



Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury (DCoE) Webinar Series

March 10, 2016 1-2:30 p.m. (ET)

Management of Sleep Disturbances Following Concussion

Operator: Thank you for standing by. At this time, all participants will be in a listen only mode for the duration of today's call. This call is being recorded. If you have any objections, you may disconnect at this time. I'd now like to turn the call over to Dr. Panakkal David. Thank you. You may begin.

Dr. David: Okay, thank you for joining us for the DCoE traumatic brain injury, March seminar. Sorry about that. Managing sleep disturbances followed by concussion. My name is Dr. Panakkal David. I'm a traumatic brain injury subject matter expert for the defense and veteran brain injury center, at the defense center of excellence, for psychological health and traumatic brain injury. I will be your moderator today for today's seminar. Before we begin, let's review some of the webinar details. If you experience technical difficulties, please visit dcoe.mil/webinars to access the trouble shooting page. Please feel free to identify yourself to other attendees via the chat box, but refrain from marketing your organization or product.

Today's presentation references and resources are available for download, from the file pod and will be archived on the online education section of the DVBIC website. All who wish to obtain continuing education credit or certificate of attendance and meet eligibility requirements must complete the online CE evaluation. After the webinar, please visit dcoe.pdf.pesgce.com. To complete the online CE evaluation and download and print the CE certificate or certificate of attendance. The evaluation will be open through Thursday March 24, 2016.

Throughout the webinar, you are welcome to submit technical or content related questions via the Q&A pod, located on the screen. All questions will be anonymous. Please do not submit technical or content related questions via the chat box. I will now move on to today's webinar: Management of sleep disturbances following concussion.

Nearly 340,000 service members sustained a traumatic brain injury between 2000 and 2015. Of these TBI, 82.5% were classified as mild TBI known as concussion. Matthias and Navarro showed that as many as 50% of people who sustain a concussion suffer from a sleep disturbance. Additionally, in a 2008 Department of Defense survey of Operation Iraqi Freedom service members, 92% of those

surveyed with a TBI history experienced fatigue. This is the Hoge et al. study in 2008.

Sleep disturbances and fatigue can lead to worsening symptoms such as decreased cognition, pain, and irritability that can ultimately affect return to work. Clinically, sleep problems may coexist with headache, traumatic pain, and other neurological symptoms that create diagnostic and treatment challenges for providers. This presentation will address assessment and management of concussion, associated sleep disturbances, and fatigue.

The speakers will present recent research on concussion management and sleep disturbance and discuss ways to enhance quality of life and function in individuals who are experiencing both concussion, sleep, and fatigue. At the conclusion of this webinar, participants will be able to describe common sleep disturbances following TBI, discuss appropriate and diagnostic criteria for sleep disorders, demonstrate knowledge of fatigue and management of TBI, particularly pharmacological and non-pharmacological treatment of sleep disturbances and fatigue, describe new advances in treatment of sleep disorders.

Dr. Michael Yochelson is the vice president of medical affairs and chief medical officer for the MedStar National Rehabilitation Work in Washington D.C. He's a professor of clinical neurology and clinician rehabilitation that is been at Georgetown University in Washington D.C. Vice chair of clinical affairs in the department of rehabilitation medicine at MedStar Georgetown University Hospital, and acting chair of the Department of Veterans Affairs special advisory board on prosthetics and special programs. He's previously a Navy neurologist and psychiatrist. Dr. Yochelson received his M.D. from George Washington University School of Medicine and health pharmacist, and his MBA from University of Maryland.

Dr. Emerson Wickwire, the director of insomnia program and assistant professor in the Department of Psychiatry and Medicine at University Maryland School of Medicine. He previously co-founded a leading interdisciplinary sleep medicine center that began a model for comprehensive sleep medicine centers throughout the country. He holds a special interest in sleep medicine population and serves as the local site director for the Walter Reed National Army Medical Center, National Capital Consortium Sleep Medicine Fellowship. Dr. Wickwire received his PhD in psychology from the University of Memphis. He completed his residency at the University Mississippi Medical Center and advanced training in behavioral sleep medicine at Johns Hopkins School of Medicine. Thank you Dr. Yochelson and Dr. Wickwire for your presentation. If you have any que-

Dr. Yochelson: Thank you Dr. David for that introduction. On behalf of Dr. Wickwire and myself, I'd like to thank DVBIC for hosting this webinar. I think this is a very important topic, as the issue of sleep disturbances and fatigue is certainly one that's very important to our patient population, those who have sustained a traumatic brain injury.

If you could just take a moment to vote, or indicate what your discipline is. Okay. It

looks like we have a large number of behavioral health providers at almost 29%, about 17% or 18% rehab providers, another 17% social workers, and then a mix of primary care providers, nurses, and other. Go ahead and move on.

I'm going to start with an overview of concussion and talk a little bit about the impact of concussion on sleep and vice versa, and then turn it over to Dr. Wickwire who will talk about sleep disorders in more detail, both in the general population as well as TBI survivors, and then finally we'll wrap up with a discussion of fatigue after traumatic brain injury.

First I wanted to start with a definition. Concussion is in fact a mild traumatic brain injury. I think most of you on the call would be aware of that, but I think it is important to talk to our patients about that, because a lot of times patients assume that a concussion is not, in fact, a brain injury. It's a complex pathophysiologic process affecting the brain, induced by traumatic biomechanical forces.

It's very prevalent in the United States, as you can see. There are about 2.5 million emergency departments per year for all levels of traumatic brain injury. Sports related traumatic brain injury is estimated somewhere between 1.6 and 3.8 million per year. The reason the discrepancy between that and the above number is that not all sports related brain injury and not all concussion seeks treatment in the emergency department. The above statistic tends to be skewed more towards your more severe brain injuries. Of those brain injuries, about 50,000 each year result in death. There's approximately 5 million people in the United States living with disability as a result of brain injury. This is a very significant issue.

There are 2 principle mechanisms of traumatic brain injury, and I include 2.5 because working with the military population, blast injury is another thing that you see more commonly. We certainly don't see that very commonly in the civilian sector in the United States. Primarily, we see contact injury and acceleration/deceleration injuries. Contact injury is when an object strikes the head, or the head strikes an object. Typically, the head is stationary if struck. It's possible, of course, that both are moving at the same time. That results, then, in contact of the brain to the skull itself.

Acceleration/deceleration injuries occur when there's unrestrained movement of the head. This results in a tensile shear and compressible forces. It can be both transnational and/or rotational. Rotational tends to have a greater impact in terms of TBI symptomatology. Motor vehicle accidents and falls are most common here.

Blast injury, I put as the half of your mechanisms. The reason being, actually, a large number of blast injuries either result in either a contact injury or an acceleration/deceleration injury. What will happen in a blast is either there's debris that hits the military member or whomever in the head, or the blast itself results in the person being flung to the ground or a wall, and hitting a hard contact force. Likewise, they can get acceleration/deceleration. The actual mechanism of inquiry can be the same in blast injury, but blast injury has the additional potential to create brain injury because for the blast waves transmission through the brain as

well as tertiary and quaternary effects of blast injury.

The damage, regardless of the type of injury, the damage can be focal or multifocal or diffuse. Some of the more common types of focal, you'll see with a contact injury where you'll have actual injury to the scalp or the skull, surface lacerations, you can get an intracranial hematoma, or essentially bleeding or bruising in a certain area of the brain. Raised intracranial pressure which can lead to vascular changes, typically raised intracranial pressure itself is going to give a more diffuse injury, but it can also result to a stroke which would then be a focal injury to the brain.

On the diffuse side, diffuse accidental injury, which is by far and away the most common result of a traumatic brain injury. You can also have hypoxic, ischemic damage, meningitis. Meningitis is less common. It tends to occur if you have an open brain injury and it's because of dirt or bacteria that gets into the opening and then results in a meningitis or other infection. Vascular injury can be more diffuse, and then changes in neuro chemistry. Some of these things are areas where we really need to focus in terms of the research of the treatment of traumatic brain injury.

Wanted to talk a little about diffuse accidental injury, because it is the most common type of injury you'll see, particularly with the mild traumatic brain injury. At the time of impact, there are rotational forces that create a shear to the axons, the axon becomes stretched, but not necessarily torn, unless there's significant mechanical loading. The damage occurs to the cytoskeleton of the axon, and then damage begins that can continue to progress over the course of 72 hours following the trauma itself. This is a very important time period for neuro protection and potential recovery. The region of high vulnerability involves axons that go through the brain stem and are involved in the reticular activating system. This contributes to coma and persistent vegetative states. This is also an area that's important in terms of arousal and wakefulness, and as we'll be talking about sleep issues, this is an important issue for brain injury. The most susceptible areas are the gray, white matter junction, and then specific focal areas include the frontal and temporal white matter, the upper brain stem, the splenium of the corpus callosum and the basal ganglia.

Some research has shown that there's neuro chemical changes, these were in animal studies. After traumatic brain injury, 19 out of 20 chemicals in the neuro cortex were shown to be altered, and 9 out of 20 in the hippocampus were. In addition to neuro chemical changes, other changes that have been demonstrated after brain injury include edema, cytotoxicity, neuronal and glial integrity, mitochondrial changes, oxidative stress, inflammation in cell membrane disruption. These are all potential areas of treatment, and again, these tend to occur as part of a cascade early after traumatic brain injury, so these are areas of importance in terms of current research and way to either minimize through neuro protection, minimize the injury that is occurring or also areas in terms of neuro plasticity, ways to allow for recovery after traumatic brain injury.

In terms of symptomatology, we categorize the symptoms of concussion in 4 categories. In some articles you might see it in 3 categories, sometimes sleep is lumped in under somatic. Somatic, cognitive, emotional, and sleep disorders. Somatic include the physical symptoms such as nausea, vomiting, dizziness, headaches, numbness, tingling, weakness, things like that. Cognitive would be issues with memory, concentration, attention. Emotional would be depression, feeling sad, feeling irritable, or nervous. Sleep disorders which we'll talk about in much more detail include issues with lack of sleep, too much sleep, inability to fall asleep, or excessive daytime sleepiness. I do want to emphasize the difference between fatigue and sleepiness, sleepiness being the need to get more sleep, whereas fatigue is more of an issue of energy. We'll talk a little bit more about that in the talk as we talk about fatigue.

What's the natural course of concussion? In a study that looked at sports concussion, they found that in a typical course, and we think of a typical course as lasting a few days to a week or so. In patients have less than 4 symptoms they typically will follow this shorter course. The duration would be about 48 hours on average. Again, typically less than a week. About 18% do have symptoms that persist longer than 7 days, and these are the ones that we really need to pay attention to in terms of appropriate counseling and treatment.

What are some risk factors for longer post-concussive symptoms? Having greater than 4 symptoms, having a headache that lasts for greater than 60 hours, and fatigue or fogginess after injury. Fatigue, which again we'll talk about later, is potentially a prognostic indicator that somebody's going to have a more prolonged period. The issue of course, is that there's a lot of different factors, so in and of itself, it is not necessarily a prognostic indicator of more prolonged post-concussive state, but it is something to pay attention to, certainly in patients who have a longer post-concussive syndrome. Fatigue and fogginess is a very common symptom.

Sleep disturbances after traumatic brain injury are very common, up to 75% of patients with traumatic brain injury have some form of a sleep disturbance. It typically is more common in the more mild traumatic brain injury, so in your concussion or mild traumatic brain injury patient, more so than in some of your more severe patients. We actually looked at this on our inpatient unit, at MedStar National Rehabilitation Hospital, and this is just our clinical experience, what we found is that approximately 25% of the time, which an inpatient should be sleeping, they in fact were not sleeping. This is based on a nursing sleep log that was being done on an hourly basis.

What we found is that it wasn't 25% of patients that were having difficulties, it was actually less than that, but they were having difficulties in which they weren't sleeping for more than 25% of the time. This led to very significant functional impairment during the day. We found that it tended to occur more frequently in patients who were agitated. Patients whose Rancho Los Amigos scale was 4, which is confused and agitated, and it tended to occur earlier in the hospitalization.

Why was that? A few of our hypotheses, one was that it was a transition to a new environment. We certainly see among patients of all sorts, regardless of whether or not they have a brain injury, they sometimes don't sleep as well in a new environment, particularly when you're hospitalized. The other thing is the lower level of Rancho at admission. They were progressing as they were in our hospital, due to both natural recovery and rehabilitation. It was not unexpected that they would have more challenges with sleep earlier on in their hospital stay.

Overall, however, we felt that it was a better environment for sleeping than in the acute hospital, because one, we don't have quite as many buzzers, bells, and whistles going off all night and day. We're not waking people up in the middle of the night to check vital signs. We're very attentive to their environment because we understand that sleep is an integral part of their rehabilitation. It's something that we focus on, we pay attention to, that's why we do the nursing logs. As a result of the information that we get from the nurses, we also adjust medications, sleep schedules and the like. We're focusing on it unlike the acute hospital.

On the outpatient side, you don't necessarily have somebody who's going to walk into your office and tell you that they have a sleep disturbance, but as you're getting the history, certain key phrases might pop up and they might just say you know, I just can't seem to fall asleep, or a spouse or bed partner might say that they're waking up several times every night or getting confused, hallucinating. Certainly want to pay attention to snoring and breathing, either the same symptoms and questions you want to ask any time you're asking about sleep, I would actually encourage that these questions should be asked on a routine basis, whether or not the patient presents with any potential sleep disturbance or not, because you want to pick up on it. It is something that's very frequently overlooked, particularly in a primary care setting where someone might be coming in for a completely unrelated problem. If you're focusing on the brain injury itself, you do want to ask about sleep issues. They might come in complaining about tiredness or fatigue during the day but not have any complaints about nighttime. Again, you want to explore that in more detail.

Often, the inefficiency of sleep leads to other problems. Problems such as that is listed here. Fatigue, agitation, depression, pain, and cognitive problems. The question is, are these problems secondary to poor sleep, or are they a result of the traumatic brain injury? These are all symptoms you can get as a result of the brain injury, or in someone who hasn't even had a brain injury as a result of poor sleep. We really need to think about what is the impact of poor sleep on the recovery of somebody who's had a brain injury.

We know particularly with mild traumatic brain injury and concussion, what's our first recommendation? It's rest. What's our second and third? It's rest and more rest. We really need to understand better how much, how long, and how do you do it? There've been a number of studies looking at this. They've shown that students who have moderate activity actually do better than those who have complete rest as well as those who have high activity levels. There's indications that even if someone is asymptomatic, they're at increased risk for a second concussion within

the first week. Certainly in terms of physical rest or not going back to competitive sport within the first week might be a good indication.

There is an increased energy demand, in order to restore some of the neurochemical changes in the brain. Again, rest is actually an important issue in terms of treatment. I would say that the best recommendations that we have at this point, and it is still a gray area, would be relative rest for at least 3 days regardless of symptoms, and then not complete rest, not bed rest for any particular duration of time. At the most, 1 or 2 days, because we do know that extended periods of bed rest will lead to other complications, may actually slow down recovery and lead to disability as well. With that, I'll turn it over to Dr. Wickwire to talk a little bit more about the sleep issues and sleep disorders.

Dr. Wickwire: Thank you, Dr. Yochelson. Thank you to Deb Beck for hosting us, and thank you to all of you who for being here. Let me make sure I can move things forward. I want to start with just giving you a little bit of background in terms of my interest into the relationship between sleep and concussion or sleep and mild traumatic brain injury. About a year and a half ago, I was asked to join a concussion and sleep disorders working group, which Dr. Yochelson was leading. You'll recognize some of the names of the participants. I'm a bio behaviorally trained psychologist. Really, a sleep disorder specialist. I don't work in the behavioral health setting. I don't do primary mental health care. I work in a sleep intensive setting. That was the expertise that I brought to the group.

The genesis of this working group was really to begin to see if we could improve outcomes in mild traumatic brain injury, by looking at underappreciated sequelae or co-morbidities in patients with concussion. There were several of those including neuro psychiatric co-morbidities and chronic pain and neuro inflammation and then of course, disturbed sleep. This was the context.

As a result, we ... I'm not sure what's happened to the slides. Okay. As a result, we've just recently published, it's now been accepted for publication, a write up, preliminary findings from our working group. This will be published in *Neurotherapeutics*, which many of you recognize as a top brain science journal. 3 things that I'd like to talk about today, with that in mind. I want to step back and think a little about sleep. First is what sleep is, second is why does this matter at all in concussion, and third, offer a few suggestions for a roadmap as we move forward.

The average American adult will sleep for 24.8 years during his or her life. For most of us, sleep isn't something that we've thought about very much. It's sort of like a reliable car. We take it for granted until it breaks down. In reality, sleep is normal, natural and necessary. Many of you are familiar with the performance triad in the United States Army that really emphasized sleep as one of three pillars, not only of health, but also operational readiness, along with nutrition and exercise.

Think about it. If sleep doesn't serve some absolutely vital function that the biggest mistake the evolutionary process has ever made. What could possibly be adaptive

about being vulnerable for 8 hours per day? Maybe there's something important going on here. Generally, we think of sleep as a time of slowing down. In fact, most physiologic functions do slow down during the evening. Body temperature goes down, we consume less oxygen, our heart rate slows, our blood pressure drops.

Sleep takes place in rhythmic organized stages. We wax and wane in and out of deeper and shallower stages of sleep. What we see here looking at this slide is increasing duration of rapid eye movement, or REM sleep over the course of the night. You'll see that from peak to peak, each of these sleep cycles lasts about 100 minutes. We typically go through 4-6 sleep cycles over the course of the evening. The REM sleep episodes get longer, as I mentioned, so what this means is that the dreams that you remember right when you wake up in the morning are typically the dreams that you were having early in the morning or very late in your sleep period.

Conversely, we have the majority of what we call slow wave sleep, or stage N3, which stands for non-REM sleep, early in the evening. Non REM sleep is broadly associated with physical restoration, along with memory formation. The brain doesn't just turn off or on like a light switch. Different parts of the brain can be more or less awake or asleep, and we'll talk about that more as we move forward.

Ultimately, sleep is governed by 3 factors. 2 primary factors, and then a third, which is particularly relevant in patients with concussion, which we'll discuss in a sec. The first is called the sleep drive, or the sleep homeostat, or sleep pressure. You can think about this just like hunger or thirst. Over the course of the day your body builds up more need for sleep. That is influenced by caloric expenditure, in other words if you're out running a marathon, you will build up more need for sleep than if you are lying at home watching a football game. It is influenced by duration of wakefulness. This is one reason why we typically encourage patients with troubled sleeping at night to avoid naps. If you nap in the middle of the afternoon, by the time bed rolls around, you've only been awake for 6 or 8 hours, whereas if you stay awake all day, you'll have been awake for perhaps 16 hours.

One factor that influences sleep is the sleep drive. The thing is that if we only were experiencing the sleep drive, we'd all keel over pathologically sleepy all the time. The body also produces an alerting signal. This alerting signal, whereas the sleep drive is generally a linear function, the alerting signal function is in a circadian fashion. You've heard of Carpe diem, the Latin seize the day. Circa Diem, about the day, as to do with endocrinology. All of our body functions that are endocrine regulated function on about 24.2 hour cycle in human adults. What that means is that sleep, wakefulness, sex drive, hormone secretion, appetite regulation, learning aptitude, these are all regulated on this about 24.2 hour cycle, which I'll tell you more about in just a sec.

You'll notice that early in the afternoon, if you look carefully at this alerting signal slide, there is a dip in the alerting signal. That is why you feel tired after lunch. It's not because you had a big turkey sandwich. It's because it's hardwired into your brain to have slightly less alerting signal early in the day. You'll notice that there's

no alerting signal during the night shift. This is emphasizing here, and we'll talk more about how this relates to concussion in just a sec, but this is emphasizing why patients are so sleepy at night and why the risk for motor vehicle crash and workplace accidents are so much higher in the evening. This slide is simply depicting an interacting of sleep drive increasing, being supported by stronger levels of alerting signal, and going down during the night and starting over the next day.

The strongest regulator of the circadian rhythm is light. It probably explains about 85% of the variance in circadian rhythmicity. This is why if you fly from the mid-Atlantic, where Dr. Yochelson and I are now, to London or Los Angeles, your body clock adjusts after a few days. It's because your retina is exposed to light at different times. You've all heard melatonin. Many patients take it because they think it's going to help them sleep, even though for the vast majority of sleep complaints, it won't. Melatonin is secreted by the pineal gland, you can see her on the right in the diagram, and what happens is that light is a very powerful melatonin suppressor. Light comes in through the eye, it travels down and then it hits the motherboard of the circadian rhythmicity, which is called the suprachiasmatic nuclei. The suprachiasmatic nucleus. Melatonin is suppressed. Even small amounts of light, particularly bright and blue light, later in the evening, will make it more difficult to fall asleep, because they suppress melatonin. Conversely, light in the morning will make it easier to get up because it suppresses melatonin.

Sleep comes in 2 flavors. Rapid eye movement sleep and non-rapid eye movement sleep. They are as distinct from each other as each is from wakefulness. In fact, there are neurochemical gateways, or switches that regulate these entirely different neurophysiologic states in the brain. They are mutually inhibitory, mutually exclusive. We're not going to talk too much about the related neurotransmitters, but what I want you to understand is, that there are well defined neurochemical processes that control wakefulness, rapid eye movement sleep and non-REM sleep, and all of these can be damaged in traumatic brain injury.

We measure sleep in several different ways. The gold standard measurement, is what's called an overnight sleep study, or a polysomnogram. Poly for many and somno for sleep. You all know someone, or perhaps you even spent the night in a sleep lab yourself, where we measure many bodily functions. Respiratory effort and blood oxygen and muscle tone and eye movement. We're really looking at a number of physiologic functions during sleep. You all also have or know someone who has a traumatic brain injury or a jawbone or some other commercially available tracker. What this is, is the commercial version of a medical research grade device called an ACTi graph. An ACTi graph is driven by an accelerometer. This doesn't measure sleep, but it measures ambulatory movement.

In healthy adults, there are over 30 papers validating activity as a reliable proxy for sleep and wakefulness. For those of you who see patients, which is the majority of you on the call, the most common and probably most effective measurement of

sleep is simply a self-report sleep diary, and so I'd like to spend a little bit of time looking at that. We want to look at daytime activities that might impact sleep. Things like naps, exercise, booze, medications at bedtime, certainly caffeine would be appropriate, particularly for young and active duty kinds of patients. Also, we want to look at a number of sleep parameters, things like what time did you go to bed and how long did it take you to fall asleep? How long were you awake in the middle of the night? What time did you wake up this morning, and how was your sleep quality?

Sleep scientists are particularly interested in the variables such as total sleep time, how much sleep did you get, and sleep efficiency, which is a ratio of how much time did you sleep to how much time you were in bed. If you slept 4 hours but you were in bed 8 hours, your sleep efficiency would be 50%. Over the course of a lifespan, this changes some, but in general, we certainly want to think of 85% for young and middle age adults as an optimal sleep efficiency target.

Remember that what we're talking about here is what is sleep and why is it important? In terms of operational readiness, one thing that's very important is the relationship between sleep and neurocognitive performance. What we're highlighting here in this slide are data looking at cumulative days of sleep loss. You'll see in this study took place over 2 weeks on the X axis, those increments move from the baseline to day 14. Participants either had total sleep deprivation or 4, 6, or 8 hours in bed. The Y axis is what's called the psychomotor vigilance task. This is a valid and reliable measure of neurocognitive performance.

What you're seeing is that over time, consecutive days of not getting enough sleep consistently, increased mental errors. Ironically, or not ironically, these kinds of discoveries often emerge in multiple locations at the same time. There was another group at the Walter Reed Army Institute of Research doing exactly the same study. Slightly different design. This is a 1 week study, looking at 3, 5, 7, and 9 hours in bed, the same dependent variable. There are a number of dependent variables that I used mistakes from the PBT because the findings were entirely consistent, and this way you can see that the findings were consistent across these studies.

No surprise, the less sleep you get, the worse you do and those effects build on each other. What might be more surprising is that even after 3 days of recovery sleep, where participants are able to sleep for 8 hours a night, you're still all worse off than you were before the experiment started. The idea that you can catch up for lost sleep on the weekends, thus far hasn't been validated in the literature.

It's important to realize that soldiers, these are self-reported sleep times from epidemiologic studies. Soldiers get a lot less sleep than the average American adult. In some ways, that's not surprising, but it's important, particularly when we think about neurocognitive performance, operational readiness, and long term medical and psychological health. There's 1 approach that I'd like to share with you, and I want to just review briefly how this study was conducted and the findings, that will potentially be helpful for you in your patient care if you work with active duty soldiers, and it will almost certainly be helpful for you in your personal life, if you

are as busy as sometimes we can all feel.

In this study, what we wanted to look at was, and I say we, it's really the authors, this is another study from the Walter Reed Army Institute of Research, wanted to look at can we prepare for periods of acute stress when we know that we're going to get less sleep than we'd like to? What happened was everyone in this study slept normally and was just monitored for 2 weeks. They completed a sleep diary and they wore an ACTi graph, and they figured out, okay, Tom, you sleep an average of 6 hours and 45 minutes, and Susan, you sleep an average of 8 hours and 12 minutes. Rather than restricting sleep, they said for the next week, Susan, I want to you to stick with your 8 hours and 12 minutes, don't do it any differently. Continue to function exactly the same way. Tom, we're going to bump you up to 10 hours a night. You were only getting 6:45 before, we now want you to get 10 every night for a week.

This experience repeated the design you just have seen. Same dependent variables, the same Y axis that I showed you in the previous studies. What you're seeing here, is that prophylactically banking sleep, over sleeping before periods of sleep loss, reduces mental errors. I'll explaining a sec why this is so important for patients with brain injury. In other words, you still do worse, not surprisingly, if you only sleep 3 or 5 hours every night for a week, but you don't do nearly as poorly as if you hadn't banked sleep. That seen during the 5 recovery days as well.

Let's talk a little bit about sleep in traumatic brain injury. As Dr. Yochelson mentioned, patients consistently complained of poor sleep quality and fragmented sleep. Sleepiness and fatigue which Dr. Yochelson will speak about in just a few minutes, and also circadian dysregulation. Let's take a look at these in a summary fashion.

First thing that you need to realize is that sleep disorders, clinical sleep disorders, not only subjective sleep complaints, are very common in patients with traumatic brain injury. Some of these prevalence rates and this was from a very well conducted meta-analysis published several years ago, some of these prevalence rates are substantially higher. They're all higher than in the general population. Some are substantially higher. For example, narcolepsy is higher by an order of magnitude.

Why this matters, is measurement really, really matters. Dr. Yochelson mentioned earlier it's hard to tell what the cause of the problem is. Is it pain, is it the brain injury, is it comorbid post-traumatic stress, or comorbid depression. The answer is, the way you measure sleep really impacts your findings, and your conclusions. Look here for example, based on clinical reports and clinical evaluation, 20% of patients following concussion have insomnia. If you objectively measure their sleep, 7 out of 10 do. I'm not going to run through these individually. I simply want to highlight for you that measurement really matters, and we really need to be thinking about assessing sleep in multiple ways.

Circadian rhythm disorders emerge when the internal body clock is out of sync with

worldly demands. I mentioned shift work earlier. Shift work disorder takes place when there is either trouble falling asleep or trouble staying asleep or excessive daytime sleepiness that is caused by work schedule. Other common sleep disorders, other common circadian rhythm disorders include delayed sleep phase syndrome, where the bedtime delays later into the evening. Instead of falling sleep at 11:00, I might not want to fall asleep until 4:00, or advances earlier in the morning. Or earlier in the evening, rather. Instead of falling asleep at 11:00, I might want to go to sleep at 8:00.

In patients with traumatic brain injury, we also end up with non-specific circadian irregularities. Sometimes these get labeled as free running disorder or non-24. What this means is that patients biology and behavior has lost its rhythmic center. This can of course, be quite problematic. In general, we treat circadian rhythm sleep disorders through teaching good sleep habits, and implementing a highly structured sleep schedule. We use melatonin to help regulate circadian phase. Melatonin is quite effective as a circadian regulator, but generally not really effective as a sedative/hypnotic, as I mentioned earlier.

Most importantly we use bright lights to regulate wake time. In patients with traumatic brain injury, bright light also can improve mood, increase feelings of alertness and decrease feelings of fatigue. Dr. Yochelson will tell you more about that in a few minutes. Patients with narcolepsy, narcolepsy is a condition characterized by overwhelming urge to sleep in spite of adequate sleep opportunity. If you recall earlier in the presentation I mentioned that sleep and wakefulness are mutually inhibitory states. In patients with narcolepsy, those switches or gates that I mentioned, are broken.

Patients, it's not narcolepsy isn't just a disorder of pathological sleepiness, because the on/off sleep switches are fluctuating back and forth, it's also a disorder of poor sleep quality. The on/off wake switches are fluctuating back and forth during night. Narcolepsy is debilitating when it's left untreated. It's not surprisingly incredibly distressing for patients who have been told for 20 years that they have severe refractory depression. Behavioral health providers, there are more behavioral health providers on the call, we'd do very well to assess sleep more systematically in their patients, and that's why it's so great that you're with us this afternoon.

When patients have narcolepsy, the standard of care is wake promoting medication that does not always mean psychostimulant. There are other adenosine antagonists and so forth. Behavioral therapies are highly desired adjudicative treatments. Parasomnias can emerge following mild traumatic brain injury. Parasomnias are acting out behaviors during sleep. Sleep walking, sleep talking, thrashing about, kicking, most violently what's called REM behavior disorder, or acting out one's dreams. There are medications that can reduce parasomnia severity, and from a behavioral side, we need to extend sleep opportunity and better manage stress.

In terms of what are treating what are called sleep related breathing disorders, what happens in sleep related breathing disorders, the most common of which is

obstructive sleep apnea, that there's not enough space in the upper airway. You're asleep, you're trying to breathe, but not enough air is getting through. This causes a number of breathing events, either called apneas, or hypopneas, depending on whether there is a complete or partial cessation of the upper airway.

The brain starts to suffocate. Blood oxygen levels drop. Because the brain is suffocating, it wakes the whole body up with a sympathetic burst to pull in more air and open the tissues in the upper airway. You are unaware of that. Your patients are unaware of that, because they are asleep, even though this can happen up to 60 or 80 times or more per hour, and you just don't get as much sleep. These are debilitating conditions that undoubtedly impair recovery following concussion.

In patients who are obese, it's an inaccurate, but it's a stereotype that only obese patients get OSA, or suffer OSA. About 70% of patients with obstructive sleep apnea are obese. We can help them to lose weight, although that's highly unlikely to eliminate the obstructive sleep apnea, particularly if it's been moderate or severe. The gold standard treatment is CPAP, or positive airway pressure, which you've undoubtedly heard of. Perhaps you even wear CPAP yourself. CPAP works by inflating the upper airway, just the same way you put air in your flat tire.

There are oral appliances that pull your lower jaw forward. Remember the problem in obstructive sleep apnea is there isn't enough space in the upper airway. The solution has to be to increase space in the upper airway. Primarily as a last resort, there are surgical interventions where surgeons try to remove excess tissue in the upper airway. It can be effective in highly selective patients. In unselected patients, it does more harm than good. It can't be recommended.

I mentioned CPAP earlier and I just want you to be clear how well it works. It works better than sham CPAP, it works better than oral appliance, particularly in patients with mild to moderate disease. CPAP takes away all of the bad things about obstructive sleep apnea, and it increases the good things the patients want in their lives. We're going to spend a sec talking about insomnia, which simply means trouble falling asleep, trouble staying asleep, waking up too early, or some combination of all of these symptoms.

There needs to be a daytime consequence to have a sleep/wake disorder, but it is your job, not your patient's job to figure out what some of those connections might be. For example, if your patients are tired or have poor cognitive performance or mood dysfunction. They're irritable, if they have somatic complaints, pain, GI problems and so forth. Your job is to ask, might this be related to poor sleep the night before? It's 8 hours every day. Historically we thought of the paradigm, the implicit paradigm of western medicine is that biology drives behavior. In other words, there is a physical injury which changes downstream behavior and cognition and emotional experience.

In few areas, is the bi-directional understanding between biology and behavior more important than it is in sleep, although I'd argue that it's important for virtually every chronic medical condition in particular. Look at what we spend health care

dollars, these are related to volitional behaviors. Sleep is no different. It's involuntary, but our behavioral choices influence it.

Let's talk briefly about how insomnia develops. Each of us, here is simply an arbitrary threshold for trouble sleeping and no trouble sleeping. What happens is each of us has a unique risk factor for developing insomnia, the same way each of us has a unique risk for developing cancer or cardiovascular disease. Along comes what I call an environmental or external stressor. Maybe this is a medical illness, maybe it's a TBI, maybe it's a loss of a loved one, maybe it's a job transition. Somehow my internal stuff interacts with life, and now I'm having trouble sleeping. What do I do? I start to do things like sleep in on the weekends, go to bed earlier, be less active. Maybe I take over the counter or prescription sleep aids, maybe I over focus on sleep. Many of us have heard patients who describe sleeping the centerpiece of their life. All of these what I call compensatory behaviors in the short run may really help. If you haven't been sleeping well, sleeping in on Saturday mornings will just feel powerful.

In the long run, after the stressor that originally caused the insomnia dies down or goes away, it's actually compensatory behaviors that perpetuate the insomnia and keep us up here in the trouble sleeping zone. This is one of the factors, not the only factor, but an important one, that CBT, or cognitive behavioral treatment is designed to target. Some of you on the call have been through CBT trainings. I used to do a great number of those for the VA. Say hello if you were in one of those groups together. What we tell patients is that you've gotten a lot of practice at being a lousy sleeper. You've gotten really good at it. We need to retrain your body how to sleep. That's what CBT is designed to do.

In terms of treating insomnia, there are a number of FDA approved medications. A detailed discussion is way beyond our scope today, but I want to let you know that there are pharmacotherapies. Those are the most commonly employed insomnia treatments, but actually behavioral interventions have much longer lasting results. In the first 30 days, these treatments are about equally effective, and at every time point after that, the benefits from CBT are better maintained over time. There are no side effects. CBT in mild traumatic brain injury is of particular interest because you shouldn't be using benzodiazepines in patients with concussion.

Some important questions in terms of the way forward, what's the role of sleep at the different time periods that Dr. Yochelson mentioned? For example, during the acute injury phase, the 0-3 days of rest, rest, rest? During the subacute phase, up to perhaps 3 months, and then what about in patients with chronic post-concussive symptoms, what about the emergence of chronic sleep disorders? From a research perspective we probably need to be thinking about these 3 phases as distinct.

Our working group, I'll also conclude with a few highlights from the working group, we made 3 recommendations, broadly. The first is we need to be doing a better job at aggregating data regarding sleep disturbances in patients with concussion. We need to be tracking patients over time from acute to subacute and chronic TBI and concussion symptoms, looking at the relationship between sleep and symptoms

over time. There were several TBI specific sleep disorders, post traumatic hypersomnia, post traumatic narcolepsy, where we really can do a better job developing targeted treatments. I was going to turn it back over to Dr. Yochelson, who will talk to you about fatigue, and then when he wraps up, we'd be happy to answer questions.

Dr. Yochelson: Thank you very much. Again, at this point we're going to talk about fatigue, and it's important to distinguish that from sleepiness or drowsiness. What is fatigue? Fatigue is the awareness for a decreased capacity for physical and/or mental activity due to an imbalance in availability, utilization, and/or restoration of resources to perform activity. That's a great definition, but if you tell that to a patient, you won't know what you're talking about. When I describe this to a patient, when I'm trying to tease out whether we're dealing with issues of fatigue or excessive drowsiness, excessive daytime somnolence, I will typically describe fatigue as more of a decrease in energy or endurance for both physical and mental activities. That's an important piece. A lot of times, they think of it only from a physical perspective.

Fatigue is the number 1 complaint among moderate to severe TBI, especially in the early post traumatic period, although, as we both mentioned, it can become a chronic issue. That's why we want to try to address it early on before they have maladaptive compensation for it. It's the number 2 complaint among outpatients. More than 60% of outpatients who've had traumatic brain injury report fatigue that interferes with function. It's not just a little bit of fatigue, it is quite substantial in a number of patients.

Again, as I said, fatigue can be mental fatigue, and it can be physical fatigue. There's a very strong interplay and a lot of people are not aware of that. Increases to physical fatigue will actually lead to increased mental fatigue, cognitive slowing and the like. I give frequently an example of one of my patients who I saw a number of years ago. He was a sophomore in college and played football and had had a couple of concussions. I'd been treating him for a while. I had cleared him to resume physical activities, not going back to playing football, but he was working out at the gym. He was doing okay with that.

He went to the gym, worked out pretty hard, the day before his final exams and he failed a couple of exams in classes that they had been doing fairly well in. He came back, he talked to me about what had happened. We got some special accommodations. He was able to retake the exam. I emphasized the fact that he shouldn't be exercising the day before, or at least not as significantly as he was. He did quite well, he got B's in his exams.

You can all imagine if you go to the gym, even with no history of traumatic brain injury, and you worked yourself really hard, you worked for an hour or 2 hours really pushing yourself, and you come out and you try to focus and think about something that takes a little bit higher level cognitive function than your normal daily activities. It's difficult for you. You put that on top of someone who's had a brain injury, and it becomes nearly impossible.

Another aspect that is important to think about is endocrine dysfunction. Endocrine dysfunction after traumatic brain injury is quite common, up to 68% incidence of hypopituitarism, and hypothyroidism can definitely cause fatigue independent of traumatic brain injury, but if we now have a medically induced or TBI induced hypothyroidism, you can certainly get fatigue as a result of that. There are not clearly established guidelines of what and when to test. We will typically test our inpatients during their inpatient stay for thyroid function and potentially some other endocrine markers.

One of the things to keep in mind is that while the incidence of endocrine dysfunction is fairly high, it often does resolve within about 3 months or so. I don't typically treat them, unless they're extremely symptomatic, or if they're still having endocrine dysfunction at a year post traumatic brain injury. I do check it early on. If it's normal, fine, if it's abnormal, I'll repeat it at about a year out, or again, if they're having significant symptoms.

The first thing to think about when someone is coming in and talking to you about fatigue is their sleep. Are they having an underlying sleep problem? If so, that's where you want to focus. You may still have fatigue issues even if you treat the underlying sleep disorder, but always work on that first, because otherwise some of the measures you're taking to counter fatigue may actually impair their sleep function as well.

You want to encourage increased physical activity and exercise. Again, within the realm of what you should be doing for gradual return to exercise following a brain injury. Now we're talking more chronic. Often what you'll see is patients coming to you who have a limited or a lost no physical activity. It's important to get them back into a good exercise program that includes aerobic, cardio type activities.

Return to work and return to school. One of the other issues is that often they've been kept out of school or very limited hours. The longer that you keep somebody, away you start to have other comorbid issues to include psychosocial issues, they get depressed, they're not with their friends and their colleagues, and they're also playing catch up when the ultimately do go back to work and to school.

Dr. Wickwire talked about the use of caffeine. You certainly want to be very careful about caffeine, but caffeine is a stimulant and it can be helpful if used sparingly. If somebody uses it occasionally when they know that they're going to have a more challenging task and they're having a lot of fatigue, it's not unreasonable. You want to think about the timing. Using it in the evening is not wise. Using it in the morning occasionally is not a terrible thing. You also want to get their history, because if they come to you with a history of I drink a pot of coffee every day and they've been doing that for years, you don't want them to stop it abruptly, but you do want to help them to taper off of it. You also want to think about the whole spectrum of symptoms, not just the fatigue. Caffeine has a very significant impact on headaches, particularly in patients who have a history of migraine. Be very careful about your recommendations for use or non-use of caffeine. In and of itself, it is

not necessarily something that you have to tell them no, don't take it.

In terms of the pharmacologic management for fatigue, again, this is different from sleep disorders. This is even different from daytime drowsiness or wakefulness. This is really low energy. What do we do from a pharmacologic management standpoint? I probably should reverse this slide and talk about non-pharmacologic management first, because that's what you want to do. Talking about pharmacologic management, we do use stimulants, things like methylphenidate, or combo drugs like amphetamine, Dextroamphetamine. They are helpful. They are particularly helpful with some of the cognitive issues like concentration and attention that can be further impaired by the fatigue.

Modafinil and Armodafinil are specifically for wakefulness. There have been studies looking at excessive daytime somnolence in TBI, and it has shown to help. Looking after fatigue after TBI, and it actually was not shown to help. Again, that's statistically speaking. If you look at the study that would show it doesn't help, I can tell you that I clearly I have had patients where it has helped with fatigue. It is something to consider. Similarly, selective serotonin re-uptake inhibitors, SSRI's, things like serotonin, like Sertraline, can be helpful with fatigue, particularly if there is a mood component.

In terms of the non-pharmacological management, we really want to try to take an interdisciplinary approach, particularly in our inpatients. The fatigue can impact their function, their ability to participate in their inpatient rehabilitation program. We do this as a multi-disciplinary approach with all of the therapists certainly incorporating to a very significant extent psychology or neuro psychology. We think about rest breaks. To be truthful, we also do consider naps. Both on the inpatient and outpatient side of things, I talk to patients about naps.

As Dr. Wickwire said, you have to be very careful, because if you're napping too much during the day, that's going to further interrupt your sleep cycle at night. If you have someone whose fatigue is so significant that they can't function during the day, a brief nap is not unreasonable. What I tell them is they need to consider taking power naps. They need a 20-minute nap. They don't need a 2-hour nap. A 2-hour nap will be more detrimental to them than no nap at all.

They should also avoid things that are overstimulating at night time. Again this goes more towards the patient who has fatigue as a result of insomnia or impaired sleep. Using your iPad or TB or video games, things that are highly stimulating, right before bedtime obviously, should be avoided. That goes back to the much larger picture of the CBT and sleep hygiene. It's certainly okay, particularly in the more chronic patients to work through fatigue in the earlier stages, in the acute and maybe subacute period, you do want to avoid aggravating symptoms by pushing through, but if you're talking 3 months plus, you really need them to actually start pushing through their fatigue, doing activities, particularly physical activities. That really is the treatment of choice.

What's new on the horizon for fatigue, there has been some work looking at blue

light therapy. Patients were given 45 minutes every morning to reduce fatigue in patients with chronic fatigue. That's an important factor. These are patients who have been dealing with this for quite some period of time. They actually demonstrated some improvement in their primary outcome which was fatigue. They looked at some secondary outcomes which included daytime sleepiness, depression, sustained attention and sleep quality, and they also found that it did improve their daytime sleepiness as well as the fatigue.

In summary, I think it's very important to remember that sleep dysfunction, poor arousal, inattention, decreased alertness and fatigue are significant sequelae of traumatic brain injury. All of these affect the patient's ability to function well. They impact their quality of life negatively. There's certainly significant overlap between TBI, sleep disturbances, and the post-concussion syndrome. Other co-morbidities that often come with it like post-traumatic stress disorder, depression and chronic pain.

Until there are more sensitive tests to really tease out mild TBI, it's important that we do consider all of these symptoms interdependently. In other words, treat the symptoms, not necessarily attributing them all to traumatic brain injury, but certainly manage your patient holistically, as I gave with the example of the caffeine. Be careful because one treatment for fatigue might actually aggravate their headaches. Always treat your patients holistically and hopefully we will help to manage them and improve their quality of life. With that I will turn it back to Dr. David for questions and answers.

Dr. David: Thank you Dr. Yochelson and Dr. Wickwire for your presentations. If you have any questions for the presenters, please submit them now on the Q & A pod. There are some questions already on the pod, and I will read them out in no particular order. The first question is why there is a higher percentage of OSA in veterans compared to general population? Percentage of OSA in veterans compared to general population.

Dr. Wickwire: I'm happy to answer the question. Just to be clear, do I see that in front of me? Should that be in front of me someplace?

Dr. David: Sorry, no.

Dr. Wickwire: Okay. Great. The answer is probably 2-fold. One, in general, base rates of obstructive sleep apnea increase with age. In that sense, veterans aren't unique. Sleep apnea tends to be more common as we get older for both men and women, particularly for post-menopausal women, for example, but men experience much more sleep apnea with every passing year.

The second reason has to do with military specific kinds of activities. Perhaps because of damage to tissues in the upper airway related to stress, for example, we see elevated rates of sleep disorder breathing in soldiers and veterans of all ages relative to matched health controls. They have much more mild sleep apnea.

If you think about the operational demands of a military career, obtaining insufficient sleep, working in high stress environments, they're not conducive to healthy breathing. Sustained stress can damage neurologic function, is probably the brush stroke answer. The last thing that I'd add for the listeners is the rates of sleep disorder breathing and obstructive sleep apnea are much higher in patients with chronic medical conditions. When you look at patients with diabetes, and cardiovascular disease, potentially psychiatric conditions, you're going to see all to more sleep apnea.

Dr. David: The next question is patients that wear glasses for photo-sensitivity for a TBI, how much do you think these dark glasses during sunlight hours would alter their melatonin and circadian rhythm?

Dr. Yochelson: It's certainly not uncommon to have photo-phobia, and I would certainly recommend for patients who have that that conservative measures like wearing sunglasses would be appropriate. There actually should be fairly little impact in terms of their circadian rhythm, because if they're outside, the vast majority of sunglasses are not going to block sufficiently. There will still be enough light getting in, both around the glasses and actually through the lens itself, but it darkens the light sufficiently that it at least reduces the pain of photo-phobia.

Dr. David: Next question is the high rate of endocrine dysfunction you mentioned, is that for all TBI or just severe TBI, and if so, what percentage?

Dr. Yochelson: That's actually among all TBI. It's a higher incidence the more severe the TBI. As you looked at the range, it was from about 15-70%. You're going to see the probably 50-70% amongst the severe TBI. You're going to probably see 15% or perhaps even lower, probably in the 5-15% for mild traumatic brain injury. You certainly can see it. I don't routinely test in mild traumatic brain injury, but if I have somebody who has persistent symptom such as fatigue or some other symptoms that can mimic, I would actually test for thyroid function, I would test for testosterone, and growth hormone as well.

Dr. David: The next question. When should military members be allowed to return to full active physical training, and resonant testing after TBI? I assume it would be a concussion rather than a severe TBI.

Dr. Yochelson: I'll take that as well. That, again, is not specific to the sleep disorders, but just to the general symptoms of traumatic brain injury. The general guideline is in terms of physical activity, you want to avoid high level physical activity. Certainly anything that would be resulting in another concussion, contact sports, things like that, until they're symptomatic.

Beyond that, I would recommend that if they're highly symptomatic, they probably need a good week of rest and then gradually returning to activity. Monitor their symptoms. Unfortunately, it's not cookie cutter. What I tell them is start going and increasing your activities gradually. If those are triggering symptoms, then we need to back down either on the intensity or number of hours that you're doing these

activities. This includes both cognitive and physical activities, so this may be time at a computer as well.

Dr. David: This question is for Dr. Wickwire. How common is the upper airway resistance syndrome?

Dr. Wickwire: Upper airway resistance syndrome, or UARS, is the most mild form of sleep disordered breathing. There are a few reasons that this is important. One, particularity in regards to fatigue and daytime sequelae, there's evidence that patients with UARS, sometimes can experience the most substantial symptoms during the day or even moderate to severe symptoms during the day. UARS requires very subtle and sophisticated measurement of breathing during sleep. Frequently patients with UARS will not meet the diagnostic criteria laid out primarily by insurance providers to provide treatment. These are patients who may have significant symptoms, who have clearly identifiable breathing abnormalities during sleep, and they may not qualify for therapy.

That's a bit of a pet peeve. I won't get on my soapbox, but UARS matters, and we need to be doing a better job recognizing it and treating it. Soldiers, particularly young, healthy soldiers are particularly at risk for UARS. This may well develop from somatization from a trauma that zaps the patency of the upper airway. In terms of prevalence rates, it's difficult to say, because the assessment is often not consistent across sleep disorder centers and across nosologies. Certainty over 10% of the normal weight men and women, normal weight US adults, have UARS and will not have obstructive sleep apnea. To put that in context that's roughly twice the prevalence rate of OSA.

Dr. David: The next question. How long can we expect to see chronic symptoms of post-concussion?

Dr. Yochelson: Again, extremely variable, and at this point we don't actually have any specific predictors for that. There are some things that put somebody at higher risk. If they have had previous concussions, particularity if it is taking less time, or rather a lower impact to create symptoms, or each time they have a concussion their symptoms are lasting longer. If they have a prior history of migraines, prior history of depression or other mood disorders, anxiety, those are all negative prognostic indicators for a more prolonged post-concussive state. The vast majority of people are going to resolve within matter of hours to days, within a week, certainly.

Even though that's a vast majority, that's a vast majority of 2, 3 million people. The numbers are still significant in terms of the percentage that do have symptoms for more prolonged periods. Generally, even for the prolonged post-concussive, it will resolve of the most part within a 1-3 month period, and then it's a very small percentage that continues beyond that. I have had some patients who seem to have a persistent post-concussive syndrome that does not go away completely, although there is some research, Dr. Leddy's group out of Buffalo uses a treadmill program, and he studied patients with chronic post-concussion syndrome, put them through the treadmill protocol and actually had significant improvement of

symptoms through physical activity, even after many months or even years of post-concussive symptoms. Physical activity on the early end may be problematic, but certainly we don't want to eliminate the possibility of increasing physical activity even if somebody is symptomatic.

Dr. David: The next question I believe for Dr. Yochelson. Would you routinely recommend stimulant medication for treating fatigue in a patient with comorbid anxiety or PTSD?

Dr. Yochelson: Was the question stimulant medications?

Dr. David: Yes, correct.

Dr. Yochelson: I would actually avoid stimulates like methylphenidate. The neuro stimulants actually will exacerbate anxiety, so if they have PTSD or anxiety disorders, I would strongly recommend avoiding that.

Dr. David: Thank you. The next question is what would be an appropriate treatment approach for patients experiencing parasomnias such as night terrors following TBI?

Dr. Wickwire: I can take that. If you recall, earlier we talked about the difference between non-REM sleep, which tends to take place early in the night, the first third of the night in general, and REM sleep, rapid eye movement sleep, which tends to take place primarily in the last third or later during the sleep period. Night terrors or sleep terrors, which are much more common in children, emerge from non-REM sleep. These are called non-REM parasomnias.

A few notes. First, if you see a patient, they describe disturbing dreams or acting out behaviors during sleep, the first question I want to ask you is when does it happen? In a non-leading way, what you're trying to look for is does this happen during the first third of the night or the last third of the night. Obviously you as a clinician are not a medical test, but that's going to give you a good insight in terms of is this likely emerging from non-REM sleep or REM sleep?

Sleep terrors take place when patients emerge typically from the deepest stages of sleep. They may be terrified. If you were watching this, and parents on the webinar will recognize some of these symptoms, child may wake up and seem entirely alert and awake. They're screaming at the top of their lungs. Their eyes are wide open. Because this is happening from non-REM sleep, from that deep sleep, the next day they won't remember it at all.

Remember that different parts of the brain can be more or less awake or asleep. In the case of sleep terrors, the vast majority of the brain is asleep. It just happens that this startle or alert or terror part to the brain is awake. In order to reduce night terrors, we need to do 2 things. First, we need to make sure we're obtaining adequate sleep. The reason is when we don't obtain adequate sleep, our body craves balance. We experience what's called sleep stage rebound. Let's just say for example that I was chronically sleep deprived over a week or 2 weeks or more. The

next time that I was given adequate sleep opportunity, my body would crave slow wave sleep, the first night would make up for slow wake sleep and the second night would make up for REM sleep.

The reason that matters is, these parasomnias are emerging from slow wake sleep, and that first night after chronic sleep loss, I'm going to have more slow wake sleep than usual, therefore increasing my risk for night terrors or similar non-REM parasomnia events. The second thing we need to do in addition to extending sleep opportunity is to manage stress. We know that life stress, work stress, anxiety can all trigger parasomnias.

Dr. David: Thank you. The next question. Are there a set of number of mild concussions after which you would recommend the patient never to return to activity that caused it?

Dr. Yochelson: The reason that I would recommend that somebody not return to a specific activity that caused the concussion in the first place, would be probably 2 fold. One is if this is a patient how has now had multiple concussions, and particularly if they have had to deal with a prolonged post-concussive state on multiple occasions. We really don't know why it is that 2 people who have a very similar impact can have very different concussion symptoms. There's probably something genetic. We don't, at this point, know what that is. That person is probably much more susceptible.

Again, with multiple concussions, we know there's a risk of CTE, and if they're getting concussions from the same activity, I would certainly avoid it. Similarly, although perhaps less strongly is if they have a very prolonged post-concussion syndrome, then I would consider telling them to avoid returning to that same activity.

Dr. David: Thank you for submitting the questions. This will conclude the question and answer session. After the webinar, please visit dcoe.pdf.pesg.ce.com to complete the online CE and download and print the CE certificates or certificate of attendance. The online CE will be available until Thursday March 24th, 2016. To help us improve the future webinars, we encourage you to complete the feedback tool that will be open in a separate browser on your computer.

To access the presentation and resource list for this webinar, you may download them from the pod file on the screen or at the business website dvbic.dcoe.mil/online-education. An audio recording and edited transcript of the closed-captioning will be posted to that link in approximately 1 week. The chat function will remain open for an additional 10 minutes after the conclusion of the webinar to permit attendees to continue to network. The next DCoE TBI webinar, Managing a Headache Following Concussion, is scheduled for April 14, 2016, 1:00-2:30 PM Eastern Time. The next DCoE psychological health webinar, deployment related [inaudible 01:26:01] PTSD and mild TBI in service members is scheduled for March 24, 2016 from 1:00-2:30 PM Eastern Standard Time. Thank you for attending and have a great day.