</td>
<td>5h39m</td>
<td>29</td>
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<tr>
<td>5</td>
<td>PLM</td>
<td>46.5</td>
<td>198</td>
<td>53.4%</td>
<td>4h40m</td>
<td>47</td>
</tr>
<tr>
<td>6</td>
<td>Insomnia &amp; EDS</td>
<td>12.5</td>
<td>35</td>
<td>87.3%</td>
<td>5h29m</td>
<td>12</td>
</tr>
<tr>
<td>7</td>
<td>Obstructive &amp; Central Apnea, Insomnia</td>
<td>3</td>
<td>59</td>
<td>88.2%</td>
<td>7h42m</td>
<td>17</td>
</tr>
<tr>
<td>8</td>
<td>Insomnia &amp; EDS</td>
<td>106</td>
<td>88.5</td>
<td>50.8%</td>
<td>3h21m</td>
<td>4</td>
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<tr>
<td>9</td>
<td>Hypersomnia</td>
<td>63</td>
<td>58</td>
<td>73%</td>
<td>5h26m</td>
<td>35</td>
</tr>
<tr>
<td>10</td>
<td>Insomnia &amp; EDS</td>
<td>28.5</td>
<td>18.5</td>
<td>88%</td>
<td>6h30m</td>
<td>20</td>
</tr>
<tr>
<td>11</td>
<td>Hypersomnia</td>
<td>10.5</td>
<td>12.5</td>
<td>95.1%</td>
<td>7h37m</td>
<td>12</td>
</tr>
<tr>
<td>12</td>
<td>Insomnia &amp; EDS</td>
<td>3</td>
<td>36</td>
<td>90%</td>
<td>6h29m</td>
<td>28</td>
</tr>
<tr>
<td>13</td>
<td>Insomnia &amp; EDS</td>
<td>53</td>
<td>121</td>
<td>61.5%</td>
<td>4h54m</td>
<td>20</td>
</tr>
</tbody>
</table>
Daily Cognitive-communication and Sleep Profile

- A series of seven 7-point Likert rating scales developed as a means of monitoring daily fluctuations in cognitive-communication function in relation to quality of sleep.

- A questionnaire completed either by the client, therapist or significant other who has the opportunity to observe them over the course of the day.

- A daily profile was found to be sensitive to subtle changes in sleep and function, and useful in identifying patterns and trends.

- Reliability and validity established on a normative population

Participants rate their subjective functional performance in the domains of:

- Sustained attention, vigilance and executive attention to spoken/written communication
- Verbal memory, retention of spoken/written info
- Speed of language processing
- Sleep quality, level of fatigue, daytime sleepiness
- Mood
Treatments

- Non-experimental
- Determined and prescribed by physician according to individual sleep diagnosis
- Unfortunately we did not have access to Cognitive Behavioral Therapy which would have been very helpful!
- Treatments included CPAP, pharmacotherapy
Results: Incidence of Depression

- **At baseline, 85%** of our participants had co-morbid depression even though 62% were undergoing pharmacological treatment.

- Exceeds the incidence range for depression in those with TBI of 14-77%, even while undergoing treatment.
Results: Group Average DCCASP Pre-Post

*p < .01, trend NS baseline, * < .05 post
Results: Sleep and Mood

- Beck Depression Inventory: Moderate at Baseline, Mild at Follow up.
- Beck Anxiety Inventory: Mild at Baseline, Minimal at Follow up.
- Insomnia Severity Index: Moderate at Baseline, Sub threshold insomnia at Follow up.
Results: Communication

- Latrobe Communication Questionnaire
- SCOLP Speed
- SCOLP Word Recognition
- SCOLP Scaled Score

Higher scores better

Baseline vs Follow up

Mild vs Moderate
Results: Repeatable Battery for the Assessment of Neuropsychological Status

Higher scores better

Immediate Memory, Visual Spatial, Language, Attention, Delayed Memory, Total Scale Score, Total Test Percentile

Baseline vs. Follow up
Results: Test of Everyday Attention

Higher scores better

Baseline
Follow up

- Selective visual attention immediate
- Selective visual attention sustained
- Auditory selective working memory
- Visual attentional switching accuracy
- Visual attentional switching time
- Auditory verbal working memory
- Selective visual attention
- Divided attention working memory
- Sustained auditory vigilance
Limitations

- Small N
- Only baseline polysomnography
- Lack of control group
Conclusions

1. Results are compelling!
   - Improvements on each subtest of every single measure (for 9/12 participants)
   - Improved mood

2. Dramatic functional and participation gains with subjectively-reported improvements in quality of life

3. DCCASP results showed significant self reported improvements across all domains
Where do we go from here?

- Results provide evidence to support the development of practice guidelines for the systematic evaluation and treatment of sleep, wake and arousal disorders following TBI.

- We need to identify better treatments.

- We need to investigate the role of sleep and sleep disorders and neuroplasticity (and neurogenesis) following TBI.
Take Home Message

1. We need to take sleep and wake disorders seriously

2. Begin monitoring in acute care

3. Screening regularly across continuum of recovery
   * Sleep and Concussion Questionnaire, SCQ  *(Wiseman-Hakes & Ouellet 2013, available in English and French)*

1. Access to comprehensive diagnosis and intervention
Acknowledgements

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