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Hello this is Windows to the Brain: The Neuropsychiatry of Traumatic Brain Injury, particularly mild traumatic brain injury as it is pertinent to posttraumatic stress disorder.

We know from this current conflict in wars in Iraq and Afghanistan, that there are many of our patients in the VA healthcare system and in the private community that are struggling with both posttraumatic stress disorder and mild traumatic brain injury.

The purpose of this particular lecture and conversation is to help the providers who are taking care of patients with both these conditions to understand the contributions of mild traumatic brain injury to posttraumatic stress disorder patients.

Hi, I'm Dr Robin Hurley from the VISN 6 MIRECC, which stand for Mental Illness Research Education and Clinical Center. I am also the Associate Chief of Staff for research and education at the Salisbury North Carolina VA Hospital.

I want to thank Doctors Friedman and Bernardy of the National Center for PTSD for inviting myself and our group, including Dr Taber to be a part of this web education and to be able to express some of the points that we have learned about taking care of traumatic brain injured patients with their audience.

Of note, and one of certain importance is to note the views in this session are strictly those of myself and Dr Taber. They do not represent those of the National Center for PTSD, Veteran’s Health Administration, Department of Defense or the United States Government.

It is also important to note that the images in this that are pictures of examples of humans are those off the Internet and free source documents for education purposes and are not pictures of any VA patients. All of the images that are MRI's and x-rays have been stripped of all identifying markers and do not have any specific reference to any one patient within the VA Healthcare System.

In this lecture today, we are going to talk about the neuropsychiatry of traumatic brain injury, our current understanding and future challenges. As I mentioned in the original introductory slide, we'll largely talk about mild traumatic brain injury. We are going to pay particular reference to the functional anatomy of
emotion, memory, and behavior circuits. We are going to talk about some of the deficits that we know occur in civilian brain injury and be able to make some reference to the military setting.

Now certainly since blast injury is a completely new phenomenon for us in the terms of the study of traumatic brain injury and its reference to PTSD, we don't know that necessarily everything that we know about civilian brain injury will translate to our patients in a military setting. We are also going to talk about the current assessment and treatment advice of experts in the field. And lastly, we are going to make some suggestions for future research initiatives.

Let’s start by doing a brief review for the next few slides of the neuroanatomy of the circuits of the emotion, memory and behavior to give us a reference point for how things may be injured with a mild brain injury that can affect a person’s behavior and their expression of posttraumatic stress disorder symptoms. So let’s begin in the very middle of the slide, with the dorsolateral prefrontal cortex.

This is in a sense, starts at the top of your brain and it goes through, as you see, through the basal ganglia of the thalamus and returns in a circuit formation to the dorsolateral prefrontal cortex. Now, our circuits in our brain work very much like the lights on our Christmas tree or the lights in our cities, such that if you break that circuit anywhere along the way than you can get the same symptoms from breaking an axon, which is a transfer path, as you can from an initial cortical injury. So for example, the dorsolateral prefrontal cortex, as I said sits on top of your head, so if the patient takes a bump to the top of the head such as a piece of wood falling on their head or a garage door, then they can get problems with cognition, with processing of information or with recall of memory. And those same things can occur if they have a injury to the thalamus and where you see here again as the pink circuit follows through to the anterior thalamus.

So this why it becomes challenging for radiologist and psychiatrist to be able to put the knowledge together of matching an exact injury with an exact symptom in psychiatric disorders. Now let’s move to the orbital frontal cortex. The orbital frontal cortex sits right above your eyes. That is the cortex that begins the emotion circuit. That’s what we know about from Phineas Gage a famous patient from the 1800’s who became disinhibited after the injury while working on the railroad tracks, which interestingly enough is there are some wonderful articles about the history of Phineas Gage and his contributions as a patient to modern medicine in particular neuropsychology. So I recommend to our audience to please go look those up on Pubmed to read about him, it’s a wonderful story and great teaching case.

So the orbital frontal cortex starts above your eyes, also goes to the more ventromedial portion of the caudate through the globus pallidus and to the more ventral portions of the thalamus and returns as a circuit. Again this is very important to emotional processing and dishinabition, to being able to control our inhibition. This is what we think about when patients are disinhibited, for example, yell at a policeman after a brain injury when stopped or at the grocery store clerk or maybe a waiter in a restaurant. Injury to frontal lobes cause patients to say things they really shouldn’t in public places as one example.

Now of course these circuits and my description of them are somewhat simplified and that our brains are incredibly complex organs. Yet I’m presenting them here in one slide. And lastly, it’s the anterior cingulate, which is listed here in green and black. Now the cingulate has two very important roles in terms of the context of this conversation today. One is the circuit for motivation. It’s what gets you out of bed in the morning. It’s what tells you that you need to go to work, that you need to take a shower after working in the garden, and if his is injured on one side, then the other side eventually can pick up some of the work in our brain. However, if a person is injured bilaterally with this they may end up as an akinetic mute and not be able to control or produce motivational activities.
You can see by the slide where the direction of the circuit runs. And also the cingulous part of the hippocampal circuit of the memory. It is a sense our memory factory and is very important to PTSD, and we're going to cover that in more detail in a later slide.

Let look at where--pictures are worth a thousand words--so let's look at where the circuits lie in terms of the frontal cortex. As you can see on the picture on the right side of your screen, the dorsolateral prefrontal cortex is the area in pink. Here we see, as I mentioned to you earlier, that it's much more lateral as its name implies and more dorsal. So, this is very vulnerable to injuries to the top of the head where things may fall on a person or their head hits something.

The area in blue on the slide is our orbitofrontal cortex which begins that circuit. That's very vulnerable to deceleration injuries such as when your car hits a tree or a motorcycle hits a car. And lastly, we talked about the anterior circuit, which we see is much more protected in the brain and is much more challenging to injury in terms of a mild traumatic brain injury. Now certainly with a moderate or severe injury it can be damaged, and we'll talk about that with some examples later in the lecture.

In looking at coronal slices, which are slices of the brain from front to back, we can look at the same circuits and get an appreciation of how they are intermingled as one goes deeper and deeper into the cortex and sub cortical tissues. So if you look in each of the slices of the brain, you can see in a sense a cheat sheet in the corner. Here you can look at the pictures of where we are in reference to the front of the brain versus the back. So what you begin to see as you move along the circuits become more and more intertwined.

So for example, in picture number 1, you see the blue section is our dorsal lateral cortex, the red is our orbital frontal, and in the picture, the cingulate is yellow. And what we see as you go along and deeper into the cortex and more toward the thalamus is the circuits become intertwined. Now that becomes important when looking at a stroke patient versus someone who has taken, for example, a bullet in the cortex and that the amount of circuitry damaged will get injured--will get much more complicated the deeper into the brain we go. For example, if you are looking at a thalamic stroke, it may be impossible for a neuroradiologist to tell you if all three circuits were injured compared to looking at the anatomy of the cortex and saying, “Yes, we believe it’s largely in the area of dorsolateral prefrontal area.”

We mentioned a couple of slides back about the cingulate’s role in the hippocampal circuit of the paths which is for us our memory factory. It’s what takes in our sensory information and processes it into memories we would keep and store in our brain. Now with that of course, is the role of the amygdala which you see in the top left section of the picture in blue which adds the emotion to our memories.

This becomes important of course in our posttraumatic stress disorder patients as one of the major theories about PTSD is that the amygdala, in a sense, gets turned on and can’t really then shut back down later. So we can see in looking at the tracts that would go from the hippocampus through the fornix to the thalamus and back to the mamillary bodies with input from the cingulate. Now, we know about the mamillary body in injury to that from our patients with alcohol disorder and those who have damages to mamilllothalamic tract and to the thalamic nucleus. We know about it in Wernicke-Korsakoff, for example.

Now, if we look at the location of the hippocampus, which is in green above, and the amygdala in blue, we can think about it terms of the physics of injury and how vulnerable it may be to deceleration injuries and to being hit in the side of the head. The temporal bone is very thin so it’s not hard to imagine how hitting the side of the jeep in a blast injury or being hit in the side of the head with a baseball bat, for example, could leave a person with injury to the hippocampus or the amygdala.

There are still slightly more to the story for everything you wanted to know about neuroanatomy and have forgotten from medical school, and then we will follow shortly after a couple more slides into much more
about traumatic brain injury. But, let’s go for a little more of the anatomy, and the story isn’t finished with the thalamus.

If you remember from a few slides back, we talked about how the circuit starts in the cortex, goes to the thalamus and returns. Well, we know from the work of Jeremy Schmahmann and others that the cerebellum is very important to our processing of emotion in the memory circuits and to behavior. And if you look at our slide titled ‘Cerebellum in Emotion’, what we see is that the cerebellum has direct input to all the big three important circuits that I have just told you about in the last slides: the dorsolateral, the cingulate, and the orbitofrontal.

Not only is there direct input to those three big circuits that we talked about, but there is also input to all the subcortical areas that are important to PTSD as well, including your septal nuclei which we know about from Alzheimer’s disease and memory to the thalamus which we talked about to the hypothalamus for the productions of hormones and to the amygdala and the hippocampus. There is also direct input to the circuits producing serotonin, dopamine and norepinephrine; our monoamine nuclei that in fact are in a sense the fuel for all of our brain circuits.

The circuits are not quite as simple as we talked about them here, although it’s a good starting point certainly in beginning to understand how our incredible human brain works. But, there are also lots of association tracks that come and go from all areas of the cortex. And what we see in this slide are some examples that are color coded to match the areas of the brain from which they come and go.

For example, one that is very important to us in terms of the cingulum, we talked about its role in motion behavior are the short and long fibers of the cingulum. And what we see is that they run not only run from the frontal cortex to temporal but also they have fibers that run to the occipital cortex and parietal. As we noted earlier, it’s role in akinetic mutism and motivation. It’s also very important to pain, anxiety, OCD, depression, as well as to memory processing and to visual spatial skills.

That’s one example of how, not only do we have the risk of danger, or injury to the main circuits but also to all these association tracts that come and go. So, our formation of memory and our abilities to process emotions and to control our behavior is all predicated on the circuits and associated tracts kind of interfunctioning all the time in a complex circuitry.

As I mentioned to you earlier, the neurotransmitters are of course the fuel to our brains and what keeps all these circuits that we talked about in anatomy working. One of the things we want to think about as we begin to study this in relationship of PTSD to mild traumatic brain injury is what happens if we damage or injure those production nuclei, in a sense, for our brains.

If we destroy the fuel factories is one simplistic way to make an analogy. The acetylcholine is in the basal forebrain, so it’s a little more protected. The dopamine is in the substantia nigra. The acetylcholine is in the laterodorsal tegmental and pedunculopontine areas. Of course the norepinephrine in the locus coeruleus. And the serotonin in the dorsal raphe. Now these nuclei you can see are largely brainstem based which makes them a little more protected from a mild traumatic brain injury.

As we understand the mechanisms of injury to date, but one of the things I want to emphasize throughout this lecture is the idea that we don’t know a lot about TBI, and what happens as far as the microscopic areas of injury. We don’t know if things are diffusely injured in the whole brain or only in small areas or if the brain completely recovers. So one of the things that I think will be a great area of research interest through the years, will be to understand what happens to these tracts and pathways as we really begin to know what happens in blast injury.

So let’s move to talking about the neuropsychiatry of mild traumatic brain injury and a few statistics on brain injury in general.
Dr. Arciniegas of the University of Colorado Health Sciences Center has helped me to appreciate the statistics over the years with traumatic brain injury in times not of war. If you look at the slide, it's very interesting that the United States in their regular civilian population, the reported cases of traumatic brain injury in the US are more than stroke, breast cancer, AIDS, spinal cord injury and MS combined. So, it's a very important diagnosis that throughout the years has waxed and waned in terms of the attention it's gotten.

Which begs the question, "Why is it now that mild traumatic brain injury has really been become the subject of discussion?" Of course, it's the interest with our soldiers and what has happened to them in Iraq and Afghanistan.

But, it's a combination of other scientific issues as well. It's a multifactorial problem that has sort of created where we are now.

You know traditional psychiatry didn't emphasize asking about it. Clinicians didn't say to patients always, "Did you have a traumatic brain injury?" It was one of those things that just wasn't emphasized in training many many years ago. And patients of course, did not know to tell. If a patient did not know to spontaneously tell, and the doctor didn't know to ask, then it was left unsaid and the patients got diagnosed with general mental health conditions and disorders that really had an anatomical basis underlying them.

And of course until recently, the circuits of our brain were not understood and in fact until the work of Jeff Cummings and others was there really a greater appreciation of the circuitry in the brain as well as it took a lot of the new imaging techniques to begin to understand physiology.

Which brings us to the last point on the slide that diagnostics are very very new. Look how recent it was that we began to use MRI's in psychiatry, particularly functional MR or PET and SPEC. It's really been the last decade that these things have come to really being used in research. And of course, our treatments in mental health have been limited particularly for the organic conditions and we'll talk about treatments a little bit later during this lecture.

So as Dr. Arciniegas tells us the picture of a traumatic brain injury patient after the injury is really a compilation of three things: the pre-injury factors, the mechanism of the injury itself, and the post-injury psychosocial environment. And as you can see from his slide, that it's really just about anything else in the DSM-4 can and does occur post brain injury. One of the things in our clinics that we have seen the least of in fact would be psychosis.

What we see is most of the other factors much more commonly than that one, cognitive problems, emotional, behavioral and physical disturbances all can occur both in the brain injured patient from civilian factors as in those that occur in the combat situation. One thing that I have not mentioned yet which is really really important to mention is that most patients who have a mild brain injury recover just fine.

If you go by that ACR criteria and know that a mild brain injury has a very short length time of unconsciousness. Most everyone recovers fine, goes about life and really will have no sequelae of it. What we are focusing on in this lecture are those patients that don't recover. And that come in to your clinics for assistance.

In taking a look at those pre-injury factors that contribute to that biospsychosocial formulation of the patient. We need to be mindful of their pre-existing cognitive function. Is this someone who was really really sharp prior to the injury or someone that wasn't as sharp beforehand? Were there any psychiatric
problems or sociopathic tendencies or “risk taking” behaviors? Were there problems with substance abuse?

If we remember back to our anatomy that we talked about in the first slides, an orbital frontal cortex injury often times leaves a patient disinhibited. So they are not just able to just say no afterwards. Another important thing is genetics. There is a lot of work in genetic studies going on right now to look at the contributions of APOE-4 to brain injury in term of whether or not a patient with APOE-4 positivity on both the alleles will be more likely or the same as likely to develop Alzheimers at an earlier age. As well as the age of injury when our brains are certainly at a pre and post milination which doesn’t finish in our brains until we are in our twenties, so that becomes important to think about when thinking about the age of injury for which the patient had his brain injured.

So in moving from the Preinjury factors to the physical factors of injury, again Dr. Arciniegas helps us looking at, and in drawing graphically, what may happen. You know our brain is almost the consistency of a thick custard or pudding. And if you think about that in terms sitting in this box with very very sharp edges, the bones of the bottom of the inside of the skull around the sphenoid in particular are very very sharp.

So if you think about something with the consistency of pudding or custard is shaken or moved across, it’s easy to imagine how those tiny axons and those microscopic nerve fibers can be injured or shredded. There’s rotation around the center of gravity around the brain, and of course it can be translationally injured as well. You know we think about it in terms of consistencies, and one thing we need to keep in mind when you look at MRI’s and other x-rays as they become more used in psychiatry is the difference in the water content of our brain. You know the cells have much more water content than does the axons.

So, axons or the nerve tracks, become much more densely packed the further down the brain stem you go. So you got something that is much more puffy and light over top of something that is very dense and very compact. So when you think about stopping a car when it hits a tree at 60 or 100 miles per hour, think about where the likelihood of injury is in shredding those tracts, and it’s usually in the areas where something very very light is connected to something very very dense.

So in looking at most common injuries that can occur to the brain, the subdural hemorrhage and the contusion are the most common, particularly in civilian setting certainly. So how does that happen? The brain is supplied by arteries that take our oxygenated blood in and drain by veins and sinuses as it leaves. Well, the brain has tiny little veins that connect to these large sinuses. And it’s easy than, if the brain is in a sense shaken and moved against the skull, such as in deceleration or being hit over the head, to shred those tiny veins, and thus blood accumulates between the brain and the skull or the brain and the adura?. The brain doesn’t like blood, so then it begins to swell and initiations can occur and it’s a very dangerous situation if there are large amounts of blood that accumulate. The second thing on the slide, on to the right, looks into contusions. Which occur in areas where the brain may hit something sharp, for example on the edges of the temporal cortex, as you see here, and it’s in a sense a bruise to the brain.

So where are our injuries? Subdural and contusions we said are the most common means of brain injuries. Interestingly, the areas that are most commonly hurt are the exact areas we need for emotion, memory and behavior processing. So if you look at the top three pictures on the slide, you see the pink areas for subdurals. That encompasses your dorsolateral prefrontal cortex. So the area that you need most for cognitive processing, for recall of memory it’s in a sense your computer and your hard drive if we may use an analogy like that. It’s the area most likely injured by subdurals. If you look at the bottom three pictures, the area most likely contused or bruised includes the temporal lobe, which we talked about in terms of memory, and emotion processing, and PTSD. We also talked about the orbital frontal cortex which is also noted in green, likely to be contused. That is an area for inhibition, for mood, for control of
our emotions. And the cerebellum, you see here as well noted, as well as the occipital cortex for vision. All of those are areas most likely contused in an accident or injury.

Here is an example from a patient that would illustrate both a subdural and a contusion in someone that was injured in an explosion and blast. And what we see on the left is a CT scan. This is a cross-section. At the top of the picture is the front of the brain, at the bottom of that of that left picture is the back of the brain. And in traditional radiologic format, the left side of the picture is the patient’s right, and the right side of the pictures is the patient’s left.

We see marked in this case, this axial CT scan, is the blood of a subdural. And it is exactly where we talked about that’s most common in terms of over the dorsolateral prefrontal cortex. The picture on the right shows an example of a contusion this is in the tip of the temporal lobe. Again illustrating to us the most common areas for which emotion and memory come together: the amygdale, the hippocampus, the temporal lobe. For naming, those areas are likely to be contused, as in the soldier’s case.

Lastly, let’s talk about diffuse axonal injury, which is an area of great interest right now in the research world, to be really be able to understand what does this mean. Well it doesn’t mean diffuse in the sense of one big large spot in one place that’s injured in the brain. But, what it means is really that its small amounts of damage or injury throughout the whole brain and maybe microscopic format or certainly in little bitty amounts in lots of different places. That’s how the term diffuse is used in this case.

Axonal meaning its injury to the fiber tracts or axons. And of course, injury to denote how it got there. The areas that we have to think about in terms of diffuse axonal injury are the areas that we talked about earlier. There is a change in consistency of brain material. When you go from something that is much heavier in water content to something that’s lighter or vice versa. Because, if you suddenly decelerate from one hundred miles an hour to zero, your area which is most likely to be injured is an area of weak physical structure. Such as that transition from a low water content to a high water content area. Or areas where they are mixed together. And you see color coded examples of that on the slide to your left.

The latest theory for how diffuse axonal injury occurs is slightly different than what it was years ago. We know that, if you look at the picture on the top of the screen to your left, you see what would be a cartoon of a normal axon. Then once it’s injured than you see the disruption in the fiberals and the structures inside the axon. You get disruption of the myelin. You get in a sense, a jumbling up, if I may use that very simple term, of the inside of the axon. And then, it breaks.

This does not happen immediately. This takes a while to happen, so there is lots of research going on to look at how we may stop this process from getting worse. The axoplasmic transport gets disrupted. There is swelling. There’s detachment. And eventually, death. Years ago, we used to think that it would happen instantaneously but it does not. There’s first a stretching that has to occur before all of this other process happens.

Once the axon is injured, or for that matter, once the cells themselves are injured, there is a secondary process that’s even worse that we hope to be able to eventually know how to stop. And that is the secondary effect of the “neurotransmitter storm” as its been called. As this figure illustrates, that’s been adapted from Yi and Hazell from 2006, what you see is after the injury, you get both hemorrhage, you may or may not get hemorrhage, but you certainly get a release of all of the neurotransmitters in the area. So, the things that speed you up and slow you down all get released at the same time. Which in a sense, cycles on itself and causes more injury because there is more of a need for oxygen, more of a need for glucose, which then creates more of an area for ischemia, which could then lead to more hemorrhage, which could then lead to vasospasm, and to decrease in blood flow. So it really can be a very very dangerous situation that occurs as a secondary injury after the primary.
There lots of interesting research going on in labs around the US right now to figure out how to stop this process from continuing. Something that maybe an ambulance or paramedic could give at the scene for example. The big challenge with that then is finding that will cross the blood brain barrier if it is injected into a vein in your arm. We, of course, have a blood brain barrier that protects our brain. And in this sense, we want to find something that can stop this process and be safe for us as well. So pay attention to PubMed and you’ll see as years go by lots of interesting research going on.

Of course, for those of us in the VA, one of the things we want to think about is how does this relate to blast injuries and to what’s going on with our newest group of veterans returning from Afghanistan and Iraq. This is an illustration from one of the Windows to the Brain papers done by Dr. Taber that tells us about how the blast wave itself happens. First, there’s a peak over pressure in the blast wind that comes through, then there’s a vacuum, and then a secondary positive pressure phase as well. So, the question is what is this cycle, in a sense, of these blast winds doing to the brain itself. You know to the tissues of the brain.

We certainly know what it does in terms of more hollow organs, such as the intestines or the ear drum or to the lungs. There’s been lots of research and work looking at that through the years. But what we don’t know, is what does this blast exposure do to the brain. So, there is a tremendous amount of research studies going on right now in both the DOD and VA to try to understand this blast wave. There are such things as blast tubes in which you can take studies in single neurons to look at what happens to them on a microscopic basis.

So there’s a lot of work going on to really understand is it the primary blast wave that does injury to the brain or is it more commonly the secondary or tertiary effects that can occur. Such as when the head hits the steering wheel or when the jeep rolls over or when a person gets impaled by a piece of shrapnel. We know about those things because they are much more similar to what happens in a civilian injury in terms of those same things. When a bullet enters whether it occurs in combat or in a city parking lot, the physics of that bullet would be the same. The big challenge for us now is to understand primary blast injury.

For our patients, let’s take a look at this more in relation to patient care and what we see in the clinics every day. As a neuropsychiatrist, I’ve been taking care of brain injury patients for approximately fifteen years. Probably the most common thing that brings a patient into my clinic is impulsivity. And it’s by way of the families.

We know that once a patient has had, for example, an orbital frontal injury, then it’s easy to become disinhibited, to have no filter on your actions or words, to embarrass a spouse in public. So, the spouse says, “Get help or else.” And that brings them into the clinic. Other things are cognitive changes. Someone now is having trouble in school or on the job. Increases in substance abuse or physical aggression. Those are things, that generally bring a patient into the clinic.

Of course, just about everything as I’ve mentioned earlier from the DSM-4 can be seen in patients with brain injury. And I wanted to remind us again, that none of the pictures in this presentation are of actual patients. These are pictures from education resources from the Internet. Everything from personality change, cognitive impairment, depression, anxiety, all of the conditions really you can have to brain can occur post injury. posttraumatic stress disorder is one of the more common ones. We know that from all the recent studies. So we’re going to take a look at really what are the most common coexisting symptoms for TBI and PTSD in just a moment.

To help set a perspective for Operation Iraqi Freedom and Enduring Freedom, let’s look at the some of the numbers for presence of brain injuries from the original 2005 statistics. 88% of those occurring injuries bringing patients to the hospitals in Iraq were due to mortar attacks or IEDs, or injury about the
head in 47% of those. 97% were due to explosions, in another study from 2005. And one group from Walter Reed, an at risk group for brain injury found 59% of those in the hospital had been exposed to conditions that might have led to a TBI. And that same study from Okie in 2005 showed that at least 20% of the wounded had some degree of brain injury.

Again, these are early statistics from 2005 and really do not show us all the ones who had a very mild brain injury and who did fine and were able to go back to work shortly thereafter and really were able to continue on without residual effect. But what we want to continue to talk about in this lecture are those that are not OK and that small percentage that do continue to have symptoms as those are the ones you are going to be treating in your clinics.

Common symptoms that we see as most prominent in mild TBI patients include problems with balance and dizziness, headaches, visual changes, memory and cognitive problems, irritability, sleep disturbances and ringing in the ears. I don't think in my many year of taking care of TBI patients have I met one yet who didn't have headaches, and almost all of them had some sleep challenges. Those have been, in my experience, have been the most common ones that we want to focus on treating.

Recent studies that give us some statistics on the rates of PTSD in this population include those listed on the screen in front of you. And the rates really vary in how you ask the question and where you ask it. For example, post card surveys of those returning back show us a rate of 11% compared to looking at VA post deployment clinic which clearly would have more patients with more symptoms up to a rate of 37.8% as you see on the slides in front of you. Probably will turn out somewhere I'm guessing, my personal guess is in the area of maybe 20%. But I think it will be sometime before we see an answer to that question.

So to bring us back a little bit to the anatomy and physiology, and the look of that combination with brain injury and PTSD, there's a couple of studies I'd like to point out. One from Morris and all in 2008, and O'Donnell and all in 2004 that tell us that beyond just that injury to amygdala we want to look at the brain stem and the locus coeruleus.

This imaging study on the left of your screen and the pictures from the right of the screen from O'Donnell really give us how important the locus coeruleus is and the brain stem to the reexperiencing symptoms and to the hyperarousal. It may be that the locust coeruleus production of norepinephrine isn’t inhibited or is put into over production in these patients with PTSD. I would recommend that for the reader to take a look at these studies.

In examining the Noradrenergic input more closely, what we see the nuclei, or in a sense, the fuel factory for the brain, the norepinephrine is in the locus coeruleus. It's in the brain stem. But, what we see, if you follow the purple arrows through the brain is that its diffuse everywhere the production where the fiber tracts go. So if you remember our slides from earlier looking at injury to the frontal lobe, you see that some of the areas where you have direct norepinephrine input are areas that are most likely injured by either subdurals or contusions.

There are very few statistics out there that look at patients that have both mild TBI and posttraumatic stress disorder. Because for years, it was felt in medicine that if a patient had a brain injury they could not have PTSD because their memory was disrupted by the injury itself. Well we know from studies in looking at our soldiers coming back in this current war that that's not true. That patient can have both. And this is one example study that's come out recently from Schneiderman, Braver and Kang which tell us that in patients with a level 2 mild brain injury, they found approximately 47% also had PTSD. So therefore, we know that in this one study that there can be patients with both TBI and PTSD. And, gives us a very early glance at what these numbers may look like.
So, common symptoms that makes the teasing apart of these diagnosing very challenging include: decreased concentration, agitation, insomnia, isolation, impaired memory, and affect and mood disturbances to name a few. Now, one of the things we don't know in thinking about PTSD and TBI is is this going to turn out to be one disease? One entity that includes features of both or is it going to turn out to be two different disorders or injuries in a patient? And each one having a different trajectory for assessment and treatment and we really just don't know enough yet to make that decision.

As a teacher, some of the things I see my residents and students and other mental health providers at times forget to ask in these patients in doing an assessment is about the factors you see listed on the screen. Now, certainly most people that have been trained in mental health don't forget to ask about substance abuse, and they know to ask about suicide. But, often times we forget to ask about seizures. The patient does not have to have a generalize cholonic seizure in order to be seizing. Partial complex seizures without secondary generalization are actually the most common. And, those the patient does not have to pass out at all. They can include such things as staring spells with loss of time, loss of memory during the episode. And what we see in patients with injury and seizures is that the families will say, “Oh, he's just having another one of his spells again.” Or, “He's zoned out on me again and I can't bring him back.”

Now of course, that takes a questioning from a provider in terms of being able to discern that from flashbacks. In which the patient is reexperiencing a trauma, so that requires some attention. We need to pay attention to verbal interactions.

And of course, asking about physical aggression, even though the patient and spouse may be fine in front of us. We need to make sure there's not something going on at home that we haven't asked about. Because remember, disinhibition and impulse control are really two of the primary things we want to think about I this population.

Substance abuse, I think I've talked about several times in this lecture already, and, inappropriate dangerous behaviors. It's hard to come from a time of high adrenaline such as in combat to coming back home where things are calm and quiet and not have an adjustment to that loss of constant adrenaline. So, we want to ask about dangerous behaviors, such as riding motorcycles without helmets.

I had a patient who was riding a skateboard up and down a parking garage during the busiest hours when cars are coming in and out of that garage to park for work, and he was not wearing a helmet.

We need to ask about cognitive functions and how our patients are doing in school. Can they follow movies from beginning to end?

Are there problems with eating, with sexual activity, or spending habits--the things we should never forget to ask about in psychiatry?

I mentioned earlier that when talking about the circuits of the brain, that that cingulate was harder to injure. Well we're going to talk about an example here with imaging in which it really was injured. Diagnostic imaging certainly has its place in the workup of a TBI patient. Not everyone with mild TBI by any stretch-needs the million dollar workup. But, there are certain patients who do. And certainly those who are not getting better in our standard assessments and treatment need imaging workups. I'm going to talk about a couple examples here of patients that it contributed to the diagnosis or to the treatments that were chosen.

The first one is the MRIs on the left. The top is what we call a T2 image and the bottom is what we call a flair image. These were x-rays done on a patient who had come to an emergency room thinking he had
just an example of food poisoning. He felt like he had a bad turkey sandwich the night before and had
gotten sick from it. Well, he had been sick and he had bitten his lip, and the ER felt he had a seizure due
to a loss of potassium from diarrhea and vomiting. And, the usual metabolic picture and his electrolytes
were off. So, he was place on the unit for IV replenishment and to really be watched for 24 hours, more
than anything else.

By the next day, the patient was having inappropriate psychiatric behavior and the consult service was
called. He had no recollection of his inappropriate behavior and had really felt embarrassed by them. One
of the first things the psychiatric team saw was dent in his forehead. It turns out that this guy had been,
many years earlier, mugged and assaulted, hit in the head by a brick in this case. And, he was now
having frontal lobe seizures due to that old injury that you see pictured here in the flair and in the T2. It’s
easier to point out on the bottom image; you see the large white area on the left side of the patient’s
brain.

And in this case, when looking at the at the axial, coronal, and saginal pictures, you really get the
appreciation of how large that injury is and that it really did cover all three of the circuits. He got frontal.
He got his dorsolateral prefrontal. He got his orbital frontal. And, he got his cingulate. So, this patient is
really vulnerable that should he have an injury in the future to the right side of losing his circuit for
motivation and the ability to control his interest in taking care of his activities of daily living.

An example on the top right side of the picture is a patient who was hit in the head with a piece of
construction equipment, who was dazed and confused but able to drive home. Progressively over the
next six months, was beginning to have more problems with depression, with stuttering, with suicidal
ideas, and really could not get better with the traditional psychiatric treatments. So, when he came to
Neuropsychiatric clinic for workup and evaluation, he had an MRI that was, in a sense, normal except for
slightly widened lateral sulcus in that temporal lobe. And what we found on the SPEC exam, the blood
flow picture that you see in the upper right, is that the patient was seizing from his deep temporal lobe.
And, once the seizures were treated then the patient’s symptoms disappeared.

There are many reasons to image patients in neuropsychiatry and you see the list on the slide. Certainly,
you can read them as well as I can. Probably, the two most important to think about are ‘presentations at
an atypical ages for the working diagnosis’, and ‘Psychiatric symptoms outside “clinical norms” or with
any unusual presentation or course’. And, those two are the most important because, if you think about
what we are taught and trained everyday of our careers, it’s about how to recognize the common injuries
and how to know when you are coming up on something that’s a zebra. So keep this in the back of your
minds as you do your assessments and treatment plans in patients, is to look at when you might need to
image. And, there are lots of good psychiatric textbooks out there to help you with that process.

In looking at imaging techniques and options for imaging patients, I mentioned earlier blood flow studies
called SPECS are one example. There are also studies of glucose metabolism and there’s functional MR
that is used in a research setting. And, there are all kinds of new techniques. But, what I wanted to
illustrate with you are just a couple of examples of where MRIs and SPEC show different views of the
injury and so both were able to contribute to the assessment of the case.

If you look at the picture on the top left hand side of your screen, what you see is a case of patient who
had been in a car accident. And, you see that the CT looks relatively normal. Then you look at the T2
picture, both early and late in his recovery course, and you see the area of white at what looks like two
o’clock if you place a clock face on the picture. Then you see a small area of injury to the patient’s brain.
You look at the flair, you see an even larger picture. Then when you see the SPEC spans of equal slices,
you see a large area of blue/black, as compared to the red area of good blood flow.
So, on a SPEC scan, the brighter the colors, the more blood flow. So, what you see is that the MRI was not able to show the full area of injury as compared to the SPEC scan in this case. The rest of the slide contain other examples of cases where the SPEC scan was able to contribute some information to the patient's case that added to the information given in the MR. And again, this is not for every patient, it's only for those which are struggling with diagnostic issues So the symptoms with don't match with what the imaging shows.

In moving on to pharmacological decisions for the patients, there are several things we have to keep in mind. The first is that there are no large double blind placebo controlled studies to look at long term psychiatric challenges due to brain injury. We certainly know that they exist. There have been studies for years that look at patients who have had, in the old words, organic conditions that caused their psychiatric symptoms. Now, it's due to a general medical condition in our DSM-4. But, there are no large studies that look at over the years the assessment or treatment for those patients with long term psychiatric problems.

There are no FDA approved medications for chronic psychiatric symptoms due to TBI. So what you get are the, in a sense, the opinions of experts in the field who treat these patients every day. You get case reports, some open label studies, particularly looking at acute symptoms.

What we've learned is like many other organic conditions, if I may use that old terminology, that the patients must be watched very very closely. Patients with brain injury are much more sensitive to side effects. You have to watch them for toxicity and drug/drug interactions.

More specific guidelines include first, and probably foremost, to rule out social factors first before getting out your prescription pad. I can't tell you how many times I've learned this lesson in life. Always ask about what's going on in the home making sure there is no neglect, there is no abuse, there is no care giver burnout. What's really happening in the environment?

In one example of this, I had a patient once who was struggling with sleeping. And he coming into the visits despite medication, saying he can't sleep, he can't sleep. I was tempted to get out that prescription pad once again and adjust the medicines. Until, I stopped and said, “Is there anything new or different going on in your home?” And it turned out there were family members now working shift work. So, there was a lot more activity in the house both day and night. There was a lot of loud music at times when people were home that were not before. So, it had really changed the environment. And patients with brain injury are more sensitive to environmental change. So that was what was leading to the patients problems with sleep.

Importantly, no large quantities of lethal medication. The suicide rate is high, the disinhibition rate is high. Please, please watch this in your patients!. Don't give them large amounts of medication that can be used to harm themselves.

The other thing we see that happens is that patient are not given full therapeutic trials of medication. That under treatment is common. Most providers know to go low and go slow. But often times, they give up before they reach a full therapeutic trial. Now, of course, if side effects intervene, then of course, common sense always has to play a part here. And, that good clinical care that you don't do something that doesn't help a patient, what you want to do is make sure that in our patients, we are we giving them full therapeutic trials as they tolerate.

Other agents we need to think about to avoid or discontinue. There's an old saying in medicine, “First do no harm”. We want to minimize benzodiazepines anticholinergic, seizure-inducing agents or antidopaminergic agents. This is really important in our brain injury patients, because benzodiazepines can certainly worsen disinhibition. Anticholinergic medicines can lead to more cognitive slowing as well
as confusion. Seizure inducing agents, if a patient's brain has been injured, then they are certainly more at risk for seizures. You don't want to give them something that makes that risk worse. And of course, antidopaminergic agents can impede neuronal recovery.

There have been studies that tell us also that patients are much more sensitive to the agitating effects of caffeine or other stimulants.

There have been a lot of energy diets and herbal products come out in the last few years that are really not good for patients with brain injury. Not only can they produce mania or aggression, or worsen those problems with inhibition, but more importantly, can lead to a hypertensive crisis or drug/drug interaction, or death. There's a lot of MAOI type inhibitors in these medications or in these products that are over the counter and unregulated. So please be careful with your patients and these products.

Some of the medications that we have found to be helpful in our experience in our clinics with brain injury patients include the SSRIs for depression, and it also gives, in some cases, some mild improvement with cognition. We know that if the patient is feeling better, of course, they are more likely able to concentrate and focus better. But we found just a general effect of help with the SSRIs with cognition.

We used the anticonvulsants both for seizure prevention and treatment, as well as for mood stabilization.

The atypical antipsychotics for aggression, agitation, and irritability. And of course, in very severe cases are those more severely injured, we've moved to beta blockers and other agents for aggression. But when it's a more mild problem, we really try to stick with the atypicals.

Dopamine agonist for concentration, for cognition, and focus.
Cholinesterase inhibitors for memory.

That brings up a really important thing to remember in patients is to distinguish the difference between problems with concentration and those of memory. The patient is not likely to tell you the difference. They're just going to tell you, “Hey Doc, I can't think anymore.” Or, “I can't concentrate or can't remember.” They are less likely able to tease the two apart. So, it's very important for the provider to ask the questions of the patient to discern the difference in those. As you can see, there are different medications that work better for the two symptoms.

And lastly, we have certainly found that in cases where there is some need of emotional stabilization, Buspirone works nicely. The interesting thing with Buspirone is that it often times not given a full treatment. If I think back on it, that's probably the likely agent that we have to choose from that is not given a full therapeutic trial in patients. And also, Modafinil is very good for concentration and focus when available to the patients.

Of course, medications alone are absolutely not the answer. The treatment of these patients must be done in a multidisciplinary rehab program and setting. VA Polytrauma System of care has a great website for which the provider can go to look at the options for rehabilitation programs and what's closest to them, and where their options for advice and help are. Patients with brain injury absolutely must have the care of folks from physical medicine and rehab, as well as from mental health.

There is an older study from 1998 that from Dr. Owensworth, that talks about initial education and cognitive behavior therapies in these patients and some of those are listed on the slide.

Also, the long term therapies are important, as well as family therapy, and taking a look at the social issues. Of course, if the finances, or legal problems, vocational problems are interfering, than it's not likely you are not going to be able to do much with medications until you solved those overriding
problems. If the patient is not able to provide food, clothing and shelter, then they are not likely to get better with the medications.

And of course, the support groups, such as the Brain Injury Association of America are super important to these patients and their families. We in the VA have the option, of course, of taking care of our patients, but we often times aren't able to provide as much support to the families as we like to, and we need to lean on our local support groups for that, including the Brain Injury Association. And, I've listed their website here.

In thinking about treatment for the patient that has both PTSD and TBI, the treatment programs for PTSD need to be altered to account for cognitive problems and the inhibition problems of patients with mild traumatic brain injury, and I've listed some of the advice that I've been given and seen work over the years on the slide.

The information must be presented to the patient at a slower pace. There's lot of cognitive assist strategies out there, and devices these days that can help, such as PDA's and writing on different colored pieces of paper, and strategies to help patients remember to do certain activities on a certain timeline. Lots of structural interventions are needed. It can't be as much free association.

Asking patients to do things and contribute on the spot is certainly more challenging. They have to be refocused, redirected frequently.

As well as the provider has to be much more structured in proving clear transitions between topics, between sessions, giving patients more breaks.

And, it's easy for a patient with mild traumatic brain injury to be frustrated if they can't recall events surrounding their trauma. So, we have to be careful in that some events may not have been encoded in long term memory because of brain injury, and it may be that the patient will never be able to recall those events. So, we have to readjust our treatment of PTSD to account for those problems with memory or condition.

So where are heading for the future? What can we look for in the next few years for our patients?

Let's start with some of the questions we don't have answers to and think about that in terms of where the strategies for research will go.

The first is we don't know if combat related blast injury will be similar to civilian TBI.

We don't know if the deficits will be permanent from blast injury.

We don't know, for example, if we can use the sports related brain injury literature as a guide. Some of the areas in the sports field have done a real good job at protecting their patients and looking after their players to make sure they are protected after a brain injury or concussion. And, we don't know if we can use that as a guide and model for us in taking care of patients that are combat related or not.

We don't know if the changes we are seeing in mild brain injury will be lifelong or whether they will be time limited.

We don't know what the best assessment strategies and tools are going to be in long term evaluation.

And, we don't know what the prognosis is going to be for this large group of our patients. So, we got a lot of work to do in terms of research and understanding.
It’s going to take a lot of biological studies to help us understand what’s going on with our patients. Those will include not only autopsy studies for those that pass away, but also, it’s going to take animal studies, neurocognitive studies. It’s going to take microscopic studies, looking at neurons in petri dishes and what happens if we stretch them. And, what happens to the production of the neurotransmitters in times of stress? So, we have a tremendous amount of work to do in understanding the neuropathology of brain injury.

It’s also going to take a much greater and deeper understanding of how to use the new imaging techniques that we have in psychiatry. You know the technology for imaging is absolutely incredible these days and there are so many wonderful techniques. In fact, the physics of it has outstretched our ability to use it in a clinical setting. So, what we have are these wonderful imaging techniques, but yet we’re not sure sometimes how to apply them clinically to the individual patients. So, there are still lots of group studies. There’s lots of work looking out to validate some of the new techniques. So, it’s really incredible and exciting what may happen in the future.

Such as, for example, diffusion tensor imaging, which you see in the upper right corner of the slide, in which the ability to identify on picture, the large axons and large tracts that run from one area to the next in the brain. And, the direction, the flow within those tracts is now available. It’s just absolutely incredible. There are PET scans which is what you see in the lower right, which allows us to image, not only glucose metabolism, but also neurotransmitters specific imaging such as the picture you see on the very bottom right, which is labeled picture C, which allows us to look for, in this case, at dopamine.

The pictures in the very middle show us ultrasound imaging of blood flow. We don’t know if there are microscopic injuries to the blood vessels in brain injury which may lead to some of the long term symptoms. There are many researchers who do believe that this may be part of the injury pattern. I talked about SPEC earlier. There is also spectroscopy which allows us to see the products produced by an area of the brain. And, there is xenon CT in the lower left corner which allows to look at both blood flow and structural imaging at the same time. So there’s a lot of wonderful imaging techniques to choose from. The questions are going to be which ones are most useful in mild TBI, particularly in the patient that has both PTSD and TBI. And what will this imaging contribute to the assessment and long term treatment plan for the patient?

We also have to continually strive to find new therapies for the psychiatric symptoms due to brain injury. We don’t know whether transcranial magnet stimulation will help. We don’t if there are new medications such as anticonvulsants or new SSRI’s that may help. We don’t know if vagal nerve stimulation may be of help. So, there’s a tremendous amount of work to do yet in understanding the pathophysiology of brain injury.

In these last three slides, what I’d like to do is show you some of the education products that are out there from our VISN 6 MIRECC to help in the assessments and treatments of patients with brain injuries. If a provider has not been, prior to this conflict, taking care of a lot of patients with organic injuries, this will give a refresher course. For students, it’s there. Teaching residents, it’s there. The address for the web is on the screen as you can see.

So, what we have are many products out there, including patient and provider handouts, there’s newsletters, there’s actual teaching cases where we go through in detail the patient’s symptoms, the imaging that was done, the neuropsychological tests. And go through exactly where in the atlas the anatomy deficits are, what that means in terms of structure, and where on the x-ray to look. So that these can be provided as teaching cases and we are constantly trying to build more of those in as each month goes by to help fellow clinicians.
There is also a section on the web that looks at patient education material and family education materials. For example, these pocket cards which list common symptoms and things to do and not do. For example, to do one thing at a time if you are easily distracted or to get plenty of rest and sleep, they are basic do’s and don’ts for the provider and the patient.

There are also much more advanced enduring education materials that are on the web, which help the providers to understand the anatomy and physiology as we know it today for brain injury and for the mapping of emotion/memory tracts in the brain. Those are also available through the same website that you saw earlier.

And lastly, I want to thank all of you for listening to us, for taking the time to take this course and to understand what can be done to help our patients. Together, we can make a difference in taking care of our patients with brain injuries and PTSD. And, I would like to once again thank the National Center for PTSD for allowing me to do this webcast.