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Traumatic Brain Injuries and Sleep/Wake Disorders

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Additional information is available at the end of the chapter

1. Introduction

Traumatic brain injury (TBI) and sleep/wake disorder/s have a complex relationship [1]. A sleep disorder may make a person more prone to TBI by making him or her drowsy or inattentive and therefore more prone to fall or have an accident [2]. A sleep disorder may also make a person with concussion more prone to develop prolonged concussion or post-concussion syndrome in which symptoms last more than 3 weeks or even more than 3 months [3-7]. Likewise a sleep disorder may make them more prone to future concussions and cumulative injury. [7]

Less known and more common and recently recognized is the sleep/wake disorder caused by TBI itself, most simply termed the post traumatic sleep disorder [8-10] We discourage the use of acronym **PTSD**, however, lest it be confused with post-traumatic stress disorder. We propose the acronym **PTSLD**. This chapter is dedicated to delineating this disorder.

2. TBI

TBI is a problem of significant and increasing proportions-recently described as a silent epidemic [1]. The number of individuals with TBI is expected to climb with the return of Iraq and Afghanistan veterans back to USA. Just like atom bomb induced cancer was the signature injury of World War II and Agent Orange the signature injury of Vietnam War, TBI is the signature injury of Iraq and Afghanistan wars. [1]

Current estimates indicate that the TBI occurs in 100–400 per 100,000 people per year in North America and Europe. Men are more often affected than women. The most common age group which suffers from traumatic brain injury is 15–35 years. It is the most frequent cause of death between the ages 1-15. It accounts for one third of all injury related deaths in the USA. [8]

The TBI may result from fall, domestic violence, street violence, during birth, motor vehicle accidents, war related injuries, a work related injury or due to sports. Falls and motor vehicle accidents are the most common causes in civilian practice. In developing countries such as India with smaller land size, more population density, lax driving law enforcement and booming motor vehicle growth per capita, motor vehicle accidents are as much as 100 times more common than developed countries such as UK or USA.

TBI could be due to a blunt or a penetrating trauma. The trauma may be direct or indirect such from a nearby explosion-as many as 59 percent soldiers exposed to improvised explosive devices (IEDs) develop TBI. [1]

Contrary to popular belief a significant loss of consciousness (LOC) is not always necessary to make a diagnosis especially in so called mild TBI. Per Center of disease control (CDC), a history of clear cut LOC is seen in only less than 10 percent of patients with concussion. [8]

TBI is often described as acute, subacute and chronic-arbitrarily according to the time elapsed. It is also rated as mild, moderate or severe. Although there is no consensus, many prevailing criteria exist. The departments of defense and veterans affairs [3] have attempted to do this as follows:

	GCS	PTA	LOC
Mild	13-15	<1 day	0-30 minutes
Moderate	9-12	>1 to <7 days	>30 min to <24 hours
Severe	3-8	>7 days	>24 hours

GCS-Glasgow coma scale, **LOC**-loss of consciousness, **PTA**-post-traumatic amnesia

Table 1. Severity of traumatic brain injury

Only thing mild about **mild TBI** is the name. It accounts for 75 percent of all TBI. It may potentially be associated with significant, enduring and sometimes devastating consequences, greater likelihood of injury from a repeat concussion and long-term risk of Parkinson's disease, dementia, depression, suicide or homicide. [8] The incidence of mild TBI, also called concussion, is believed to be 6 per 1000 but this may be an underestimate. Per the center of disease control (CDC), a total of 1.4 million visits to hospitals/ER per year in USA are related to concussion/mild TBI. Additional 1.6-3.8 million never visit hospital or the ER. Mild TBI is often considered to occur when Glasgow coma score (GCS) at 24 hours after trauma is 13-15, LOC is 0-30 min and post-traumatic amnesia (PTA) is less than a day. It is often used interchangeably with the term concussion. Sports teams often use the acute concussion evaluation (ACE) questionnaire to evaluate the symptoms of concussion in the sport field.

The ACE questionnaire scores the individual on characteristics of Injury (such as severity and type of trauma, LOC, amnesia and presence or absence of seizures), presence and severity of physical symptoms (such as headache, photophobia, dizziness, nausea, blurred vision etc), cognitive symptoms (fogginess, confusion, forgetfulness, perseveration, slow

cerebration, lack of concentration), emotional symptoms (irritability, sadness, emotional lability, nervousness) and sleep-related symptoms (such as insomnia, hypersomnia, drowsiness, daytime sleepiness, hyperarousal, flashbacks, nightmares), whether they are increased by exertion and how the person feels as compared to before injury on a seven point scale (0-6) and risk factors such as previous history of concussion, headaches, depression anxiety, sleep disorder or developmental disorder such as ADHD or learning disability. This may also be used for serial follow up.

The military equivalent of this scale is called MACE. A score of 25 or above is considered indicative of concussion in MACE. Symptoms persist from 3 weeks to 3 months and are called post-concussive syndrome if they persist beyond 3 months. Although it is believed that concussion results from biomechanical alterations in the brain and there is no structural damage, neuropathological and MRI data with tractography (diffuse tensor imaging or more sophisticated constrained spherical deconvolution) refute this thesis. If *conventional* neuroimaging such as head CT or MRI of the brain is abnormal, the TBI is no longer mild. However moderate to severe TBI may occur with or without abnormal conventional neuroimaging.

Moderate TBI is defined as LOC greater than 30 min but less than 24 hours, GCS 9-12 and/or PTA 1-7 days. It is variously graded by Global assessment of functioning or GAF scale [4] (scored from 0-100) or some regional scales such as Rancho Los Amigos Scale [5] which assesses head injured patients on 8 levels of cognitive functioning (LOCF). The GAF score would be expected to be 51-60 with moderate TBI.

Severe TBI is defined as LOC greater than 1 day, GCS 3-8 and/or PTA greater than 7 days. Seizure occurring acutely during the head trauma does not necessarily make the TBI severe but chronic seizure disorder starting 3 months to several years after the head trauma certainly qualifies the TBI as a severe injury. Likewise macro injury, infarction, encephalomalacia, hematoma, persistent focal or lateralized neurological signs, dementia, severe personality change or new onset severe psychiatric disorder stamp an injury as severe. GAF score of 50 or below will indicate a severe head injury even when the neuroimaging is negative. There were 5.3 million people in USA living with severe TBI by 1999 [6]. The number must certainly be higher now. Severe TBI is of 2 types: closed and penetrated.

TBI may occur alone or may be associated with involvement of not just the brain but also skull, scalp, meninges, eyes, ears, sinuses and other neighborhood structures as well as injuries to neck and body.

3. TBI and sleep/wake disorders

Sleep/wake disorders may, in fact, potentially make folks more prone to TBI by making them sleepy and/or inattentive and therefore more likely to be subject of an injury or accident. A preexisting sleep disorder also makes the likelihood of concussion being prolonged and persistent. However, this chapter will mainly deal with the issue of sleep wake disorder/s caused by TBI, a far more common and as yet not well defined problem.

Sleep related problems secondary to chronic TBI have been described anecdotally or in case-report format since 1941. [11-19]. Some commonly reported disorders include hypersomnia, narcolepsy, delayed sleep phase, insomnia, fatigue, alteration of sleep-wake schedule, and movement disorders. It has been found clinically that, insomnia [20], hypersomnia [21-28] and excessive daytime sleepiness (EDS) are common [29, 30] in TBI and may at times occur in the same patient at different intervals from traumatic insult (see below). Only more recently in last 30 years, attempts have been made to explore this relationship in detail. Guilleminault et al in 1982 [13] described impaired daytime functioning and somnolence in 98 percent of all patients with TBI and further expanded their findings in year 2000, [21] extending their observations to even those with cervical whiplash and commenting on the medico-legal dilemma.

Post-traumatic sleep/wake disorders may significantly impair the rehabilitation potential of an injured individual and need to be accurately diagnosed and treated. Organized literature in this important area is sparse and fragmented. An organized account of these disorders is essential not only to improve the rehabilitation potential of these unfortunate individuals but to protect their medical coverage from auto insurers, as they encounter significant skepticism from adjusters regarding their sleep/wake issues to be causally related to their accidents and injury.

To be perfectly accurate, the sleep/wake disorder may not only result from head injury but neck and bodily injuries may cause or contribute to sleep/wake issues equally or even predominantly. [21]

The post-traumatic sleep/wake disorders may evolve, recede or be persistent after TBI. In a prospective study [31], there was found to be a high prevalence of sleep disorders (46%) and of excessive daytime sleepiness (25%) in 87 subjects at least 3 months after TBI [23]. 47% of the subjects in the aforementioned study was found to have a sleep disorder: OSA (23%), PTH (11%), narcolepsy (6%), or PLMS (7%) and 26% of the subjects had EDS [23]. In immediate post-traumatic period, hypersomnia may be common in hospitalized patients due to medications and interrupted nocturnal sleep due to pain and frequent nursing evaluations. Later on, it may be replaced by insomnia. Parasomnias may occur as well. *TBI is now known to cause nearly the entire spectrum of any or all sleep disorders and further may aggravate a pre-existing sleep/wake disorder by potential mechanisms enumerated elsewhere in this chapter.*

4. Acute TBI and sleep-related symptoms

Watson et al in 2007 [32] found in a prospective study of 514 patients that sleep related symptoms are common during acute phase of TBI. As much as 54 percent patients have daytime somnolence, more in those with more severe injury. They result in daytime somnolence which in turn may lead to poor daytime performance, altered sleep-wake schedule, heightened anxiety, and poor individual sense of well-being, insomnia, and depression. Half of these individuals are still sleepy at the end of one year. Relationship with severity or localization of head injury was disputed by Baumann et al [28] who evaluated patients

prospectively as well, but their study ended at 6 months instead of one year in Watson's study.. However, similar to Watson study, they also found that quality of life was impaired by these symptoms.. CSF hypocretin-1 was found to be significantly reduced levels in those patients with excessive daytime sleepiness (EDS) symptoms.

5. Chronic TBI and sleep related symptoms

Verma et al in 2007 [10] in a retrospective study found that sleep changes and deranged sleep architecture are common in *chronic* TBI patients, arbitrarily defined as 3 months to 2 years after head trauma.. The sleep disorders seen in this population are similar to those seen in the general population but individual percentages are higher. Hypersomnia accounted for 50 percent of all patients and insomnia and parasomnia for quarter each. Global assessment of functioning (GAF) scores correlated with some (stage N1 percentage, impaired sleep efficiency and wake during sleep), but not all (stage shifts and wake before sleep) measures of sleep disruption, indicating a complex and multifactorial pathogenesis.

6. Pathogenesis

The possible pathogenetic mechanisms of TBI causing sleep disorders include: direct brain injury, indirect brain injury, collateral damage to neck and back and resulting pain interfering with sleep, [13] weight gain (secondary to head trauma or medications used to treat head trauma or its sequelae such as posttraumatic mood, anxiety or stress disorder), pre-existing genetic propensity for narcolepsy, which may be clinically aggravated or precipitated by head-trauma [11], a pre-existing anatomical abnormality of sleep-related brain mechanisms, oropharyngeal abnormality aggravated by head trauma or resulting weight gain, anatomical abnormalities caused by head trauma such as jaw dislocation, TMJ problems, and brainstem and forebrain lesions induced by TBI.

Direct brain injury was first described by Strich in 1961 [22] as diffuse degeneration of white matter subsequently termed the diffuse axonal injury (DAI). This was later determined in animal experiments to be the consequence of inertial loading of the head by prolonged coronal angular acceleration [23] with brunt of abnormality in septum pellucidum, corpus callosum, deep gray matter and dorso-lateral pons and midbrain, areas closely associated with sleep-wake mechanisms. The biochemical basis of this injury is excitotoxicity, [24] inflammation, [25] free radicals/eicosanoids, [9] hyperglycolysis, [26] hyperglycemia, [26] and apolipoprotein E e4 synthesis. [27] These mechanisms most likely operate in sleep disorders associated with mild head injury. MRI with tractography may provide a direct evidence of such injury. It has also been hypothesized that the hypocretin system may be partly responsible for the pathophysiology of sleep wake disturbances present post TBI [28].

7. Classification: We propose the following classification of post-traumatic sleep/wake disorders

1. Post-traumatic sleep wake disorder/s-resulting from TBI
2. Post-traumatic sleep/wake disorder/s resulting from neck and/or bodily injuries
3. Post-traumatic sleep/wake disorder/s resulting from both-TBI and neck and/or bodily injuries

Each group has 2 subtypes:

Primary: This group consists of patients who never had any sleep/wake related issues what so ever prior to the accident.

Secondary: These patients have a preexisting sleep/wake disorder which is either aggravated or altered by the accident and in fact may have contributed to the occurrence of accident by making patient inattentive and therefore prone to have an accident. A pre-existing sleep disorder also makes the likelihood of an enduring concussion more as well as increases the proneness to further and cumulative deterioration after repeat concussion.

8. Clinical features

Insomnia: This is the most common consequence of the TBI. It is pretty much universal in all patients with mild TBI at least in initial stages. It is associated with headache, dizziness, mood changes, imbalance and blurred vision and flashbacks in various combinations. It usually resolves in 3 weeks to 3 months in most mild cases but sometimes may be nagging and persistent. It may be sleep onset or sleep maintenance or associated with premature awakening in the morning-the so called the “ terminal” insomnia. It may be contributed to by associated anxiety and depression as shown by Verma et al [10] based on Hamilton Anxiety Scale (HAS-appendix 3) and Beck’s Depression Inventory (BDI-appendix 4). Nightmares and flashbacks may also contribute. At times it reflects more serious pathology such as sleep apnea caused by TBI and/or neck or spinal injury or periodic limb movements induced by medications used to manage the patient. The medications such as topiramate, methylphenidate etc themselves may aggravate or cause insomnia. Circadian rhythm disorder may complicate insomnia or cause it either due to direct injury to the biological clock or patient’s sleep hygiene suffering from frequent examinations by nurses, therapists and other workers, not going to work or office and irregular bedtime and wake up time.

Many patients with more severe head injury initially have hypersomnia due to medications, TBI itself, complicating sleep apnea or narcolepsy but later on after several months or even years develop insomnia. Same factors as listed above operate. Reverse is also true. Patients with mild TBI may develop hypersomnia/ parasomnia or narcolepsy later on even though they had insomnia to begin with. Thus the natural history of sleep/wake disorders is more complicated than the sleep/wake disorders in general as the type of disorder may switch over time.

Although, sleep studies are not generally indicated in patients with most cases of insomnia from other etiologies, the post-traumatic insomnia requires a sleep study for many reasons. It requires documentation as the adjusters frequently look for objective confirmation of subjective symptoms. Also post-traumatic insomnia may not be just pure insomnia but contributed to by sleep apnea, narcolepsy, periodic limb movements, parasomnias such as the REM behavior disorder or a circadian rhythm disorder. In addition, the insomnia may be replaced by hypersomnia or parasomnia and/or even nocturnal seizures later on. The polysomnogram (PSG) should be done with expanded EEG montage with simultaneous video-taping. Traditional investigating methods such as sleep diary, actigraphy and scales such as Hamilton anxiety scale (HAS -appendix 3) and Beck's depression inventory (BDI -appendix 4) also help in dissecting, intellectualizing and treating the issue at hand.

Hypersomnia: This is the second most common consequence. It is quite universal in acute stages of moderate to severe injury as patient is often kept intubated and sedated, on pain medications and primary brain and brainstem pathology from TBI may also contribute. Weight gain from medications to use the consequences of TBI such as antidepressants, anxiolytics or anticonvulsant medications, lack of activity, not working or going to office, being sedentary due to severe TBI and/or neck/bodily injury, overeating due to injury to satiety center of the brain may result in development of obstructive sleep apnea even when there are no oropharyngeal anatomical risk factors. Direct or indirect injury to sleep centers and breathing centers may also contribute. Lowered hypocretin levels may be operative as stated elsewhere. Neck injury may impair diaphragmatic function and add insult to injury. Associated high spinal cord injury may be devastating but cervical whiplash itself is known to cause obstructive sleep apnea [21]. Narcolepsy may be precipitated in a person who is genetically predisposed for it or even be caused by TBI, sometimes even mild TBI. After several years it may be replaced by insomnia in some patients. Hypersomnia with prolonged sleep and even Klein-Levin like syndrome might occur. The periodic limb movements (PLMs) are common either due to medications used to treat TBI or due to unknown reasons such as inactivity or complex chemical changes/alterations, not yet known. Circadian rhythm disorders may contribute. Video-polysomnography with expanded EEG montage and frequently a multiple sleep latency test (MSLT) is addition if the Epworth Sleepiness Scale (ESS-appendix 1) is 11 or more is essential for the diagnosis and should be in-lab and not portable. Actigraphy and sleep diary might help as well.

Parasomnias: These are third most common complications and often co-exist with hypersomnia or insomnia. Each patient may have more than one parasomnia. They may also develop as a remote complication of TBI. As repeated concussions are known to predispose to Parkinson's disease and Parkinson's disease is associated with or even preceded by REM behavior disorder (RBD) by as much as 3 years, this is not entirely unexpected. Sleepwalking, nocturnal eating disorder, nocturnal seizures, nocturnal enuresis either as a part of post-traumatic OSA or due to TBI itself and confusional arousals all are seen and common. In-lab video-polysomnography (video-PSG) with expanded EEG montage is essential for the documentation and diagnosis. The family may also be encouraged to use their smart phones to record these events to help in diagnosis.

9. How to approach a patient with PTSLD

Detailed history is important. One should carefully ascertain if sleep related symptoms started after TBI or preceded that. If latter, document any changes in severity of symptoms or change in symptoms. The routine scales administered in our practice are: Mini mental state examination, ACE questionnaire, Hamilton anxiety Scale (appendix 3), Beck's depression inventory (appendix 4), Epworth sleepiness Scale (appendix 1) and Berlin questionnaire (appendix 2). Careful determination of LOC, PTA and GCS is done based on hospital, ER and other previous records. Computerized psychological and neuropsychological testing (easily administered by even a medical assistant using the 'neurotrax' system) to determine the global assessment of cognitive functioning and levels of anxiety and depression is important to establish a baseline and future follow up. Physical examination should pay careful attention to the HEENT examination, TMJ, neck size, chin (prognathia, retrognathia, micrognathia), oropharyngeal examination for tonsillar size from 1-4 and Mallampati score 1-4, focal and lateralized neurological signs and cardiopulmonary examination. Sleep/wake related history should include details about snoring, witnessed pauses in breathing, bedtime, wake up time, circadian rhythm, gasping and choking in sleep, hypnagogic hallucinations, hypnapompic hallucinations, nightmares, nocturnal incontinence, seizures, sleep walking and acting out of dreams, any falls from bed, restless legs and periodic limb movements (by asking questions such as do you have creepy crawling sensation in your limbs and feet which improve by movement). Wakefulness should be evaluated for alertness, drowsiness, dozing, napping, daydreaming and automatic behaviors. The ESS (appendix 1) is helpful in quantitating sleepiness and Berlin questionnaire (appendix 2) about the probability of sleep related breathing disorder. Sometimes the sleepiness scales are not reliable in patients with severe head injury. Caregiver's input is needed in those situations. Current medication list is critical.

Ancillary tests include an MRI of the head with tractography (diffuse tensor imaging or preferably constrained spherical deconvolution), EEG, an overnight in lab video-PSG with an expanded EEG montage and a 5 nap daytime multiple sleep latency test (MSLT) if ESS is greater than 10. A seven day sleep diary and actigraphy is obtained in those with insomnia or circadian rhythm issues. CSF hypocretin levels may be useful.

Initial follow up visits are monthly for 3 months and then 3 monthly times two. Six monthly visits are obtained after that. Annual ancillary evaluation is more limited and defined by patient's clinical symptomatology. However, sleep disorders may change their characteristics during the course and re-evaluation may need to be tailored accordingly. Therefore a cook book approach is not useful. Maintenance of wakefulness test may be useful in quantitating residual daytime sleepiness.

10. PTSLD

We propose this term as an acronym for post-traumatic sleep/wake disorders to distinguish it from PTSD or post-traumatic stress disorder.

1. Post-traumatic sleep-related breathing disorder:

This is fairly common in general population affecting 2-4 percent of all adults. In patients with TBI, sleep apnea defined as apnea-hypopnea index (AHI) of 10 or greater may be present in up to 30 percent of all patients. Seventy five percent of apneas and hypopneas are obstructive in nature. This condition may present as hypersomnia, insomnia or may only be seen on laboratory evaluation as an unexpected finding. It may cause a secondary REM behavior disorder (RBD -a parasomnia) which may potentially be injurious to the patient if not recognized and treated and further compound the TBI. Mechanisms of post-traumatic sleep related breathing disorder are several. Patient may have pre-existing anatomical abnormalities which were insufficient to cause the sleep related breathing disorder prior to TBI but the occurrence of TBI provides a sufficient milieu for it to clinically manifest. Sedative medications such as clonazepam may potentiate apnea, antidepressants such as sertraline and mirtazapine and anticonvulsants such as valproic acid cause weight gain which is a known risk factor for this condition. Weight gain may also result from physical inactivity and direct damage to hypothalamic centers related to feeding and satiety. Tracheostomy, if done, during the acute management of TBI may further increase the risk especially in children by causing tracheomalacia, as seen in one child by the senior author of this chapter. In addition to known risks of this condition such as premature death, hypertension, heart attack, stroke, dementia and diabetes, this condition may impair the control of patient's seizure disorder if present. Newborns with perinatal head trauma and abused children may develop central apnea due to direct injury to the breathing centers in the brain. In general, more severe the head injury, higher the apnea hypopnea index and hypoxia are. ESS (appendix 1) may be unreliable in those with moderate to severe head injury and should not be used as a sole criterion to order or not order the sleep studies. [10] Berlin questionnaire (appendix 2) also helps in predicting the probability of sleep related breathing disorder.

2. Post-traumatic narcolepsy:

The incidence of narcolepsy in general population is about 1:2000 in the USA. Hormonal change and minor head trauma at puberty are long known to be initiating factors for narcolepsy in neurology text books as the genetic propensity of narcolepsy usually manifests clinically at or after puberty 90 percent of the time. In addition, most patients with narcolepsy remain the same throughout their lifetime. Post-traumatic narcolepsy is different in that it is far more common than general population (it is seen in up to 6-9 percent of all patients with TBI) [10, 11] and down the road, after several years in our experience, symptoms may sometimes abate and even be replaced by insomnia. Hypocretin levels are known to be reduced by TBI and may well play a pathogenetic role. New onset cataplexy might occur after TBI, increasing the risk of falls and therefore repeated TBI. Nightmares are common in TBI and careful history is needed to distinguish them from hypnagogic and hypnapompic hallucinations seen as auxiliary symptoms of narcolepsy. Occurrence of narcolepsy is not correlated with the degree of TBI.

Polysomnogram (PSG) will nearly always show some degree of sleep disruption such as increased percentage of N1, frequent awakenings, reduced sleep efficiency (less than 85

percent), reduced N3 (delta) percentage (less than 15 percent) and sometimes SOREMP (sleep onset REM period or REM sleep occurring with 15 min of sleep onset). The MSLT will show a sleep latency of 8 min or less and 2 or more SOREMPs in 5 naps. [33]

3. Post-traumatic hypersomnia.

Idiopathic hypersomnolence syndrome is long known to often follow TBI and conditions such as Guillaine Barre Syndrome (GBS) or infectious mononucleosis (IM). The PSG shows relatively normal or even improved sleep efficiency sometimes greater than 95 percent, increased or normal delta percentage, relatively few awakenings, minimal sleep disruption if any but severe daytime somnolence on MSLT with no SOREMPs. Medication effect needs to be excluded and one has to be careful not to misdiagnose 15 percent cases of narcolepsy in whom MSLT is initially negative as post-traumatic hypersomnia. The PSG features described above are helpful in distinction and there is no history of hypnagogic or hypnapompic hallucinations or cataplexy. Autonomic symptoms are sometimes present. [33]

4. Post-traumatic periodic limb movement disorder (PLMD):

These may a solitary abnormality on PSG but more often are associated with other conditions such as OSA and narcolepsy. They may have been present premorbidly but are often worsened by medications used for the treatment of TBI. They may be asymptomatic and may not require any treatment or cause significant patient insomnia or spousal discomfort and need treatment. Lower extremities are affected and sometimes only one side but upper extremities may be involved in addition or alone. Neurologic deficit such as hemiparesis or paraparesis may worsen or cause this condition. Anemia of chronic disease may compromise the serum ferritin level and may compound the issue. They are considered significant if more than 15/hour in an adult or 5/hr in a child. [33] Up to 30 percent of all patients may have this condition. [10] They may or may not report RLS in addition when awake.

5. Post-traumatic REM behavior disorder (RBD):

This condition was first described to occur in cats when lesions were created in periolocus coeruleous area to interrupt impulses going down the ventral reticulospinal tract to spinal motor neurons in REM sleep [10]. Similar mechanisms are operative in humans with TBI. Associated Parkinson's, alcoholism and medications may also contribute. Up to 13 percent patients show symptoms of RBD and/or show increased tone in chin EMG on PSG [10]. Patients typically act out their dreams during last third of sleep at night when REM percentage is the highest and potentially fall from bed, climb out of windows or walk out in freezing weather. It may be secondary to post-traumatic OSA and then it responds to CPAP. If not, RBD precautions and medications are necessary. It may be a precursor of Parkinsonism in patients with punch-drunk syndrome and may precede that condition by as much as 3 years. It should be distinguished from sleep walking which usually occurs during the first half of sleep and there is no dream recall. It should also be distinguished from NREM sleep related confusional arousals which are similar to night terrors.

6. Other post-traumatic parasomnias:

They include sleep paralysis, cataplexy, sleep walking, nightmares, sleep enuresis and nocturnal eating disorder. [33] All parasomnias (these plus RBD) occur in 25 percent of all patients with TBI, either by themselves or in addition to other disorders. Birth injuries to the head may be associated with head banging disorder. [16]

7. Post-traumatic insomnia:

At least one quarter of all patients with TBI have insomnia either sleep onset or sleep maintenance or a combination thereof. [10] Hamilton anxiety scores (appendix 3) are typically elevated in those with sleep onset insomnia and Beck's depression inventory scores (appendix 4) in those with sleep maintenance insomnia. Physical factors such as frequent examination by nurses and respiratory therapists during ICU stay may be the cause at least in acute TBI. Medications such as bronchodilators, anticonvulsants such as topiramate or stimulants such as methylphenidate may cause insomnia. Circadian rhythm abnormalities and not going to regular work and physical inactivity leading to frequent daytime naps may cause insomnia at night. Post traumatic sleep related breathing disorder both of obstructive type or central type may cause insomnia as well. Severe restless leg syndrome (RLS) may cause sleep onset insomnia and PLMs, sleep maintenance insomnia. Patients with post-traumatic narcolepsy may sometimes present initially as insomnia at night and only a careful history uncovers the diagnosis. For example, a patient treated by the senior author was treated for 2 years as insomnia by various physicians, until she disclosed to the author additional history of severe daytime sleepiness and napping since TBI and disturbing "nightmares" (actually hypnagogic hallucinations) with automatic behavior which prevented her from holding onto any job and not succeed in her new marriage. She responded beautifully to sodium oxybutate and was immensely grateful.

8. Post-traumatic circadian rhythm disorder:

This is a fairly common complication. The disorders include a delayed sleep phase syndrome (DSPS), irregular sleep wake cycle, advanced sleep phase syndrome (ASPS) and non-24 hour sleep wake cycle. [33] Irregular sleep wake cycle is common during the acute phase of TBI in moderate to severe cases as nurses and respiratory therapists check on the patient frequently and patient is on medications including sedatives or anesthetic agents such as propofol. It is also common in chronic TBI patients with a psychiatric disorder or blindness. Otherwise DSPS is the most common complication related to circadian rhythm abnormality in patients with TBI and a direct injury to suprachiasmatic nucleus may well be the cause. ASPS is quite frequent in elderly patients with TBI. Non-24 hour cycle is a rare complication in some patients showing a stepladder pattern on actigraphy. [33]

11. Differential diagnosis

Lack of pre-existing history of sleep related symptoms is critical for the diagnosis of the primary post-traumatic sleep disorder, although the TBI may aggravate a pre-existing sleep/

wake disorder or make it more difficult to treat. Secondary gain may need to be excluded but objective confirmation from tests as outlined above, obviates that possibility. Interviewing the family members, friends, golf buddies etc and previous medical records are helpful in determining whether the disorder is primary or secondary. Previous anatomical abnormalities do not automatically exclude a primary post traumatic sleep/wake disorder as patient may have been compensated before and the TBI may have been the “last straw which broke the camel’s back”. Likewise, a positive HLA testing does not automatically make narcolepsy pre-existing or genetic, as head trauma, even mild or minimal is known to be the initiating factor for narcolepsy. Please refer to the international classification of sleep disorders [33] edition 3 for further help in differential diagnosis of post-traumatic sleep disorder/s from non-traumatic etiologies as detailed discussion of that would be tangential to the intent of this chapter.

Treatment : Once it is realized that TBI may cause or aggravate a pre-existing sleep/wake disorder, management is simple. It is treated like any other sleep disorder of another etiology by adding medications, reduction of medications, meditation, machines, devices or behavioral techniques. Treatment is important as it will interfere with rehabilitation potential of the patient unless addressed head on. The treatment modalities outlined below are well described in standard text books of sleep medicine and in the practice guidelines of the American Academy of Sleep Medicine [34] and would only be briefly outlined below without individually referring each modality to prevent unnecessary expansion of the reference list and dilute the intent of this chapter.

Medications and reduction of medications: Mild sleep apnea may be managed with proprietyline. Periodic limb movements may be helped by Clonazepam, dopamine agonists, gabaergic agents, tonic water and vitamin D. Nocturnal eating disorder often responds to topiramate. REM behavior disorder responds well to Clonazepam and/or melatonin. Nocturnal seizures require anticonvulsants. Carbamazepine is most effective. Hypnagogic hallucinations and nightmares may require clonazepam, imipramine or more complex pharmacological remedies as NMDA agonists.

Reduction of medications may also help by reducing weight, decreasing excessive daytime sleepiness, lessening the aggravation of OSA or reducing PLMs. Some medications such as amitriptyline may induce or aggravate RBD in TBI patients and that might improve by this strategy. Sometimes, reducing topiramate, certain antidepressants, stimulants and wakefulness promoting agents etc may improve insomnia.

Meditation: simple meditation techniques such as Hong-Sau which do not require any special equipment or posture or more complex such techniques such as yoga exercises requiring exercise mats and lotus position may be useful at times in reducing anxiety and improving sleep onset insomnia.

Behavioral techniques: 11 principles of sleep hygiene (appendix 5), 6 Bootzin’s principles (appendix 6) and cognitive behavioral therapy for insomnia (appendix 7) are often useful for the management of insomnia. In fact most enduring relief of post-traumatic insomnia comes with non-pharmacological behavioral techniques.

Patients with RBD may require padding around their beds, alarms and double locks at doors and boarding up of windows (RBD precautions). Those with nocturnal eating disorder, may need to have a lock on the refrigerator.

Phototherapy: It is useful in the treatment of post-traumatic delayed sleep phase syndrome and advanced sleep phase syndrome, non 24 hr sleep/wake cycle and insomnia caused by post-traumatic depression. Morning exposure to a standard 2500-10,000 lux lamp from a distance of about 18-24 inches for 30-60 minutes is used in all of these conditions except ASPS in which evening exposure is required. Nausea and queasiness may occur and the duration of exposure may need to be optimized upwards gradually.

Chronotherapy. It will be useful in managing circadian rhythm disorders resulting from head trauma. Advancing the bedtime by 3 hrs a day may help the treatment of DSPS over 8-10 days. It may be used alone or in conjunction with phototherapy and/or melatonin.

CPAP: Continuous positive airway pressure it is the mainstay of treatment for moderate to severe OSA. Patients may experience difficulty in using this device due to facial or TMJ injuries or chest trauma or CHF or if they are claustrophobic.

BIPAP and BIPAP-ST (NIPV)- Bi-level treatment is necessary in some of the patients who have co-morbid muscle disease or CHF. It provides a lesser pressure to facilitate exhalation in an individual with weak muscles or CHF. The inhalation pressures (IPAP) are at least 2 cm of H₂O or more than the pressure for exhalation (EPAP). BIPAP-ST or NIPV provides additional protection by backing up ventilation if the respiratory rate falls below a predetermined rate such as 10/min.

Adaptive servo ventilation (ASV): is often useful when nothing else works in complex or central sleep apnea caused by TBI by overwhelming the apneas not only simply by pressure but also volume of the inhaled air and mostly obviates the need for tracheostomy except in acute stages. This device is quite expensive but well worth it as the senior author has never prescribed tracheostomy for sleep-related breathing disorder ever since this device has been commercially available. Prior to that, it was needed at least in one patient every year in our clinic.

Jaw advancement devices: may be useful in those with mild post-traumatic OSA with TMJ issues.

Ongoing follow up is essential by at least 3-6 monthly office visits and yearly sleep studies since post-traumatic sleep disorders are notorious to change during their natural history and may require altogether different treatment as the time passes by.

12. Discussion

A spectrum of sleep disorders are a common finding after the acute phase of TBI [9]. They result in daytime somnolence which in turn may lead to poor daytime performance, altered sleep-wake schedule, heightened anxiety, and poor individual sense of well-being, insomnia

and depression [10] Sleep changes and deranged sleep architecture are more common in *chronic* TBI patients as compared to the general population [10]. Sleep disturbances can compromise the rehabilitation process and the ability to return to work. [20] A high index of suspicion may lead to a diagnosis and subsequent treatment of these disorders and contribute to physical and cognitive rehabilitation of these patients. [10] A proper diagnosis and greater awareness of this complication protects patient's rights for medical care under auto-insurance laws in states such as Michigan [2]. This will also be critical in the management of TBI related symptoms of returning veteran of Iraq and Afghanistan war since TBI is the signature injury of those wars and has become a silent epidemic. [1]

13. Directions for future research and efforts:

The future research and efforts should concentrate on primary prevention of TBI, better delineation of premorbid sleep/wake status by some scales (similar to those which predict premorbid IQ), early identification and accurate diagnosis of post-traumatic sleep/wake disorder, its exact impact on physical, cognitive and occupational rehabilitation, convincing the auto-insurances not to be stingy in the care of these unfortunate individuals and look at sleep/wake related complaints as a medical issue and not a malingering issue, and the US government to provide greater research and medical funds for this important medical condition.

Appendix 1. The epworth sleepiness scale

0 = no chance of dozing

1 = slight chance of dozing

2 = moderate chance of dozing

3 = high chance of dozing

SITUATION	CHANCE OF DOZING
Sitting and reading	_____
Watching TV	_____
Sitting inactive in a public place (e.g. a theater or a meeting)	_____
As a passenger in a car for an hour without a break	_____
Lying down to rest in the afternoon when circumstances permit	_____
Sitting and talking to someone	_____
Sitting quietly after a lunch without alcohol	_____
In a car, while stopped for a few minutes in traffic	_____

Any answer followed by double asterisks (**) is a positive response.

Category 1 is positive with 2 or more positive responses to questions 2 through 6

Category 2 is positive with 2 or more positive responses to questions 7 through 9

Category 3 is positive with 1 or more positive responses and/or a BMI>30

2 or more positive categories indicates a high likelihood of sleep apnea

Bottom of Form

Appendix 3. Anxiety rating scales

1. Background

1. Authored by Max Hamilton in 1959
2. Public domain anxiety rating scale

2. Symptom Rating Scale (0=Not Present, 4=Disabling)

1. Anxious Mood

- 1.1. Worries
- 1.2. Anticipates worst

2. Tension

- 2.1. Startles
- 2.2. Cries easily
- 2.3. Restless
- 2.4. Trembling

3. Fears

- 3.1. Fear of the dark
- 3.2. Fear of strangers
- 3.3. Fear of being alone
- 3.4. Fear of animal

4. Insomnia

- 4.1. Difficulty falling asleep or staying asleep
- 4.2. Difficulty with Nightmares

5. Intellectual

5.1. Poor concentration

5.2. Memory Impairment

6. Depressed Mood

6.1. Decreased interest in activities

6.2. Anhedonia

6.3. Insomnia

7. Somatic Complaints: Muscular

7.1. Muscle aches or pains

7.2. Bruxism

8. Somatic Complaints: Sensory

8.1. Tinnitus

8.2. Blurred vision

9. Cardiovascular Symptoms

9.1. Tachycardia

9.2. Palpitations

9.3. Chest Pain

9.4. Sensation of feeling faint

10. Respiratory Symptoms

10.1. Chest pressure

10.2. Choking sensation

10.3. Shortness of Breath

11. Gastrointestinal symptoms

11.1. Dysphagia

11.2. Nausea or Vomiting

11.3. Constipation

11.4. Weight loss

11.5. Abdominal fullness

12. Genitourinary symptoms

12.1. Urinary frequency or urgency

12.2. Dysmenorrhea

12.3. Impotence

13. Autonomic Symptoms

13.1. Dry Mouth

13.2. Flushing

13.3. Pallor

13.4. Sweating

14. Behavior at Interview

14.1. Fidgets

14.2. Tremor

14.3. Paces

3. Interpretation

1. Above 14 symptoms are graded on scale

1.1. Not present: 0

1.2. Very severe symptoms: 4

2. Criteria

2.1. Mild Anxiety (minimum for Anxiolytic): 18

2.2. Moderate Anxiety: 25

2.3. Severe Anxiety: 30

4. Other Anxiety Scales

1. Zung Self Rating Scale for Anxiety

2. Beck Anxiety Scale

3. GAD-7

Appendix 4. Beck depression inventory

1. Background

1. Twenty-one question survey completed by patient

2. Answers scored on 0 to 3 scale

1.1. Minimal: 0

1.2. Severe: 3

2. Questions

1. Sadness

2. Hopelessness

3. Past failure

4. Anhedonia

5. Guilt

6. Punishment

7. Self-dislike

8. Self-blame
9. Suicidal thoughts
10. Crying
11. Agitation
12. Loss of interest in activities
13. Indecisiveness
14. Worthlessness
15. Loss of energy
16. Insomnia
17. Irritability
18. Decreased appetite
19. Diminished concentration
20. Fatigue
21. Lack of interest in sex

3. Interpretation

1. Score <15: Mild Depression
2. Score 15-30: Moderate Depression
3. Score >30: Severe Depression

Resources: Beck Depression Inventory

1. General
 - 1.1. Intended for use by licensed professionals only
 - 1.2. Copyrighted by the Psychological Corporation
2. Available for purchase from Psychological Corporation
 - 2.1. <http://www.psychcorp.com/>

5. Reference

1. Beck (1996) Beck Depression Inventory, Harcour

Appendix 5. Eleven principles of sleep hygiene

1. Wake up and go to bed at about the same time every night. Bedtime and wake-up time should not differ from working days to weekend nights by more than approximately an hour.
2. Avoid sleeping in on weekends to “catch up” on sleep. This makes it more likely that you will have problems falling asleep.

3. If you take naps, they should be short (no more than an hour) and scheduled in the early to midafternoon. However, if you have a problem with falling asleep at night, napping during the day may make it worse and should be avoided.
4. Spend time outside every day. Exposure to sunlight helps to keep your body's internal clock on track.
5. Exercise regularly. Exercise may help you fall asleep and sleep more deeply.
6. Use your bed for sleeping only. Don't study, read, listen to music, watch television, etc., on your bed.
7. Make the 30–60 minutes before a quiet or wind-down time. Relaxing, calm, enjoyable activities, such as reading a book or listening to calm music, help your body and mind slow down enough to let you get to sleep. Don't study, watch exciting/scary movies, exercise, or get involved in “energizing” activities just before bed.
8. Eat regular meals and don't go to bed hungry. A light snack before bed is a good idea; eating a full meal in the hour before bed is not.
9. Avoid eating or drinking products containing caffeine from dinner time on. These include caffeinated sodas, coffee, tea, and chocolate.
10. Do not use alcohol. Alcohol disrupts sleep and may cause you to awaken throughout the night.
11. Smoking disturbs sleep. Don't smoke at least one hour before bed (and preferably, not at all!).

Appendix 6. Six Bootzin's principles for stimulus control in the treatment of insomnia

1. Go to bed when sleepy.
2. Use the bed for sleeping; do not read, watch television or eat in bed.
3. If you are unable to fall asleep, get up and move to another room; stay up until you are really sleepy, then return to bed; if sleep still does not come easily, get out of bed again. The goal is to associate bed with falling asleep quickly.
4. Repeat step 3 as necessary throughout the night.
5. Set the alarm and get up at the same time every morning regardless of how much you slept through the night. This helps the body acquire a constant sleep-wake rhythm.
6. Do NOT nap during the day.

Appendix 7. Cognitive behavioral therapy for insomnia: weekly for 8-10 weeks:

Sleep hygiene-see above-appendix 5

Stimulus control-see above-appendix 6

Sleep restriction or curtailment

Relaxation, meditation, hypnosis

Reducing muscle tension and hyperarousal by biofeedback

Relapse prevention:

1. Don't compensate for sleep loss
2. Start stimulus control procedures immediately
3. Re-engage sleep restriction should the insomnia persist beyond a few days.

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