ARTISS SYMPOSIUM 2014

Psychiatry and Pain Management

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Department of Psychiatry, Walter Reed National Military Medical Center

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Center for the Study of Traumatic Stress
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From the Conference Series:

ARTISS SYMPOSIUM

Psychiatry and Pain Management

Editor's Note: This transcript has been edited, however, as in most transcripts some errors may have been missed. The editors are responsible for any errors of content or editing that remain.

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First Edition

* * *

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The Editor would like to thank K. Nikki Benevides, MA, Center for the Study of Traumatic Stress, Department of Psychiatry, USU for her editorial assistance.

Contents

History of the Artiss Symposium

Kenneth L. Artiss (1913–2001), the namesake of this symposium, was an Army officer, a research psychiatrist and instructor at Walter Reed Army Medical Center. Dr. Artiss, who served for 21 years in the Army Medical Corps retired in 1964 as a Lieutenant Colonel. He was Chief of the Department of Psychiatry in the Division of Neuropsychiatry at Walter Reed's Institute of Research. His work included development of treatment methods for combatants with severe psychiatric disorders.

After his retirement from the Army, Dr. Artiss was a senior consultant for many years to Walter Reed's psychiatric residency training program. Dr. Artiss created an award in 1983 to spur military psychiatry residents to conduct high quality research. This award still exists today and was presented at the conclusion of this symposium.

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For their support the committee wishes to thank:

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- Mr. Vernon Woods
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- The Command at WRNMMC for providing a climate where we are allowed the space and creative license to think about complex issues.
- Dr. Robert Ursano for his support and encouragement to document this important symposium.
- All the patients that continue to inspire and teach us.

PREFACE

Biopsychosocial Approach to Pain Intervention

Harold J. Wain, PhD

We will begin with pain and the biopsychosocial approach to diagnosis and treatment. It will integrate everything that, hopefully, we will cover today. We are not just looking at the physiological part of pain and things that transpire biologically, we are also looking for a way to integrate the biopsychosocial aspect. How do we put brain, mind, and body together? It took me a long time to actually understand what pain was all about, not just on an academic level, but on a personal level as well.

What is the definition of pain? Pain is an unpleasant sensory and emotional experience which is associated with actual or potential tissue damage or described in terms of such damage. I had two really interesting patients this week. One was a woman with phantom pain, subsequent to an above the knee amputation (AKA) after a traumatic accident where she lost her leg. She came in with severe pain. How do you treat it? Nerve blocks all failed. She used the TENS unit. All narcotics failed to help her. The medical student and resident who saw the case with me recognized that I had seen this patient 20 years ago for vocal cord dysphonia. What do you do with a patient like this? During the interview she also said that two years ago her daughter committed suicide. How do you integrate this data together and recognize that you have to come up with a treatment approach?

There are several myths about pain. 1) The physical behavior signs of pain are more accurate in a patient self-report. We know this is inaccurate. 2) Pain cannot exist in the absence of tissue damage. We know this is not correct. 3) Pain without an obvious cause, which is more severe than expected, is psychogenic. This is inaccurate. 4) Patients on medications who frequently visit the emergency department or take opiates for a long time are addicts. Some are and some are not. 5) Patients whose pain is in response to placebo do not have true pain. This is one of the biggest myths because patients who respond to placebos also have true pain.

How do we diagnose pain? Most of us know that you perform a thorough physical evaluation. That reminds me of a story of individuals who begin psychiatric care because of their headaches. One noted individual in the history of music did that. His headaches were attributed to his background or childhood when he in fact had a brain tumor. The idea is to get collateral information and make sure you look at the physiological and the radiographic data. I tend not to look at a patient until somebody else in the specialty evaluates them. If they have headaches, I want neurology to evaluate the patient first.

What is the problem? What is the most common reason that patients come to see us? Frequently, the first intervention occurs in the emergency room. Do we under treat or do we over treat pain? From the behavioral health role, is pain out of proportion to physical findings? Frequently it is. Is it functional pain? I think, as one of my mentors taught me, that the significance of a symptom is for the preservation of life, rather than for its destruction.

Pain is very significant. It tells us many things, either biologically or psychologically. Is there depression, anxiety, and/or somatoform spectrum? Let us not negate DSM Axis 2 behavior as well, because those behaviors become significant in understanding the patient with pain. Frequently, we get requests for stimulators from anesthesia and surgery. Another patient comes to mind that we saw recently. She also lost her daughter two years ago and had severe physical, emotional, and sexual trauma as a child between the ages of 12 and eighteen. She was abused, yet, she is an E9 and doing beautifully; however, subsequent to the failed stimulator, she was paralyzed on her right side and now walks with a limp and with severe pain. We were able to use some hypnotic techniques with her that were transient, which I will discuss in a moment.

The biopsychosocial approach was coined by an internist, George Engel, who was also a psychoanalyst. I had the privilege of observing Dr. Engel when he ran the psychosomatic unit at Rochester. The biopsychosocial approach systematically considers biological, psychological, and social factors in the complex interactions in understanding health, illness, and the healthcare delivery system. One thing that has helped me understand a great deal about the biopsychosocial paradigm is looking at hypnosis. In the 1800s, Esdaile described over 300 major surgical procedures done with hypnosis alone. Why? People said suggestibility, but that is not it. Not everybody can do that, but there is an integration of biopsychosocial parameters along with physiology. If you look at some of the EEG patterns and some of the PET scans during hypnosis you will see alpha and theta waves. Why does that occur and how do we set the stage for that to transpire?

I have had the privilege of partaking as the anesthesiologist in about 36 surgeries. I still wonder why hypnosis actually works. Why can some people go in to the operating room without any anesthetic? To me the most significant surgery was a septoplasty because in that surgery you use a hammer and chisel. Why was the patient able to tolerate this procedure? The patient was a physician who graduated first from his medical school class. I do not know why, but it is he who had the gift to do that.

Some of the factors that affect pain are fatigue, sleep, anxiety, depression, fear, and worry about illness. Is the patient seeking drugs? Is there a history of substance abuse? What is the cultural background? There was a patient in the emergency room this morning who said that she was talking to God after her husband left her for another woman. The comment that came back was that this was cultural. Some would think that the behavior was psychotic since she was talking back and forth with God. However, this behavior was part of her cultural background that we need to evaluate and understand with the patient. Ethnic background is important.

Exploring past experience is also important. How did the patient respond in the past? What are their previous traumas? Are they reenacting a trauma for all of you to reenact for them by giving them nerve blocks or by doing some minor or major surgical procedure? Do patients want a stimulator, based on the fact that they have been traumatized before, and is this another way of being traumatized? What is the meaning of the situation for them?

Sometimes when we go on rounds we ask patients about their pain levels. We are really bringing attention to the patient. Why not instead ask them, what is their comfort level? What are patients expecting? What about patients with tics? Are they expecting them to occur? Are patients looking internally or externally? There is not a uniform threshold for pain except in the laboratory.

"Tell her she's dead. I don't want to talk to her about the relationship." Often in a behavioral health evaluation we ask patients about their past. Some people do not want to discuss their past even though it would be helpful. What is the somatic representation of the internalized conflict that is being manifested externally? What about repetition compulsion? Are some patients repeating the past? Is this their way of repeating or projecting their transference upon their provider? What about the patient's psychopathology? Often we negate the personality structure of the person. Just because they have obsessive traits or some sociopathic traits that does not mean that is their diagnosis. You want to look at what traits they project and what traits they present with.

A patient's medical memories are important. Do they like going to the emergency department? Some patients love being a patient. They may reenact their childhood by getting all of us to take care of them. We have one patient on the ward right now that comes in every three or four weeks. This is classic behavior for this type of patient. How do you handle that? Does birth order make a difference? The youngest of the family tends to have more somatic complaints. That is not a "Wainism;" that is evidence-based. When we observe the pain do body activities increase or decrease? Does the patient protect their painful areas when they talk with us? What kind of facial expressions do they have? What about patient communication? What are patients telling us about their pain? What is the metaphor associated with pain? Listen to their words. What does their pain interfere with?

When you interview the patient make sure the environment is a safe place and use an informal approach. Accept their comments without confronting them. Is there anatomical consistency? Review the chart, review the medications, review sleep, look for metaphors, and clarify ambiguities. Respect the right of the patient to maintain their symptom. Be Colombo rather than Kojak. Just be benign. Wear a raincoat into your office. Do not bring a resume. I do not like to dwell on the past; however, the best predictor of the future is the past. It is important to understand the past with a patient and how they became injured and why. What is the patient's perceived trauma? Is there alcoholism in the family? Parents who are alcoholic tend to bring forth somatosizers. What about their illnesses as a child? That may be a model for some patients. Do they have difficulty expressing emotion? Are there any alexithymic conditions you want to explore? Is there antisocial behavior? Are they injuring themselves? Are they abusing drugs? Ask about the type of abuse they may have experienced, or if they have abused others. What type of models do they have in their parents, grandparents, or significant others who are in their home? What is the patient's history or use of medications? When did it start? Always ask when it began. Did it begin when you got angry at your boss? Did you have a paralysis of your hand or pain in your hand when your mother scolded you? Patients will recall very clearly. A classic patient had atypical facial pain because her mother slapped her frequently on her right side. When did the pain begin? What does it feel like? Patients need time to tell us what we need to know. They want to be taken care of and if they think we are dismissing them, this can create more problems.

We must also address the transference and countertransference issues. One of our jobs in clinical liaison is helping staff who are angry at their patients. Patients with pain and patients who use drugs can be challenging. We have to deal with the staff, and ourselves, and our feelings. We have to be aware of what kind of transference and countertransference issues are present. How do you manage them? How do you manage your colleagues? We go back to the behavioral health diagnosis model. These are things we want to understand in our patients. We want to understand how and why these issues develop. Remember, pain may be a way of coping.

Today we will talk about many different types of treatments and techniques. For me the therapeutic alliance and building a relationship with the patient is probably the most important thing we can learn. If we demonstrate caring for another human being our treatments and techniques become more effective. But without that empathic approach and the understanding of what we are doing with the patient, these techniques are not successful. We think because we are writing in the chart, or doing cognitive behavioral therapy (CBT) or exposure therapy that we are being productive. I guarantee you, we are not.

A nice study was done at UCLA looking at patients who did well with acupuncture and those who were high hypnotizable, in the context of the biopsychosocial approach. It is fascinating to note that the higher the hypnotizability, the greater the results are with acupuncture. Narcan reverses the impact of acupuncture. Narcan does not reverse the effectiveness of hypnoanalgesia or hypnoanesthesia. Therefore, hypnosis is actually mediated through a different receptor site than the opiate receptor sites.

I will conclude with this brief scenario. We have a soldier who came back from Iraq with significant injuries and was able to tolerate his pain pre-operatively, operatively, and post-operatively using only the hypnotic technique. Why? Hopefully, by the end of the day we will answer that question.

Introduction to Psychodynamics and Pain Intervention

Russell B. Carr, MD

I am looking forward to hearing from our numerous speakers today and I am pleased to see a multi-disciplinary approach to the topic of psychiatry and pain. At Walter Reed we have learned the extent to which complex situations require complex care and multi-disciplinary care. This is something I have seen evolve through our efforts during the War on Terror in the last 10 years. When Dr. Wain asked me to talk about psychoanalysis and pain for 15 minutes, the first two thoughts that came to mind were what in the world do I, as a psychoanalyst, have to say about pain management, and if I do have something to say, how am I going to say it in 15 minutes?

That initial response is black-and-white thinking, meaning that all the treatments are biologic and there is no psychological component to what we do. At times even I have that knee-jerk reflex and we need to, as Dr. Wain so eloquently pointed out, offer in psychiatry a biopsychosocial approach. Maintaining a biopsychosocial approach is very important in pain management and in complex chronic pain management.

For the psychological component, in psychoanalysis, I want to focus on two areas. What is the meaning of pain for patients, and what is the relationship between patients and providers? Psychiatrists are the experts in these areas. In analysis and therapy this is our focus. Thinking in this way is important in pain management as well. What do I mean by the meaning of pain for a patient? How do we help someone who has suddenly found themselves in chronic pain? Soldiers and marines are returning home with severe injuries, some of whom may have been dealing with chronic pain for extended periods of time or perhaps they have dealt with pain of various sorts throughout their lives. What is the meaning of pain for them? How does it impact their sense of self and their experience of the world? How has it changed, perhaps, how they view themselves and how they interact with others?

Dr. Lande, our service chief for Psychiatry Continuity Service (PCS), and I were discussing this recently concerning a patient with severe chronic back pain. No one had talked to the patient about how having this pain prevented intimacy with his wife and what that meant for him and how he perceived himself. Maybe he lost his sense of manhood, of being a man, and of being a good husband. Was there guilt and shame that may have come with that?

Honing in as close as we can to our patient's experience is something we need to think about. The other piece of that is *context*. Dr. Wain provided a great example about a patient whom he saw recently. Her daughter had just committed suicide and the patient had her own previous mental health issues. Placing pain that suddenly does not seem to respond to standard treatments into a context in a patient's life is very important. It is crucial to ask what else is going on in their lives. What other meanings could this have for the patient? Perhaps there is lingering unresolved grief and loss. How might that be manifesting now? Perhaps talking with the patient about these things and processing her loss with her, both the amputated limb in this case and the loss of her daughter, may have remarkable effects in how she engages in her pain management and her overall medical treatment.

The meaning in context is important, but the relationship between the patient and the provider is also important. This is the other aspect that we assess. What is going on between you, as the provider, and the patient? One thing I learned in my psychoanalytic training is that the derivative of the word for patient is "to suffer". We are seeing patients who are suffering. We are trying to walk with them in their suffering, perhaps dwell in the suffering to some degree, and recognize it, and understand what is going on.

As Dr. Wain pointed out, we also need to understand what patients bring to the relationship and what we bring to the relationship. How has pain been handled in their families in the past? How was being hurt handled in their family? Was their pain dismissed? Was their pain actually mocked? Or were they supported and did someone help them? Did someone make them feel that they were not alone with their pain?

Frequently, the patients we see that are struggling with chronic issues feel utterly alone. Pain can be a chronic issue. If they have had a sense in their life that they are alone with their pain, or that they are required to solve it themselves it makes it very difficult for them to respond to treatment. It makes it difficult for them to accept treatment and, for them to be engaged in a way that does not have shame for them, or that does make them feel they are being looked down upon in some way.

The other piece to think about is what we, as providers, bring to the patient. I think about this with patients that may be struggling and not responding to treatments, or not responding to what I or other doctors are trying. My thoughts are, what are we bringing to this setting? What are we doing? I do not like the phrase that a patient has failed therapy. I think we have failed them. Therefore, I try to sort out how we failed them. I think about how I am acting with them as well as specific treatments that may not have worked. Is there something about them that makes us minimize their pain or feel anger towards them? How can we understand that dynamic better and understand our responses to patients? We could call this countertransference. How are we responding to patients that could be interfering with treatment success? Perhaps we could be reenacting an experience with them that has been recurring throughout their lives that relates to being in pain and being rejected for pain. Attempting to step outside of that paradigm with patients is important to recognize.

In summary, I want to emphasize that we need to focus on the meaning of pain for a patient and the context of suddenly being in pain. Perhaps patients may be facing pain for the rest of their lives. How does this fit into the context of their lives overall, and what has been leading up to it? How have they responded to these things in the past? What the psychiatrist brings to the relationship is important to think about as well. I talk to our residents frequently about a very important part of the biopsychosocial model. I think it is important that complex chronic pain has a multidisciplinary approach. Everyone has a seat at the table for managing it.

Rehabilitation of the Combat Casualty and its Implications for Behavioral Health Specialists

Paul F. Pasquina, MD

The topic of psychiatry and pain management is extremely important. Whenever we talk about pain there is a physical, psychological, and an emotional component. As Dr. Carr said, we cannot effectively take care of patients unless we understand the context of their experiences. Often when we are taking care of patients in rehabilitation, we just say, "They are going through rehab." We do not necessarily understand the scope of the experience of rehabilitation and what that means to our patients.

Everyone knows we are still at war. We have been at war for over 13 years. People are still putting their lives in harm's way and sustaining horrific injuries. Understanding these patients and what they are going through, what they have gone through, and what their families have gone through is important. What are their experiences? It is important to understand, in context, what it means to take care of severe trauma over great distances with the team of people that impact on the care of patients. What we can and cannot do and how that might influence patient outcomes is also important to understand in the context of patient care.

It amazes me that soldiers with severe combat injuries can receive immediate care and return to the United States; however, we, in rehab, have to think about the discharge plan from day one. In rehabilitation medicine the patient is met when they enter the hospital to begin planning the next steps. Bones need to heal and medicines need time to heal other injuries. We have to address the discharge plan so patients can move forward. The discharge planning is usually coordinated by social workers and case management staff. They typically know all the resources in the community. In any community practice this is how it works. However, in today's context, we are caring for patients in Washington, D.C. when patients' families may be dispersed all over the world. They might have an uncle in Germany who is their closest ally. Their fiancé may live in Maine and their stepmother might live in

Texas. Where are they going to go? Discharge planning becomes extremely complex with these patients.

Everyone should be aware of Level 1 to Level 6 care centers. Walter Reed National Military Medical Center (WRNMMC) is a Level 5 care center. A Level 5 facility is where you receive definitive care. A Level 4 care center would be Landstuhl Regional Medical Center in Germany. Level 3 is the highest level of care in combat, or in the theater, and Landstuhl is a combat-support hospital. Level 2 is where you have a laboratory, and Level 1 is your medic buddy. Has anybody heard of Level 6? Level 6 is thought to be the VA, but as folks who have been practicing over the last decade know, there is a strong relationship with patients going back and forth between the VA system and the DOD system. There are three main Level 5 facilities where our most severely injured combat casualties go: WRNMMC, The Center for the Intrepid at Brook Army Medical Center in San Antonio, and the C5 Program at San Diego Naval Medical Center, all of which have comprehensive holistic rehab programs.

Unfortunately, it is more the norm than the exception to have patients with bilateral lower limb loss and patients with severe upper limb injuries who have gone through multiple reconstructive surgeries. It is not uncommon for patients to have a brain injury or for them to have other sensory disturbances that involve vision and hearing. Clearly, the emotional component to all of these traumatic injuries needs to be taken into consideration as well. Patients with extreme injuries help me focus every day when I wake up because this is what we should be thinking about. As I pick up the milk on my way home, or as I fill up the gas tank or pay a bill, I think about some of these challenges and the call for all of us to treat these patients.

I want to tell you about a patient I will call DJ. DJ was a recent West Point graduate and an Airborne Ranger who was deployed in Iraq. His vehicle was struck by an IED, but he was not injured so he got out of his vehicle to help the guy behind him that was trapped in the vehicle. A sniper shot him in the neck. He came to WRNMMC a C3 tetraplegic and was on a respirator. DJ met with us, met with our team, with his family, and his wife, and said, “I don’t want to live like this. I want to withdraw life support.” We called the Ethics Committee and met again with his family, and DJ decided he would give rehabilitation a chance. We were successful at transferring him to a spinal cord injury rehab center in Seattle, thought to be the best by many in the VA system. After two months the director of the program called me to say that DJ had decided to withdraw life support. Our Ethics Committee met, and DJ, holding the hand of his wife, decided to withdraw life support. As much as we have had success with combat casualty care, there is still much more to learn. DJ was a man of faith. His family was a family of faith and that was the decision they made. These are the types of emotional scenarios that people are dealing with.

Another soldier, James, came to us at the old Walter Reed location after he was involved in a blast explosion and lost both of his arms. Because of a very high transradial level, right below the elbow, he was not a good prosthetic candidate. James also lost both of his eyes and had a significant traumatic brain injury. His wife was eight months pregnant when he returned. These are our soldiers. These are the extremes of our soldiers, but these are the people that we are entrusted to care for. We have made progress in our medical care, our surgical care, our rehab care, and our behavioral healthcare, but there is still much more we need to know. There is much more we need to understand in order to meet the needs of our most severely injured patients.

There are some good stories to share as well. Bob Woodruff, embedded news reporter, had a severe brain injury and was treated at Walter Reed. He went through extensive rehabilitation and reached the limit of what we could do for him. That was before the NICoE (National Intrepid Center of Excellence) existed and the resources that we now have. His best therapy was saving his life and engaging him in rehab, but when he was discharged he really had to get back into his work. He had to challenge himself to get back into work, and he was successful in that goal. We have seen many people return to high-level functioning even after severe injuries.

Brain injury remains a significant problem for our patients. How the actual physical injury of the brain impairs and interferes with pain perception and how it affects the psyche are extremely important. There is a post-concussive syndrome called chronic traumatic encephalopathy (CTE). Hopefully, people are familiar with the disease, or the term, but this fairly new entity has now become mainstream information and knowledge. We have taken care of patients who are ten years out from a mild traumatic brain injury in addition to multiple other types of injuries. Their families are reading about professional athletes who seem to have everything going for them, but then take their own lives. These professional athletes exhibit aggressive behavior, and they are irritable and impulsive. We still have a great deal to learn about the brain. For example, is tau protein deposition causing a problem? What is happening with proteins that are forming, and why is the body not excreting them? There is a great deal of good work being done to look at CTE.

Extremity trauma is the most common type of physical injury that we see in combat casualties. Often it is not clear if the limb is salvageable. Patients may endure multiple surgeries. Obviously, the perioperative period is a time when patients are in a great deal of pain. Nutrition becomes another important aspect when patients are in and out of surgery every other day. They are not allowed food after midnight (NPO), and when they wake up after surgery they do not feel hungry.

Returning to the biopsychosocial model gives us a great deal to think about. What about limb salvage versus amputation? Everything is done to attempt to save a limb, and we have expert surgeons doing all kinds of creative skin flaps, muscle grafts, and reconstructive surgeries. There are some studies suggesting that these patients may not do so well, and I will discuss the study that Dr. Wain and I were involved in a little later.

Military patients with amputations are different from patients you see in civilian practice. Soldiers have a higher rate of multi-limb loss and a higher rate of upper limb loss. Since we increased our forces and our numbers in Afghanistan there are many more patients with multiple limb loss and proximal limb loss. We also see dismounted, complex blast injuries and we need to be prepared to take care of these types of patients. Typically this is somebody who is on a patrol who steps on a land mine, loses both lower limbs at a very proximal level, and frequently has genitalia injuries, as well as upper limb injuries. During the years when we were more involved in Afghanistan genital injuries increased exponentially. Dr. Wain will tell you, when you begin with an 18-year-old male that has problems with sexuality and now has problems with genitalia injury, things become extremely complex.

The age distribution of our military patient population is also quite different from civilian patients with limb amputations. The majority of the military population is under the age of 35, which creates its own challenges, but also some great hope because technology that may be 20 years out may eventually help them. If I am 20 and new technology is going to take 25 years to develop, I will only be 45 when it is available. We need to be thinking about short term as well as our long-term impact on patients.

There are many changes imposed by amputation including change in body image, self-concept, sexuality, functional changes in lifestyle, worries about finances, moving forward, and constant problems with comfort related to prosthetics. How patients see their role in life, what they had expected of themselves, and now, what they may or may not be able to do has also changed. Accompanying all this is a sense of loss of control.

There are major emotional responses to injuries involving limb loss: grief, anxiety, and depression are common and normal. The incidence of depression in people with lower limb loss is typically around 30 percent. Chronic pain is also a high predictor of developing depression or behavioral health problems, as well as a number of other comorbidities.

When we study outcomes of limb salvage versus limb amputation, patients in the limb salvage group actually have worse outcomes than those with an amputation. Does that mean we are going to amputate everybody's limb even if we can save it? No, however we need to be thinking about patients that have multiple surgeries. Their muscular performance level may be compromised with multiple interventions over an extended period of time.

There are numerous outcome measures. As an organization, in the DOD, we do not do a very good job looking at outcomes. I think everybody can say that. We are doing ourselves a disservice by not looking at outcomes very well. There are many outcome scales in use, many of which include quality of life measures. If you look at any outcome studies that have been done with amputees or people with disabilities, we learn their quality of life is not as good as able-bodied individuals. Amputees and patients with disabilities are significantly challenged in life and we need to be able to measure that.

In a study done by Reiber and colleagues in the DOD-VA system we looked at some of the health concerns and prevalence of comorbidities of people with lower limb amputation. The study showed that the incidence of low back pain is extremely high in patients with limb loss. Patients also have a high incidence of phantom limb pain and residual limb pain. As people age with disability they will have pain from arthritis. They also have a much higher incidence of depression and PTSD. Soldiers, by virtue of deploying, have a very high incidence of PTSD, depression, and anxiety. If you add components of physical impairment to that, the patient's assessment becomes much more complex.

Military service members also have unique psychosocial needs. They are younger, they are adjusting to body image changes, and they are dealing with things like depression, anxiety, and PTSD. They are separated from their unit. They are not sure if they should stay in the military. Should they go through a medical board? What does that even mean? "I did not understand what the VA counselor told me. Was I supposed to be taking notes? I am on a lot of medicines. I do not really understand this." We encounter many scenarios in our patients' hospital rooms. We may see a patient who has lost multiple limbs, and their mother and father are having an argument about something that happened 15 years ago. Many factors come into play when we are taking care of patients. Do they have children? Do they have a mature relationship with a partner? These are other issues to explore.

Visits from dignitaries can be helpful. Former Secretary of the VA, General Shinseki, is a Four Star General who lost his foot in Vietnam. General Franks, also a Four Star General, lost his leg in Vietnam. Visits from dignitaries actually play a positive role, so try not to shelter your patients from them. If visits from the President or Four Stars do not help, then Ozzy Osbourne might. Celebrity attention has been very positive. I think the communities at large have been very welcoming of our injured service members. I am reminded of an individual who lost his right arm and his left leg. From the time of injury until going through his rehab, he got married and had two children. Engaging people in life and participating in the community is one of our goals.

Often we have a stoic patient population. They are struggling and what do they normally do? They may reach for alcohol; not an uncommon behavior. They are anxious and they do not know what to do. They are at a party and have a glass of wine or beer and they feel better. The next morning they may feel a little jittery again. They remembered that the alcohol worked pretty well at the party so they may have another drink thinking this behavior will help. We have to address this type of behavior with our patients and recognize that alcohol abuse is a serious issue. Our patients want help. They do not want to become alcohol abusers and we need to think about the problem in this context.

There are many pharmacological interventions for pain management and we try to teach all of them. It is important that the entire team be involved and not just behavioral health specialists. The point I want to make is that our psychiatrists and our behavioral health specialists are dealing with many patients with multiple complications. It is everyone's role to participate in the care of patients with pain. That is why we have interdisciplinary team meetings. That is why we have a behavioral health specialist at the table saying, "When this comes up in therapy, use this approach, or use that approach." We are in this together.

How important is creating centers of excellence and what role do they play? Patients need to be functionally independent. They need to feel dignity and need to be taught independent skills. Centers of excellence have resources to help us teach patients these skills. Part of that is having, for example, an activities of daily living (ADL) apartment where patients can work on skills in occupational therapy. They can work on independence, cooking, cleaning, and toileting with and without their prosthesis. When they go home, they feel comfortable. The symbolism of great buildings like the National Intrepid Center of Excellence (NICoE) and Walter Reed National Military Medical Center (WRNMMC) mean something. It means we are here for our wounded warriors. The Computer Assisted Rehabilitation Environment (CAREN) is an excellent example of state of the art technology. We are still discovering the role of CAREN. People with multiple injuries, including brain injury and sensory perception, can use the virtual environment of the CAREN system and simulate multiple systems simultaneously. In CAREN patients can work on things like balance, strength, visual acuity, and cognitive skills in a single 40 minute rehab session. How does this affect pain? Taking an active approach is felt to be helpful. The feeling of progress definitely has a role in recovery. Mirror therapy is artificial feedback that may make it possible for patients to "move" the phantom limb releasing it from potentially painful positions. The idea is that if you can see your missing limb and you can process that, you can help decrease the pain. Therapists should be aware of therapies other than the traditional pharmaceuticals.

You may hear patients say that their HO is acting up. HO, or heterotopic ossification, is a very common condition affecting 40-60% of blast casualty patients. Bone forms where bone should not form and the condition can be severe especially when bones are intertwined with muscles, nerves, and soft tissue. HO can be problematic for fitting and wearing prostheses. Surgery may or may not be helpful.

There are some differences between upper and lower limb amputation that we need to learn. There may be some increased pain and body image issues with upper limb loss, however the biggest problem with upper limb loss is the high rate of prosthetic abandonment. If a patient relies on one arm to do all their activities of daily living, the risk of developing overuse injuries in that one arm or the neck may be much higher. Hand dominance can also be extremely challenging for patients. If a patient is right handed and they lose their right hand, they now have to use their left hand for everything. As you go about your day think about how it would feel if you lost your dominant hand. There is an optimal time period for fitting patients with prostheses that may help prevent abandonment. For the upper extremities we typically use myoelectric prostheses that are designed to mimic human anatomy and motion with electronic technology. What are most patients going to do, particularly when the prosthesis is hot, uncomfortable, and heavy? They will abandon their prosthesis and use their other hand. Over time this becomes problematic.

Choosing a prosthetic component is difficult. Will patients choose a hook or a hand? You have probably seen patients with both and the question becomes why does someone prefer one over the other? Many times the hook is a functional terminal device. Remember there is no sensory feedback from a prosthesis. The entire sense of touch, whether it is emotional touch or whether it is for activities of daily living, is gone. Patients need to be able to see what they are picking up, and a hook gives them much more visibility performing that action.

Rehabilitation for lower limb amputation is extremely complex. We have some patients with four limb amputations. What do you do? You follow similar principles that you do with every other patient. You form a team and talk with your colleagues and by collaborating you figure out the best way forward. There are no magic answers. The process is a day-by-day, adjust as you go process.

The basis of prosthetics usually begins with a clear socket that you can mold and adjust to the limb. You can adjust it before you get to a definitive socket. The residual limb will mature, change in size and dimension, and increase its tolerance for weight bearing. The socket is extremely important because it is the interface between the patient and his prosthetic limb. If the socket is not comfortable it does not matter what all the other components are. There are different ways to secure the prosthesis. Some patients use a pin lock suspension. They put on a roll-on liner with a pin at the end and it locks into the prosthesis, or they can use something like a seal-in liner and a vacuum suspension. Is it comfortable walking around with a plastic thing around your leg all day? No, it is not, especially in the hot months of the year.

The choice of components becomes quite complex and overwhelming to many of our patients as well as our providers. It is like going to a shoe store. We have what we call dynamic response feet that store and release energy as the user ambulates. The dynamic response foot provides a good "energy return," meaning that a high percentage of the energy expended when the user steps forward is stored within the foot system and then is returned as momentum for each successive step. We also have high-tech prosthetic knees with microprocessors. The microprocessors control resistance. If users want to walk fast, they do not want a great deal of resistance in their knees. When walking slowly, users increase some of the hydraulics and increase the resistance. The devices have to be programmed and patients have to be trained. Most people do not understand that walking with a prosthesis uses a great deal of energy. It is taxing on the cardiovascular system and can be challenging. Many of our patients do not appreciate this at first. It takes patients a long time to be proficient walkers, particularly those with bilateral lower limb loss. We usually start patients walking on what we call shorties. The idea is that a patient's center of mass is lower so if they fall, they can get back up. They can work on their stability and their balance with shorties. As patients get more comfortable with stability and their socket, their residual limbs become much more able to accept weight. At that point we will advance them in height.

For people who have multiple limb loss we often have to incorporate some very creative technological solutions. Does technology make a difference? When you see someone not just walking, but having the confidence to put their child on their shoulders and walk through a busy parking lot, that speaks volumes. Another inspiration is a patient who lost both his legs above the knees in combat in Iraq. He competed as a paralympian alpine skier in Sochi in 2014. Even though he is a very fit man, it took him a year to learn how to walk again. Technology is used in wheelchairs and training patients to use them. Technology is used to customize and adapt cars for driving. Technology is used to help patients with activities of daily living and to help patients return to recreational activities. Often recreational motivational activities are the first activities outside the hospital that patients attempt. Many patients come back from recreational activities reinvigorated and more committed to rehab to continue to learn the things they can do.

The story I will close with is a personal one that highlights the depth and breadth of some of the programs that we have in the creative arts. A close friend of mine from West Point lost both legs in a combat injury. He was a football player and a big guy. I saw him almost every day while he was in the hospital, and subsequently took care of him. A year or two after his injury we were talking about what to get my wife for Valentine's Day. He told me to get her a camera and a specific lens. He was telling me all about photography. He said, "Paul, believe it or not, I lost both of my limbs and everything else, but the thing I was most concerned about the whole time was a radial nerve injury." He was concerned he would not be able to operate a camera when he recovered. The take-home message is do not underestimate the importance of what might not be obvious. Here is a man that I felt I knew pretty well, and he was reluctant to tell me about one of his most important concerns. I would have discussed and alleviated his worries, had I known.

In the social context of rehabilitation we have many peer visitations that can be helpful for patients. It is helpful to see other people with similar issues making progress and reaching their goals. There is another component of this to understand. Many soldiers do not want to be celebrities, yet suddenly they are engaged in celebrity-ism. When they return to their hometown they are celebrated during a time when they are still struggling a great deal. We need to help our soldiers through that process.

In conclusion, I would like to say that we have many interesting and complex therapies to offer. Hopefully, these therapies will help some of our most severely injured patients. I appreciate everyone's help in taking care of our patients and their families.

The Use of Spinal Cord Stimulator and Pain Clinic Interventions for Pain Patients

Scott R. Griffith, MD and Christopher Spevak, MD, MPH, JD

DR. GRIFFITH: Our goal is to provide people with enough pain relief for them to focus and participate in rehabilitation in order to return to activities of independent daily living. Pain relief is one of the major goals of rehabilitation. I asked Dr. Spevak to assist with the presentation today because he has a background in both academic and private medicine as well as being our embedded wounded warrior pain doctor for a number of years.

I brought some of the equipment that is typically implanted. I hope, as the presentation unfolds, it will make some sense. [*Equipment passed to the audience.*]

Dr. Spevak will begin by describing how we might choose a patient for an implantable pain system, and also, how we interact with behavioral health to try to identify the patients that may benefit the most from this approach.

DR. SPEVAK: Our objectives today are to describe the indications for spinal cord stimulation and intrathecal delivery, talk about the mechanisms underlying spinal cord stimulation, and discuss some of the complications. To get us started, I have three questions for you to consider. First, which of the following is the best indication for spinal cord stimulation? A: compression fracture; B: aseptic necrosis of the hip; or C: complex regional pain syndrome or trigeminal neuralgia. The correct answer is C. Question two: patient is a woman with an implanted pump delivering 25 milligrams of morphine per day. She has failed back syndrome and is complaining of increased pain and weakness. What is your suspicion? A: morphine withdrawal due to fractured catheter; B: catheter tip granuloma; C: recurrent disc herniation; or D: morphine-dependent hyperalgesia. The answer is B. Here is your last question: patient is 72-years old, has low back pain with prostate cancer metastasis, and is best treated by: A: intrathecal morphine; B: decompression laminectomy; C: spinal cord stimulation; or, D: TENS. The correct answer is A: intrathecal morphine therapy.

Patients are referred to the Walter Reed pain clinic for many conditions.

The most common conditions are post-surgical chronic back pain, radicular pain, radiculopathies, arachnoiditis, complex regional pain syndrome, peripheral causalgia, and phantom limb pain.

There are different types of pain. We artificially make the distinction between two types: neuropathic pain and nociceptive pain. Neuropathic pain may result from direct nerve root injury, radiculopathy, and peripheral deafferentation pain. This is the type of pain we see in patients with multiple sclerosis, certain strokes, trigeminal neuralgia, and diabetic peripheral neuropathy. Nociceptive pain is derived from tissue damage such as cuts, bruises, bone fractures, and burns. We know that most chronic pain that patients experience is combined components of post-surgical chronic back pain, idiopathic chronic pain syndrome, and cancer pain syndromes.

Spinal cord stimulation delivers electrical signals to the epidural space. There are several proposed mechanisms. Modern theories suggest spinal cord stimulation works because pain signals are inhibited before they reach the brain and are replaced with a tingling sensation. This is indicated for the management of chronic, intractable pain of the trunk and/or limbs.

For you historical buffs, the origin of neurostimulation began with electrically charged torpedo fish, and the first electrostatic investigations were conducted by Otto von Guericke in 1672. This was followed by electroacupuncture and the invention of the Leyden jar to store electricity. More modern uses arrived in the 1700s. John Wesley, father of the Methodist movement, championed the use of electricity to treat angina, bruising, cold feet, and gout. My favorite is the electric hairbrush that promised when you brushed your hair you would grow more hair. Fast forward to 1965 and here is where modern pain research really begins. The gate control theory was proposed by Melzack and Wall. Gate control theory asserts that activation of nerves that do not transmit pain signals (non-nociceptive fibers) can interfere with signals from pain fibers, thus inhibiting pain. The gates, the small afferents coming in, are composed of at least two kinds of fibers. Some are fast and somewhat thick Aδ fibers that carry messages quickly with intense pain. Others are slow C fibers that carry the longer-term throbbing and chronic type of pain. Larger Aβ fibers do not transmit pain stimuli and inhibit the effects of firing by Aδ and C fibers. Some areas located in the dorsal horn of the spinal cord that are involved in receiving pain stimuli from Aδ and C fibers also receive input from Aβ fibers. The non-nociceptive fibers indirectly inhibit the effects of the pain fibers, closing a gate to the transmission of their stimuli. In other parts of the laminae, pain fibers also inhibit the effects of non-nociceptive fibers, opening the gate.

Neural stimulation began with Norman Shealy in 1967 when he laid a copper electrode along the spinal cord in a laminotomy. This technique was popular in the ‘70s and ‘80s. We were very fortunate to have Dr. Shealy attend grand rounds and journal club, as well as lecture here, a few years ago. We talked about some of the early days and some of the advances.

The North American Neuromodulation Society Conference (NANS) is an annual conference where dedicated researchers show us what is new in the field. Some of the new stimulation patterns show us that we might be able to stimulate the ascending pathways that motivate emotion which is the affective component of pain. Perhaps we will be able to do a better job in that area. This is groundbreaking research. One of the things I hope we can convey to you is our excitement and enthusiasm because this is an area of pain research that is in its infancy.

We have multiple societies in addition to the Food and Drug Administration (FDA) that specify indications for approval of spinal cord stimulator for the management of chronic intractable pain of the trunk or limbs. Spinal cord stimulation can be effective for neuropathic pain indications, failed back syndrome with radiculopathy, painful neuropathy, complex regional pain syndrome, postherpetic neuralgia; and there is minor evidence that spinal cord stimulation can be effective for non-nociceptive pain.

What are the indications for spinal cord stimulation? A slide was shown of the "ideal patient." He is a frequent smoker, a beer drinker, and he is overweight. He also does not exercise. This is our perfect patient for spinal cord stimulation, right? Wrong. How do we select patients for spinal cord stimulation? Ideal patients have failed acceptable conservative therapy, have no active infection at the site of implant, have no untreated drug addiction, are psychologically stable, and have no other contraindications to implantation.

There are several studies testing the effectiveness of spinal cord stimulators currently in development. Dr. North, a neurosurgeon from Baltimore, is one of our best clinical researchers in this area. In one of his studies Dr. North looked at 50 patients, all of whom previously had a failed surgery and returned with pain, making them candidates for another surgery. What did Dr. North do? He randomized them to re-operation or spinal cord stimulator with voluntary crossover at six months. After six months, what happened? Sixty-seven percent chose to receive a spinal cord stimulator. Only 17% of patients whose first surgery had failed and who were randomized to the spinal cord stimulator asked for a second surgery. That kind of difference was one of the first studies that started us down this path.

Spinal cord stimulation for vascular disease was first reported in 1976 by Albert Cook. Eleven months after follow-up, patients reported a reduction in pain and healing. What is new and on the horizon? We expect to see stimulation either on the peripheral nerves or in the field, but not stimulation in the spinal cord. At this point, Dr. Griffith will talk about neurostimulation trials.

DR. GRIFFITH: What do we look at when we conduct a trial once we have decided that a person is a reasonable candidate? We assess several things. What is the patient's general response? Do they feel overall that this was good for them? We are also looking for objective measures. Do they have less pain? Typically we use a cutoff of 50% reduction, but we tend not to be too dogmatic about that since there can be other important end points. People can be a great deal more functional when they are walking around testing this out. The reduction in opioid use drives a great deal of our interest in the military-specific community. Many people stop using opioids altogether, and the majority of people are actually glad they received an implant.

The goal of an implant is to create a paresthesia, or a buzzing sensation in an area where pain usually occurs. This process has become more complex; consequently representatives from the companies that make the various stimulators will come to us and actually help program the systems. We talk about amplitude and frequency. The amplitude is how strong the stimulation is. The frequency is basically how fine and how far the stimulation penetrates the tissue. Can you stimulate something deep versus superficial? Pulse width addresses whether something feels relatively smooth or bumpy. When you move your body, the electrical characteristics change in the epidural space which is several millimeters wide. Therefore, as something moves in the epidural space, you can change some of the electrical characteristics. Many companies have done some fairly sophisticated things with accelerometers that are used in sports cars to be able to quickly adjust the amount of energy being delivered to try to maintain a steady sensation even though the amount of power needed to do that is changing.

One of the big advances today is there are many more contacts on a lead. When we had four contacts on a single lead it was fairly easy. Today things are much more complex in terms of interplay between the two leads that you may be using and interplay between multiple contacts. Another advance is that leads have become longer so that you can cover more areas. However, the biggest advance is in rechargeable battery technology. Today, as opposed to the '90s, the systems have a battery that is similar to your cell phone instead of a car battery. Battery technology has changed some of the other possibilities for patients in a good way. If a patient has a high energy need to get pain relief that is not as problematic because you can just recharge the battery more frequently. While you can do trials with two leads — and sometimes we do — we will most frequently do a trial with a single lead, both for cost and because it is typically effective.

There are some variations among trials. Sometimes trials are done with surgical leads where you actually put the lead in, you have an extension, and then you can use that lead for a permanent system if needed. We tend not to do that. We typically will have a trial lead, take that completely out, and put in a new permanent implant system if the trial is successful. The controllers for the implant systems generally work like a remote control for a television. Patients can change the electrical parameters within programs. There are many programs that can be set up, however most patients use three or four. They might use one when they are walking and another one when they are at rest.

[*A video was shown to the audience.*]

NARRATOR: This is a video of a minimally invasive, percutaneous spinal cord stimulator. A spinal cord stimulator is a device to help manage chronic pain. The device will help turn a painful, abnormal sensation into a non-painful sensation. In the operating room, the patient is prepped and draped in a sterile fashion, and through a needle the electrode wires are placed with a standard loss-of-resistance technique. A glass syringe is attached to the needle and using the aid of fluoroscopy, which is an x-ray, the physician can feel and guide the needle to the appropriate epidural space. Now the electrode wire can be passed to the previous site of the successful trial using the aid of an x-ray. The x-ray screen shows the separate eight contact electrode wires being placed.

Companies make a variety of different electrode arrays that can be placed through a needle percutaneously, which is a less invasive style of surgery. Once the electrode wires are placed in an appropriate position, the device is connected to a cable, and in a sterile fashion with the patient awake and talking, the device is analyzed to make sure that the patient has a comfortable, appropriate sensation in the area of previous chronic pain. Once proper placement is ensured, sedation is deepened and a small skin incision is made between the needles and at the predetermined level in the buttock for placement of the computer battery. Then the needles are removed and the wires are pulled into the surgical site. Sutures are placed to hold the battery down and the wires are tunneled from the back to the buttock site and anchored to the muscle. In this surgery, we cut down to the muscle but we do not cut muscle, and there is nothing cut other than skin and fatty tissue. The battery is anchored two centimeters under the skin. Once it is confirmed that the device is in full working order, the incisions are closed in layers with suture material. Although it is a minimally invasive surgery, the patient will have two small incisions. Patients can go home the same day, and we will generally follow-up in one to two weeks.

[*Video playback ends.*]

DR. GRIFFITH: We have talked a great deal about the benefits of spinal cord stimulation but there are some complications or problems. The most common problem is lead migration. About 15-20% of patients have lead migrations depending on what study you read. To a certain extent, that is not the worst complication. Typically, lead migration happens when a patient is very active. It is not the most difficult thing to fix, but it is something we worry about since solving the problem requires another surgery and additional cost.

Infection is one of the more feared complications because you are implanting material over a period of years. Infection rates are comparable to other similar surgeries. Dr. James Rathmell in the Harvard System has published rates of approximately five percent. In our practice we see similar rates of infection. Infection is potentially a big problem but most infections are fairly superficial. Occasionally a patient may develop a significant deep epidural and intrathecal infection, but fortunately those kinds of complications are rare. Another complication we see with regularity is pain at the implant site. If a patient is predisposed enough to pain to be getting an implantable pain system, then pain from the system itself is something you really have to be concerned about. Our population tends to be thinner than the general population so we sometimes have a cosmetic concern. If a patient is very thin it can be disruptive for them to have a lump from the generator, and the lump may also be experienced as disfiguring.

The foot is a good example of an area where we can get good coverage with an implanted system. Patients do well over a period of time, but as all of you know the nervous system is very plastic. Over time, patients can come to a point where stimulation that was working well does not work well anymore. Fortunately, the increased number of leads, the increased number of contacts, and the ability to have more settings helps mitigate that somewhat. When the stimulation becomes less effective it is often possible to reprogram the system so that the patient can achieve benefit again.

When therapy does not meet patients' expectations that is the point at which behavioral health can be very helpful. If a patient says we have solved all of their problems 100% this is a red flag. If a patient says, "I am now able to do more and this therapy has helped about 60% of my pain," this is a more realistic story. We are encouraged by these stories since it typically means we will be able to help the patient in the long-term.

Intrathecal drug delivery systems and therapy is done primarily for cancer patients, but we have used it with a number of patients that have been very refractory to other treatments. We currently have a patient who is implanted with an intrathecal pump that pumps ziconotide, which is a neuropathic pain medicine derived from a snail poison. Ziconotide can be helpful but it has a narrow therapeutic index. We also have a patient with trigeminal neuralgia who has failed a variety of interventional medication treatments, including opioids, but has done very well with an intrathecal drug delivery system. He has been able to hold down a steady job. He has dealt with transitioning out of the military, the deployment of his spouse, and caring for their child. He has been able to deal with the stressors in his life in the context of having some relief from his pain.

Pumps generally have a life span of five to seven years. Most pumps are used for patients with extreme pain from cancer. The pumps can be powerful tools to help patients go home and spend what time they have left with their families. The main drugs that we infuse are ziconotide, opioids, local anesthetics, and baclofen. It takes about 300 times as much morphine orally to get the same effect you would have with a single unit delivered intrathecally.

There are some misconceptions about intrathecal drug delivery. One is that it works on opioid-insensitive pain. That is not the case. It is another way of delivering opioids and it does opioid things. It does not prevent tolerance. People become tolerant over time and may require increasing doses. There are dose-related complications that concern us. Itrathecal delivery and dosage does not eliminate the need for oral analgesics. We do have fancier pumps now where you can get some bolus dosing, but in general people may still require boluses, especially cancer patients, for episodes of severe, activity-related or disease-related pain. Opioid-induced hyperalgesia is a phenomenon associated with long-term use of opioids, which is a concern. We have known since the 1980s from a variety of studies that you do have induced hyperalgesia no matter how the medication is delivered.

Other concerns with an intrathecal system are an increased risk of spinal fluid leaks. You may also see dislodged catheters and/or blocked catheters. Acute withdrawal of medication can also cause many problems. It is important to address medication issues immediately. Drug side effects can often be mitigated by adjusting the pump or by applying other medications. For example, applying an antiemetic may help with the side effect of nausea. In the past there were many pump treatments for patients with post-surgical pain. That has changed over time since it is not a very good long-term treatment plan.

In summary, patients who have neuropathic pain and concordant anatomic distribution typically respond best to neurostimulation, whereas patients who have nociceptive pain and a concordant distribution may respond best to intrathecal drug delivery systems. Trials are helpful because they are reversible and the treatments in general are reversible as well. Some of our best outcomes are patients who improved and then eventually no longer needed their implantable pain system.

Transcranial Magnetic Stimulation (TMS) Use for Pain Disorders

Geoffrey G. Grammer, MD

Today we will discuss transcranial magnetic stimulation (TMS) and how it came to be a tool used in psychiatry. Like all the presentations today the content does not represent that of any organization or body. I have no financial disclosures that are relevant to this presentation.

Transcranial magnetic stimulation is a form of neuromodulation; the idea being that we can affect certain areas of the brain with specific tools or devices. TMS is different from medications with a systemic distribution that affect brain chemistry. With neuromodulation we can affect specific areas of the brain and change how that specific area functions. Many people think of neuromodulation as electroconvulsive therapy (ECT), and ECT is a form of neuromodulation. ECT sends electricity through a huge area of the cortex, and induces a generalized seizure that leads to systemic adrenergic receptor changes. The Jack Nicholson portrayal in the film *One Flew Over the Cuckoo's Nest* remains the bane of ETC providers everywhere when trying to consent patients for the procedure.

Vagal nerve stimulation is another form of neuromodulation in which the vagus nerve is directly stimulated, impacting the brain by increasing brain-derived neurotrophic factor (BDNF). Vagal nerve stimulation is approved for the treatment of epilepsy and refractory depression. Unfortunately the weight of evidence for depression has not been as robust as the manufacturer or most providers would like. Deep brain stimulation is used on a humanitarian basis. It is a fairly extreme procedure that involves inserting a wire into the brain and inducing a pulsating electrical current in order to change how that area of the brain works. Transcranial electrical stimulation has a broad definition. Many people in the field of psychiatry may think of this as alpha stimulation. I generally prefer transcranial electrical stimulation closer to the cranium, but, either way, the idea is you are causing subtle changes in brain function with electrical signals.

What is the rationale for TMS? It is not science fiction. When we pair psychiatrists and magnets it can seem strange, but it is not. TMS follows Faraday's Law which states that if you pulse a magnetic field over a conducting substance you will induce an electrical current within that substance. Nerves are essentially biologic wires. They conduct electricity, so when we pulse a magnetic field onto nerves we cause those nerves to activate or fire, regardless of what the resting state action potential is at that time. By doing this repeatedly at certain frequencies we can bring about long-term changes in the brain. TMS is FDA approved for the treatment of depression. After several medication failures we can begin to think about augmentation with TMS. TMS is a labor-intensive process for depression that involves treatment every day for approximately five weeks.

How did the idea of TMS begin? When TMS first came to the United States from Europe people used it as a brain-mapping tool. By placing a magnet over a patient's scalp and pulsing a magnetic field down, we could ask patients to tell us what they saw or to recite the alphabet. We could ask patients to stop talking and figure out which side of the brain was dominant for speech. During brain mapping some patients said, "This is helping my mood a little bit." We began to think perhaps we could use TMS not only as a diagnostic device but as a treatment device.

We know from advances in functional imaging that patients with certain psychiatric disorders have functional imaging patterns different from those who do not. Knowing this brings up a theoretical and neurologic basis of how these disorders manifest. By using TMS we can go into the brain and directly attend to the theoretical pathophysiologic mechanism of action.

It is important to address advances within the TMS technology. Old pictures of TMS show a large magnet held over the patient for about 30 minutes by an unfortunate graduate or medical student. There was a huge external cooler that made the entire room hot, but the magnet cool, and it was very labor intensive. Technology had to advance to make it portable for clinical practice.

By pulsing a magnetic field onto a neuron you cause the neuron to fire. There are second-order effects of neurotransmitter release. We know that when we stimulate areas of the dorsolateral prefrontal cortex we increase transmission of the monoamines dopamine, norepinephrine, and serotonin. It is important that we not think of the brain as a two-dimensional structure. When the cortex is stimulated, this has downstream effects on a variety of nuclei and other structures causing either up-regulation or down-regulation, somewhat unpredictably. When reading the TMS literature, it is important to think of the brain as a whole, and not as a flat map. As we studied this in more detail, we found that initial theories of TMS were overly simplistic. Brain research is like using a microscope to study how a microscope works, therefore it is somewhat of a paradox. The very tool that we are using to analyze the brain is the brain. It is humbling.

When we stimulate certain areas of the dorsolateral prefrontal cortex, we get activation in deeper structures like the cingulate, the orbitofrontal cortex, the insula, and the amygdala. Again, when we think about stimulating one area, remember the stimulation has a "branching-out" effect. When we stimulate repeatedly there are several things that occur. Like anything in the body, if you continue to use it over and over again, it is more readily activated when used in the future. I can run a mile one day but if I run every day I can run five miles. Running becomes easier and I can run faster. Something similar happens in the brain. If we make one area of the brain work, it starts working a bit more readily and a little more actively. In addition, when we stimulate nerves repeatedly we see an increase in BDNF, which essentially facilitates arborization of nerves and interconnectiveness. BDNF is like a fertilizer for nerves.

We can down-regulate nerves with certain pulse sequences. There are nerves that cause tonic inhibition called GABA interneurons. If we only stimulate those nerves with specific frequencies, we can shut down an area of the brain. For example, we can interrupt a patient's ability to produce speech by placing the coil over Broca's Area while they are reciting the alphabet. With a single pulse we can interrupt the person's production of speech.

[*Several TMS system devices were shown to the audience to demonstrate the variety of specific nuances and techniques that allow delivery of specific pulses.*]

TMS is a non-invasive procedure. Unlike ECT, patients are not asleep when they receive TMS treatment. Patients remain conscious the entire time and afterwards they can drive home. Unlike ECT, there are no cognitive deficits with TMS. Typically, TMS treatment is administered in an office-based practice setting. Because we do not necessarily need an MRI to identify landmarks, you can take a coil and put it over an area that approximates the motor cortex and begin sending down a pulse. You will find that you can make different areas of the body twitch. If we localize specifically to the thumb, there are many landmarks that come off of that area that correspond to different treatment sites. When treating patients, I will ask them to hold their hand in front of their face and every time the coil pulses at a specific spot their hand will twitch. This is a direct activation of the primary motor cortex. From there we can branch out with measurements to plot where we want to treat.

There are specific terms that are important to understand when discussing TMS. TMS typically refers to a single pulse of a magnetic field. When someone talks about rTMS, they are referring to repetitive pulses over time. Pulses are given in pulse trains per second. They are given in specific trains of a certain duration: one, two, three, four seconds. There is also an intertrain interval where brief pulses are typically administered for 2-4 seconds, and then there is a rest period anywhere from 18-30 seconds depending on the pulse sequence. Regardless of what condition you are attempting to treat, most treatment sessions last 20-60 minutes. Most people will receive treatment five days a week in order to effect the long-term changes that you want within the cortex. Stimulation with five hertz or more is fast stimulation that tends to be activating for at least the superficial neurons underneath. One hertz is slow stimulation that tends to be inhibitory. As I mentioned before, there are downstream effects that are somewhat unpredictable. For example, though you may inhibit the motor cortex, it may have an unintended upregulation further downstream.

Is TMS safe? There are no systemic side effects. The most common side effect is scalp pain. There are many nerves between the cortex and the scalp, therefore when we stimulate nerves on the brain we inadvertently stimulate the nerves in the scalp, so it can be uncomfortable for patients when they begin treatment. Repeated treatment leads to attenuation, making the treatment more comfortable over time. Causing nerves to be polarized underneath the coil involves the risk of secondary generalization causing a generalized tonic-clonic seizure. Those who have an underlying predilection for a seizure disorder are certainly at greater risk. Stimulating the dorsolateral prefrontal cortex can inadvertently cause discomfort around the eye if you hit different branches of the trigeminal nerve. There are certain methods you can use to mitigate that, such as rotating the coil to take it off a perpendicular axis.

There are some contraindications to TMS treatment, therefore it is important for patients to undergo a complete medical and neurological evaluation. TMS uses a powerful magnet, about a 1.5-3 textile magnet, depending on the energy delivery in a specific coil. Because of the strength of the magnet, you want to make sure that there is no metal anywhere near the magnet. The magnet will heat up a metal by producing eddy currents around the metal. In our patient population with war injuries this becomes important if they have retained shrapnel or if they have a titanium prosthesis on their scalp. You have to exercise caution in patients who have a history of seizure, a recent stroke, or a severe head injury. Patients with other neurologic diseases, with an altered seizure threshold, or who take medications that cause seizures may not be good candidates for TMS and should receive a thorough evaluation. Implanted devices also create concern, particularly pacemakers and spinal stimulators. You have to be careful not to get an electromagnetic interference because the electrosignal that goes through the coil is powerful. That being said, there is an increasing case series demonstrating safety in those patients, and if you can avoid getting within 30cm of the coil you can likely treat safely. If the distance is less than 30cm, you must weigh the risks and benefits. With distances less than 10cm you are running the risk of interfering with the underlying device.

What is pain, and what are the pathways of pain? It is important to understand this because when we use TMS, we are disrupting the neurologic transmission and processing of the pain signal. If a person has pain in their right arm, that signal will interface with the dorsal horn of the spinal column. At the dorsal horn there are some regulating mechanisms, one of which is descending fibers. This is believed to be part of the mechanism of action of tricyclics where there are noradrenergic fibers that will inhibit the pain signal at the dorsal horn. Serotonin also interfaces at the dorsal horn but it tends to be a yin and yang where it stimulates and inhibits at the same time. In addition, GABA interneurons in that area can lead to tonic inhibition of the pain signal. Medicines like gabapentin are believed to have their mechanism of action there. From there, pathways cross over and go up the spinothalamic tract through the midbrain, impacting the reticular activating system.

When someone is in pain, often their overall sense of well-being is changed. This is because of the interaction with the reticular activating system. These signals then impact the thalamus. The thalamus is the operator of the brain that connects different signals. From the thalamus, the signal goes to the primary sensory cortex in addition to other areas. Once the signal hits the primary sensory cortex, your body figures out what is happening and will interpret the signal as a pain signal and localize it. Then the signal typically goes to association areas where you begin to determine that this feels like a cut or this feels like a burn, and this feels exactly like when my child stomped on my foot yesterday and he must be stomping on my foot right now.

There are two types of homunculus: sensory and motor. This becomes important when we talk about localization for treatment of pain because we can identify and target a specific area that processes a pain signal that corresponds to the anatomy. How do we use TMS to disrupt a pain signal? We can impact the descending tracts through enhancing the endogenous opioid system. We can interfere with the transmission at the level of the thalamus and we can inhibit the processing of the signal at the sensory cortex. I want to delve into more detail for each of these. The descending tracts come down and cause inhibition that is enhanced by tricyclics, but part of the mechanism of action of opioids is also enhancing this tract. It is a convoluted, indirect mechanism, but it is believed to actually lead to gating at the level of the dorsal horn. The dorsolateral prefrontal cortex then becomes a site we can treat that interferes with the system.

How we measure the effectiveness of TMS is somewhat controversial. The good news is that the action of TMS is similar to the action of a grenade. It is one of the few things in medicine that if you get close, it is "good enough" because the area that is part of the magnetic signal allows for some margin of error. There is an interesting study that was conducted by Mark George's group at the University of South Carolina. Twenty-four volunteers were randomized to receive either active TMS or "sham" TMS. They were given either saline injection or naloxone. If they got saline one week they came back two weeks later and received the naloxone, or vice versa. Subsequently, participants' skin was treated with capsaicin to induce pain, whether it be a thermal or cold stimulus. The average visual analog scale rating was 8/10 in the patients who received "sham" treatment. What was phenomenal to me was that volunteers participated as study subjects with no disease knowing they would be given pain stimuli in the 8-10 range. When TMS treatment was administered to induce a pain signal, the average visual analog pain rating was four. Subjects reported approximately a 50% decrease in pain, which is fairly dramatic. Here is the interesting part. They took the same patients who had a decrease in their pain sensation and pretreated them with naloxone, and then administered TMS followed by the pain stimulus. Their pain rating went back up to 8/10 as if they had never received TMS. It was from this experiment that a theory was developed arguing that to induce the natural opioid process, the treatment location appears to be the left dorsolateral prefrontal cortex.

The dorsolateral prefrontal cortex is used for the treatment of disease processes that cause more system pain. Fibromyalgia probably has the greatest weight of evidence showing trends towards benefit with TMS. A study was done of patients with post-operative pain following gastric bypass surgery. Patients were randomized to receive either active or "sham" TMS. Patients who received active TMS while they were still recovering reported less pain and less opioid usage.

There has been some debate among the TMS community about where to treat for neuropathic pain. Alvaro Pascual-Leone, a leader in the field, argues that you should treat in the primary motor cortex. The primary motor cortex is one of the most epileptogenic areas of the brain so it is not without risk that you stimulate this area. When we stimulate the primary motor cortex two areas are activated in subcortical structures: the thalamus and the anterior cingulate. By activating the thalamus you are disrupting ascending spinalthalamic tracts from ever getting processed and sent to the sensory cortex. By disrupting the anterior cingulate, you may help some of the emotional valence that occurs when patients are in pain. There are a variety of studies that show a benefit in using the primary motor cortex for treatment of pain, especially for neuropathic pain. There is modest evidence showing benefit for deafferentation pain syndromes, particularly nerve root evulsion and brachial plexus injuries. Recently there was a study using primary motor cortex stimulation that showed a convincing benefit for migraine prophylaxis.

In my mind everything ends up in the sensory cortex where your body processes the signal and tells you what you are feeling. One of the "experiments" that we did early on used some normal controls — meaning my friend and some medical students who could complete a visual analog scale of 8/10 — and we administered TMS over the sensory cortex. We found that about 60% of participants had some anesthesia of their extremity or even some heavy neglect that lasted for several hours. This result gave us the idea to use TMS in other conditions, particularly phantom limb pain. What happens in phantom limb syndrome? When a limb is amputated a person loses the input to the sensory cortex that organizes that area. The most common theory says what happens is that the brain spills into surrounding areas of input, therefore your hand is no longer receiving input from the hand but is receiving input, say, from the tongue or the face. The problem is the hand is not the tongue or the face, and people are left with confusing, nonsensical signals. Patients with a phantom limb pain report that they are not experiencing pain per se, but uncomfortable sensations. They may feel that their limb is in the wrong position or an uncomfortable position, or that it itches or twitches. The theory is, why not go into the specific area that has been deafferented and inhibit it using the inhibitory pulse sequence? The interesting thing is we can map an approximation of where this would be by going to the non-amputated side and mapping down the homunculus to correspond to the same level as the phantom limb pain. In 2009, we did this on a 24-year-old male who sustained a severe blast injury and a right upper extremity amputation. This gentleman was on multiple medications, was sedated, had trouble staying awake, and was appropriately frustrated. As early as the first week of treatment the patient had a decrease in his phantom limb pain intensity from 5/10 down to 2/10 and by the end of treatment he was down to one.

We followed this up with a second case, a 22-year-old male who had sustained a severe left upper extremity injury from a blast. He had a graft down to his waist to try to preserve some of the tissue. When the graft was removed from his waist, he woke up in the PACU (post-anesthesia care unit) screaming in pain. He was taken to the ICU and placed into an induced coma because the severity of his pain could not be controlled with other measures. Each time his doctors tried to wake him up intense pain returned. When we saw the patient, he was grimacing and in agony. We put him in the treatment chair and administered inhibitory pulses over the area corresponding to his injured tissue. Within minutes, the patient visibly relaxed and fell asleep. His family was amazed that he had reached a level of comfort where he could relax again. By stimulating this area he had a sustained pain relief for about four weeks at which time he would return for a little tune-up.

In summary, we have three treatment sites with TMS and each site may treat a slightly different type of pain. When we want to induce the natural opioid process, the treatment location appears to be the left dorsolateral prefrontal cortex. When we are trying to disrupt the signal at the level of the thalamus, we are talking about stimulating the motor cortex using 10 hertz, but that carries with it an increased risk of seizures compared to other TMS protocols. Finally, we are looking at directly inhibiting areas of the primary sensory cortex for conditions associated with deafferenation and potentially things like regional pain syndrome where you might end up with cortical hypersensitivity to pain stimuli.

I have not presented studies involving hundreds of patients because they do not exist. TMS is a non-invasive method of treatment of pain for some patients that does not cause sedation, does not add to polypharmacy, and does not interact with other medications. Clearly more research is needed to learn how to use TMS most effectively and in whom to use it. We have identified three sites which seem to be the predominant treatment sites that people are targeting, and hopefully, over time, we will learn the optimal pulse sequences and the optimal locations for treatment.

Pain Treatments and Prescription Opioid Abuse: Challenges and Solutions

David L. Thomas, PhD

I am affiliated with the National Institute on Drug Abuse (NIDA), and I am part of the National Institutes of Health (NIH) Pain Consortium. There is no pain institute at the NIH, but the Pain Consortium consists of about 25 institutes with representatives that work across institutes on matters of pain. The Pain Consortium was created by an Act of Congress in either 2000 or 1999. My presentation is not about how to use opiates effectively. Instead I will outline the problems that exist with opiates, and how we, at the Pain Consortium, are trying to balance pain treatment with the fight against the prescription opiate abuse epidemic.

The bad news is that we have an opiate epidemic. This epidemic has occurred in the last 20 years in terms of opiate prescribing. Today opiates are prescribed much more often. Approximately 219 million prescriptions for opiates are written each year and 2.1 million Americans are addicted to opiate pain killers. Sales of opiates have risen dramatically, deaths are skyrocketing, and treatment admissions for overdoses are paralleling these increases. In high school students, marijuana and hashish are most often abused. Vicodin, Oxycodone, and many other prescription drugs are also abused, but overall opiates lead the way. There are more than 16,000 deaths from opiate overdose each year. That number is greater than the number of overdoses for heroin and cocaine combined. Four out of five new heroin users or addicts will have previously abused prescription opiates. In the reverse direction, only one out of one hundred prescription drug abusers began with heroin.

There has been a great deal of discussion over the years about gateway drugs like marijuana, but is marijuana a gateway drug? Defining a gateway drug is difficult. In the case of heroin, the abuse of prescription opiates does look like a gateway. It has all the features that you would expect. The biggest feature is that heroin is readily available and inexpensive. In contrast, prescription drug abusers pay a great deal more for each pill; up to $80 for one pill. Abusers quickly run out of pills, and an easy alternative is to buy a bag of heroin for $5 or $10. Prescription drug abuse is a gateway in that context.

The Institute of Medicine (IOM) reports that there are approximately 100 million people in chronic pain. When I mention that number, I often get the eye roll meaning, "Seriously? 100 million people in chronic pain?" Try to think of a disease without a pain component. Pain is everywhere. Part of the problem is that people do not believe the number. Pain is a silent epidemic. It is all around us, but the patients in pain are not visible, or they are not showing their pain, or perhaps they are suffering at home. Approximately 16,000 people die from prescription opiates each year and that number continues to grow. We have 100 million people in pain. These two problems are colliding and there is no consensus about what to do with opiates. That is why I cannot present and say, "Here's what we do, and it's easy to do, and if you follow these directions you won't have any problems." We are not at that point yet.

NIDA and the Food and Drug Administration (FDA) share a similar position in the debate over what to do about pain. We are asked, "Why aren't you doing more for people in pain?" We are trying. "Why aren't you doing more about prescription opiates?" We are trying, but we do not want to do one to the detriment of the other. We have four times as many prescriptions written today than 20 years ago, which is good if the drugs are working. It is not good if the drugs are not as effective as promoted. Currently, there is a push to reduce prescription opiates, but there is not enough consideration given to people in pain.

There are several initiatives that NIDA and the NIH Pain Consortium are developing. They are initiatives to stop prescription drug abuse and to identify and promote more effective pain treatments. The first iniative is the Health Electronic Registry Outcome (HERO) pain registry. The Pain Consortium is the lead on developing HERO. This pain registry operates in a clinical setting where many aspects of a patient's pain and history are taken in a unified way. Questions are standardized and the people that take the information are trained to take it in an identical manner so databases can be compared. This also allows for comparison of medical records between subjects and patients much more easily. The patients may participate by reporting their pain symptoms with an iPad or an iPhone. Patients can mark where their pain is and talk about the location of their pain.

Patients use the Pain Reported Outcomes Measurement Information System (PROMIS) pain measure which is used by the NIH that allows for an in depth pain assessment beyond the 0-10 reporting scale commonly used. PROMIS looks at how pain affects overall function, depression, anxiety, sleep disturbances, and many other areas associated with pain. The NIH obtains a great deal of data from each patient in a standardized way without spending too much time, which bolsters compliance. We are beginning to fund Stanford University to use PROMIS. Stanford will then take PROMIS and make it available freely across the United States to other healthcare organizations.

With the pain registry a clinician will have, in their office, access to the clinical experience with patients as though the patient were standing in front of them. They will be able to see the pain patterns in the clinical situation with data that can inform treatment on the spot.

In the future the pain registry will be used beyond the clinic. For example, instead of doing experiments on patients we might know from a patient's genetic makeup if they are likely to respond well to opiates. We will also incorporate things like cell phone daily sampling. We will have information from the clinic and how patients present, how patients self-report their pain symptoms, and information about daily life to learn what factors predict success. We think gathering many types of information will help assure that patients who need opiates will get them. Patients that are identified as potentially having a problem with opiates could be steered in another direction.

The second initiative is a conference called Pathways to Prevention that was held in September, 2014. This is not a typical conference on opiates. If you attend a conference on opiates people argue about opiates and say, "They're good. They're bad," and nobody agrees on anything. At this conference people do not have to agree. We have a jury. This conference took two years to plan with the NIH, the FDA, and outside stakeholders. Each group created a list of questions about opiates that we wanted to answer. What are critical things we need to know about opiates? Do they work? What are the side effects? What are the risks of addiction?

In parallel with Pathways to Prevention, we hired a Center of Excellence to review all the literature on the questions we posed. Finally, we came up with panelists and a jury for the conference. The jury members selected were smart and ethical, and they could not have any involvement in or with the opiate field. The jury looked at a yearlong report and heard experts sharing opinions about the report. Finally, the jury deliberated and presented their conclusions. No one person controlled the process. It was gratifying to know that the entire process, as elaborate as it was designed, was aimed at reaching some truth, and providing us with the best information about the literature. The literature is not perfect. Where it was not perfect the jury said, "We need more research," and they told us in what areas research was needed. The key questions were patient-centered. Are opiates effective? How do we minimize side effects? What are the short-term/long-term risks, including risk of addiction?

As of last year, the FDA has the authority to require post-market safety studies on products that the agency has approved. The FDA has now required the nine companies that make long-acting or extended release opiates to look at the safety of the drugs that they make. We all want studies on safety to be credible. At the end of the day, if the drug companies fail to follow procedures that NIDA and the Pain Consortium think are appropriate then we may say, “This isn’t up to our expectations.” We fully expect that the drug companies will do what we want, and that in the end, these valuable studies will be credible.

The first study is very exciting. It is the holy grail of studies that we have been looking for. If you take pain patients prospectively and give them opiates for pain, do they misuse it? Do they start abusing it? Do they become addicts? How many of them die? The estimate, based on retrospective data, is that somewhere between 0-40% become addicted to opiates. That range is not precise enough. We are trying to refine that number within two or three percentage points. What population will transition from use to abuse? If we can answer that question, then how do we stop use-to-abuse? What might be the genetic factors involved? Opiates are powerful medications and they do stop pain, but they may not be good for everyone. How do you separate groups of people in pain?

There are studies that tell us how to evaluate abuse and addiction using different measures. You can study terminologies used in medical coding to see how predictive that is of abuse, addiction, and overdose. Doctor shopping is an interesting phenomenon that can also be studied. Patients sometimes go to multiple doctors. Is that good or bad? Some people do it because they have different conditions and they are seeking treatment. Others doctor shop because they are trying to get pain medications. Still others doctor shop for diversion. One study is assessing how prevalent doctor shopping is and what impact it has on patients’ outcomes.

The last study is a prospective one that will address the question of opiate-induced hyperalgesia. If pain is originating from opiate-induced hyperalgesia, it is probably wise to terminate the opiates and try something else because patients do not need a pain medication that is actually producing pain. How common is hyperalgesia? How can you predict who has hyperalgesia? How do you help a patient once they are in that condition?

Studies like these are very expensive. Nine drug companies are pooling their resources and moving forward since the studies are scheduled to be completed by 2018. The consensus conference gave us a picture of right now, and these studies will fill in some of the research gaps that we know exist.

In 2011, the Institute of Medicine reported that we need more pain education incorporated into medical school education in the United States. Beth Murinson and collaborators looked at how much time was devoted to pain education in medical schools across the United States and Canada. She called every school and studied the curriculums. In this country the median number of hours devoted to pain education over four years of medical school is approximately eight hours. In Canada, the median number of hours is fourteen. We have 100 million people in pain seeking care from healthcare providers who receive, on average, one day of pain education. We are trying to change that. In veterinary schools in Canada students receive ten times more training on aspects of pain.

In 2012, we funded our Centers of Excellence. In the same year we had a kickoff meeting that brought everyone together with a common goal. Those involved wanted to be part of the movement to change pain education and produce a cultural shift in how we think about and deal with pain in the United States. Even though we began as an initiative focused on increasing pain education, we soon found ourselves in the midst of a broader goal to change how pain is dealt with in America.

The three main goals of the Centers of Excellence are to develop curriculum materials for medical schools, to create an online resource so that other schools can more easily adapt their materials, and to disseminate and evaluate what was created. At the core of this are case-based interactive learning modules that will be accessible online. We plan to make 50-100 of these types of teaching modules. Our first module is Edna, and she is online now. Edna is an older woman with hip pain. She has sclerosis and her back looks terrible, but the pain is actually in her hip. Each one of these online cases has some teaching moments in them where you say, "Wait, just because the back looks bad doesn't mean that's the cause of the pain. We have to do the right diagnostics with this."

A research study was done using the module Edna. Medical students studied Edna, and then were put in a different setting and asked to perform objective standardized clinical examinations. Students moved from station to station evaluating "patients" who were pretending to present with a medical problem. Students learned how skilled they were at evaluating these patients. Medical students that had studied Edna, which is a one-hour course, performed significantly better on the examinations with fake patients than the medical students that did not take the Edna course. A one hour course made a significant difference. These findings were published recently in a journal of geriatrics.

Another module in development is Mrs. Mondragon. She has leg pain caused by a fall. She does not speak English so her son translates for her. Her son is very emotional and reports that his mom says her pain is minor and is no big deal. But Mrs. Mondragon does not want to tell her emotional son the real extent of her pain. This is an interesting module due to language/translation difficulties and the communication style between the mother and the son.

Each module contains a mystery in a way with teaching moments scattered throughout. Collectively, we think that a great deal will be learned from each of them. Each module can also stand alone. For example, if I am teaching a course, I could use Tylee's module because I am interested in sickle cell pain. Tylee is an actual sickle cell patient who was followed for ten years. Videos from a ten year period were used to make Tylee's module. We have many other modules in development and we will introduce each of them when they are ready.

In 2011, the Department of Health and Human Services (HHS) tasked us to develop a comprehensive population health-level strategy for pain prevention, treatment, management, education, and reimbursement that includes specific goals, actions, time frames, and available resources. Working groups were formed to present recommendations to HHS that are implementable. The final recommendations were sent to HHS, and they will determine which of the recommendations will be implemented. No matter what they choose, there will a great deal of good done for people in pain.

Returning to the original paradigm presented earlier, often we say, "Let's worry about people in pain and forget about prescription drug use," or, "Let's fight prescription drug abuse and stop all these opiates from getting out there." What we really need is to do both. Too often the push is to just eliminate opiates. However, if you had a pill that would improve the lives of cancer patients or a pill that would cure cancer, you would not debate about whether cancer patients should get it because somebody else might abuse it. You would administer to those who would benefit and worry about the abuse separately. But with pain it is a different story. Patients in pain are feeling their access to treatment might be limited because they are not valued. They worry that the prescription drug abuse problem will take priority, and they will be denied treatment. Because we do not want that to happen we are trying to find out where opiates work, where they do not work, and how best to deliver treatment to patients in pain.

Phantom Limb Pain: Theories and Therapies

Jack W. Tsao, MD

Today I will talk about some of the research on phantom limb pain that we are conducting at Walter Reed along with other collaborators in the military health system. I will discuss my personal opinion and that of my collaborators, which does not constitute the official position of the U.S. government. In 2004, when I first arrived at Walter Reed, we had a litany of medical treatments for phantom limb syndrome, none of which seemed to work. Now, a decade later, 1,645 military amputees have come through either here, San Diego Naval Medical Center, or San Antonio Military Medical Center.

The definition of phantom limb pain is the sensation that an amputated limb is still present accompanied by uncomfortable feelings such as pain, itching, or electric shock-like sensations. Some people have described phantom limb pain as feeling like a spike going through the hand or the foot. Others experience a frozen limb sensation like the limb is still present, but they cannot move it. It feels like the limb is stuck in an uncomfortable position. About 90% of amputees at Walter Reed experience phantom pain. The typical time of onset is immediately after an amputation. Over the course of about three months the pain typically goes away on its own. Sometimes it is accompanied by the entire memory of the hand or the foot disappearing as well. Some people feel like they never had the amputated limb.

Phantom pain was described as early as 1510 by the French barber surgeon Ambroise Paré. Back then the barber was essentially the surgeon. When soldiers went to the battlefield, the person who cut your hair was also in charge of performing all of your operations. The best description of the phenomenon of phantom limb pain was given by a physician and Civil War surgeon named Silas Weir Mitchell. There were many amputations on the battlefield during the Civil War. After the war, Mitchell became a neurologist. He noted that phantom limb pain was typically seen after a traumatic loss of the limb. Since that time, we have learned that you can also have phantom limb pain with cancer, diabetes, and other causes of amputation. Similarly, people who have a hysterectomy or mastectomy may also report phantom sensations. However, the limbs are the body parts that are most noticeable and that have been traditionally described when people talk about phantom limb pain.

It is interesting to note that doctors originally thought this type of pain was purely psychiatric. The interventions were predominantly mental therapies. We now believe the cause is in the brain, and that there is a neurological basis for phantom limb pain. Similarly, during the Civil War period, people did not believe that this phenomenon was real. They thought, "Maybe it's due to neuromas that have formed at the end of the residual limb." The procedure performed at the time was to serially shorten the limb to remove neuromas to see if that would eliminate the pain. Because phantom limb pain is a cortical phenomenon, unfortunately that was not very effective.

Many people have written about phantom limb pain but the person I want to highlight is Weir Mitchell. Descartes, the French philosopher, first theorized in the 1600s that phantom limb pain was actually in the brain. Herman Melville wrote about it in the 1850s in his novel *Moby Dick*. In the late 1800s Weir Mitchell wrote, "Nearly every man who loses a limb carries about him a constant or inconstant phantom of the missing member, a sensory ghost of that much of himself, and sometimes a most inconvenient presence. Very many have a constant sense of the existence of the limb." I think that description depicts it best. When you ask patients with an amputation they will say, "My foot is still present," or, "My hand is still present."

I will describe two examples of patients with phantom limb pain. The first patient is a Marine with phantom limb pain who came in for a disability evaluation. He lost his right hand during a gun battle due to a rocket-propelled grenade. He described a clear sensation that his finger was stuck in the firing position on his rifle, which is what he was doing when he lost the limb. He went on to say, "It felt like I was firing the gun. I couldn't let go, and then I had cramping in the thumb." The patient was describing the area of the thenar muscles and his description was very complete. "It was painful," but he also had a sensation that his hand was still doing something physically. As I talked with more and more amputees, that was the consistent story. Patients could give you a complete phenomenological description of sensations that included more than just pain.

The second example is a 20-year-old soldier who lost his right foot. Again, a rocket-propelled grenade was the weapon of choice for the insurgency. He felt that his toes were curled into the bottom of his amputated foot. Interestingly, his foot had been stuck in this position pushing on a dirt retaining wall during the fire fight that took his limb.

Why does phantom pain occur? There are three primary theories, but the exact cause is unknown. The most prominent theories are: 1. phantom pain is due to new cortical neuronal connections, some type of neural plasticity, or neuronal reorganization in the brain that occurs after the amputation; 2. phantom pain is due to mismatched signaling in the neurons responsible for vision and those responsible for proprioception, i.e., a sense of your limb in space; 3. phantom pain is due to a phenomenon called proprioceptive memory. We will discuss parts of all three theories.

The cortical reorganization theory has been best researched over the years. The idea is that you have changes in functional properties because you are taking away, or modulating, the peripheral inputs. From the peripheral nervous system, you receive feedback to the brain. When you take away the hand or the foot, the arm or the leg, as in an amputation, neurons are making new connections with other neurons. Most of the work in this area has been done with non-human primates and other mammals following deafferentation of nerves. Research was done by Merzenich and Jenkins in the 1990s with monkeys. If a monkey had an amputation of digit three, when they did anatomical studies later, they found that the areas that previously controlled digit four and digit two had expanded to take over the area that used to be digit three. The question is, if you see this pattern in non-human primates, do you also see it in humans? The answer is that there is definitely evidence of reorganization both from behavior as well as functional imaging studies.

In terms of behavioral reorganization it helps to go back to a map of the brain. The Penfield Homunculus is a good example of how the brain is organized with specific regions of the brain mapped to specific motor and sensory functions. A large part of our primary motor cortex is devoted to the hand and to the face, which makes sense. We do things with our hands, and we use facial expressions to convey meaning, thoughts, and many other emotions. There is less motor cortex area involved in working the legs and the feet. On the homunculus for the somatosensory cortex there is a small area for the foot as well as the genitalia, a larger area for the hand, and much larger area for the face. If reorganization occurs, what do you think might happen? If you take away a hand, neurons might be expected to either link up with the face or with the abdomen/trunk area.

The neurologist, Vilayanur Ramachandran, at the University of California, San Diego conducted an experiment. He had several people who had lost an arm and asked himself, "If you have remapping, what might you expect to see? If you take away the hand, you might expect to see something on the face." He began sensory tests on subjects' faces to see if there was anything there. In some cases, when touching their face, they felt that they were also touching their phantom hand. That experiment was evidence that there is, in some cases, remapping. Ramachandran could actually map out where the thumb, the pinky, and the index finger all were on subjects' faces.

Ramachandran also described something called telescoping. After an amputation some people gradually feel that the hand or the foot is no longer the same length as it was before, and they end up with a hand representation dangling at the end of their residual limb. If you touch the end of the residual limb, subjects say, "You're touching my thumb," or, "You're touching my toes."

Ramachandran found, with remapping, that when subjects were complaining of itching or other sensations, they were able to scratch their face, thereby also scratching the itch on the hand. Clearly there are clinical implications. However, Ramachandran found that about only a third of the amputees had remapping. The question remained, how common is remapping, and how quickly does it occur? These are some of the research questions.

In terms of lower limb amputation and remapping, what might you expect to happen?

PARTICIPANT: Trunk.

DR. TSAO: Right, it might go to the trunk. Where else might it go?

PARTICIPANT: The genitals.

DR. TSAO: To the genitalia or the toes. We asked our amputees with lower extremity amputations what triggers their phantom pain. It turns out that urination, sexual intercourse, and defecation could trigger phantom pain in some people. One person said that when he had relations with his wife it was so painful he broke down crying. When we explained this phenomenon to the couple they felt much better about the whole episode. They were happy to know that there was a neurological reason for their dilemma.

The best imaging studies have been done by Dr. Herta Flor's group in Germany. They looked at upper extremity amputation and said, "If there's remapping to the face, if you move the lips maybe you can trigger a hand sensation." In healthy controls they reported activation on both sides of the brain when they moved their lips. Amputees without phantom pain look similar to the healthy controls. In amputees with phantom pain, they were able to see an extra area of activation. There is some suggestion that there are functional changes that can be detected with imaging that would indicate evidence of neuroplasticity. We see neuroplasticity both in humans and nonhuman primates, but does it have anything to do with the cause of phantom pain? That question is still not answered.

Now we turn to the second theory of why phantom pain arises: mismatched signaling. I am holding a clicker which doubles as my laser pointer. If I were to put it down and then decide I wanted to pick it up again, what is involved in the movements? Two things are involved. One is that I see where the target is located, and two, I am going to move my hand out to that target. There are two major components to movement — vision for your target, and then while my hand is moving through space to grab an object, I am receiving proprioceptive feedback as to where in space the object is. If I take away my sight by closing my eyes, then I am depending solely on proprioception.

Because I can see, vision overrides proprioception in terms of signals to the brain. Even if I had no proprioception but I had motor control of my hand, I could guide the pointer into the target. The theory states that when the limb is absent visually your brain says, "I don't see the hand or the foot there anymore." However, you are still getting peripheral feedback from the residual limb or the nerves saying, "Yes, there is still something going on down in the hand or the foot region." Now the brain is receiving conflicting signals. The brain interprets these mismatched signals as, "The hand must still be there because I'm getting some feedback from the arm, but my eye tells me it's not there." The phantom is created from the interpretation the brain receives from the signaling.

The final theory is proprioceptive memory, which goes back to the patient case exams that I presented. The phantom phenomenon is the feeling that the hand or foot has been resurrected. Patients also experience muscle cramping, a sense of position, and/or an inability to move the amputated limb. The brain is pulling in all memories of the whole experience of having a hand. Not only does the hand exist but there is a complete set of memories associated with the hand. There is memory of what position the hand or the foot was in before the loss. That is the idea of proprioceptive memory.

There is evidence to support all three of these theories, but there is no definitive answer yet as to why phantom limb pain occurs. We do not need to know what the theories are in order to create a treatment plan, though it does help. When the Iraq insurgency picked up, men and women came home with amputations. Some of them were on heavy doses of methadone. Many reported, "I'm on 60mg a day of methadone, and it's not touching the phantom pain." We tried Neurontin, Lyrica, and other medicines, but nothing worked consistently.

Ramachandran reported a case series where he used a mirror to resurrect the phantom limb to treat people with upper extremity amputations. He built a little mirror box and said, "If you put your hand in, the right hand looks like the left hand, and vice versa." If you are a right handed amputee and you put your left hand into the mirror box you have visually resurrected the right hand. I asked Ramachandran how he came up with the mirror idea, and he said he was trying to figure out how you actually moved a phantom that is not there. One day he was getting out of the shower and he stood in front of the mirror. He realized that his right hand looked like the left hand and vice versa, hence the idea of working with a mirror. He resurrected the mirror box and asked people to move their hands around, finding that some of the patients experienced a decrease in pain.

When we went back to the literature, it turns out that after his initial report in the mid-1990s, no one ever did a controlled clinical trial to prove whether or not this worked. Ramachandran abandoned this line of research because he could not explain why the mirror box worked and it was too expensive to do a large scale clinical trial, especially since there were not many subjects to study. We, unfortunately, had a skyrocketing number of war injured and decided that we could probably do this study to learn whether or not it works, and if it does work, why does it work?

If you think about the setting in Ramachandran's case, you had a person with an amputation and one intact hand, you had the phantom hand, and you had the mirror box. The participant is looking in the mirror, moving their intact hand, and trying to move the phantom hand. There are three components to this phenomenon. There is visual feedback from the mirror, movement of the intact hand, and movement of the phantom. We decided we could easily break down the components and figure out which, if any, seemed to be the most effective.. We designed a study with a three group trial focusing on the leg as the initial limb because we had a greater number of leg amputees. Group one used a mirror; group two did not use a mirror (it was covered), taking away the visual input or feedback; and group three was asked to close their eyes. All three groups were asked to move their phantom limb.

Because Ramachandran described his treatment as 15 minutes a day for three weeks we decided to do the same thing. We added an extra week to give ourselves the best chance of seeing some level of success. We measured pain on a visual analog scale, which is a basic ten centimeter line. Participants drew a line indicating roughly where they thought their pain was on a scale of zero pain to worst possible pain. We monitored what medicines subjects were taking. We also gave the covered mirror and the mental visualization groups the chance to swap over and use the mirror after four weeks. We were initially challenged thinking how to build a box that would accommodate a leg. Finally we asked, "What is the key thing with this therapy? It is not the box, it is the mirror."

[*A video was shown of a patient with a left leg amputation to demonstrate what happens during mirror therapy.*]

"He's moving the right leg, and then he's telling us that he feels that his left foot is moving." We could look at the residual limb muscles moving, and that was our indirect way of verifying a participant's subjective self-report of, "My phantom is moving."

A group in Canada has studied electromyography (EMG) signals to identify which muscles actually move in the residual limb. During mirror therapy the movements correlate with the exact muscle movements of the contralateral, or intact, limb. Participants are activating the same muscle patterns that would normally be activated to perform the movements if, anatomically, they had both limbs intact.

What did we find in our experiment? Twenty-two people signed up but four dropped out early, giving us six people in three groups. Luckily all the participants started out at essentially the same pain levels. With group one using the mirror, we found that within two weeks pain levels had dropped by 50%, then levels continued to drop up to four weeks, and then even up to eight weeks for the people who continued with therapy. With group two using the covered mirror, we found essentially no benefit, but when this group began using the mirror their pain levels were reduced. In the mental visualization group (group three), two of the patients experienced increased pain and had to stop and switch to the mirror therapy. Why did this happen? When there is a mismatch between proprioception and vision, mental visualization is actually making that mismatch worse because not only are you taking away vision, but you are forcing proprioceptive movements by asking participants to move their phantom limb.

The study showed that subjects were able to move their frozen limbs. After doing mirror therapy for a month subjects had good range of motion, and they were able to move the foot around freely. We also found that you could initiate movement by having vision drive the whole process. Lastly, we found that for the few subjects that experienced the telescoping phenomenon, we were able to rebuild limb lengths. By the end of their mirror therapy, the leg was full length again. Somehow vision is modulating this process. If you take away the visual feedback, you get the covered mirror situation (group two). Mental visualization also takes away vision (group three). We learned that vision is the key component of the entire process. We found that all six subjects in the mirror group improved to varying extents, and that eight of nine subjects who crossed over to mirror therapy improved. Granted, this is a small study, but we had a good response.

Most subjects did not change their medications during therapy. Two of the mirror subjects were able to stop their methadone, which was good news. One subject in the mental visualization group had to increase his pain medication but was able to stop the medications when he switched to mirror therapy.

The first change we found with mirror therapy was that the intensity of the pain decreased, followed by the number of daily episodes of pain, and then the length of each painful episode was reduced. The severity of the pain was what we were able to impact first. Two people who started in the mirror group experienced grief reactions, which is not surprising since suddenly we resurrected a leg that they had lost. We stopped the therapy immediately when this happened, but participants said, “Nope, I’ll come back tomorrow, and I’ll be fine.” Sure enough they were able to continue the mirror therapy.

Based on our results, we rolled this out as one of the therapies we offer to our wounded warriors at Walter Reed. What have we done subsequent to this? We have tried to duplicate Ramachandran’s study with upper extremities to see if the response is as robust. The mirror therapy is carried out in the same manner. So far results are similar to lower limb amputations. We are comfortable stating that mirror therapy is beneficial.

What is mirror therapy doing? We are in collaboration with the NIH to see what is happening in the brain before and after mirror therapy. If we return to the concept of cortical reorganization, which is the work that Herta Flor's group proposed with imaging studies, we can say that the cortical reorganization causes phantom pain. If so, we should be able to see other activation. Knowing the homunculus and how the leg is mapped, we could test this idea of reorganization. Basically when you take away the foot, you get new connections to either the leg, the hip, or the genitalia. Since the pain goes away, if it is due to plasticity, we should theoretically be able to rebuild the cortical map back to its original state.

How did we design our experiment? We scanned participants' brains before their mirror therapy, two weeks into their mirror therapy, and at the end of their mirror therapy, tracking their pain along the way. We did somatosensory mapping with a microfilament. We showed participants videos of feet moving and asked them to either move the intact or the phantom foot in conjunction with what movements they were seeing. We did a third control for anatomical localization, which means we showed them static images of hands and feet because certain regions of the brain are known to light up when you look at body parts, and those regions do not light up when you look at buildings or other objects. Part of the process of mapping is to figure out anatomically where we are. When we stimulate the leg are we stimulating somewhere else unexpectedly? Or is there extra activation being detected?

What do we see in the amputee? When an amputee moves their intact right foot, we see activation on the left side of the brain and some activation on the right side. Similarly, when the phantom left foot is moving we see right-sided activation, but we also see a great deal of left-sided activation. At the end of the participant's third scan, after four weeks of mirror therapy, activation is decreased back to its original state. In the control group, with visual presentation of limbs, we see activation of the body areas that are supposed to be activated. With the amputee, when we see the left foot we see activation on the left side of the brain. This disappears by the time the pain is reduced and the mirror therapy sessions have ended. We think that we now have a functional measure of responsiveness to mirror therapy, and we also know we are detecting excess activation occurring in the brain that goes away after mirror therapy is completed.

We know that phantom pain comes on quickly after amputation which brings up the idea of neural plasticity. However, I do not think that we can make new neuronal connections that quickly after an amputation. I think what we are seeing is unmasking of synapses. There used to be connections, or there are dormant connections, or there are connections that are inhibited between various regions of the brain. Somehow an amputation takes away the inhibitory input and very quickly we see extra activation. Mirror therapy somehow restores the original anatomic map. This is the basis for the latest hypothesis. The question is whether the excess activation is causing the phantom pain. Unfortunately, we are not able to answer that yet.

We are also conducting a genome association study because we know that some people never experience phantom limb pain. Other people have pain that persists past the typical three month time course, and that has also been reported in the civilian medical literature. We think that there may be a gene or genes we can identify that could allow more effective pharmacological intervention for pain.

In bilateral lower extremity amputees, the working hypothesis is that vision is driving the treatment. Since these amputees do not have an intact leg to use mirror therapy, what would happen if we gave them somebody else's feet to look at? We set up a study using mental visualization as the visual therapy. Participants looked at volunteers' limbs in motion. You do not have to match gender or even skin color. The important part is the visual of the moving target. The response for this group was not as robust as the group that was able to use mirrors but we feel comfortable saying that vision is still modulating the pain response in some manner.

Lastly, we believe the future of our upper extremity prostheses will come from work funded by the Defense Advanced Research Projects Agency (DARPA). For this type of advanced technology we provide a virtual training environment. Participants see an avatar moving on a screen. Our original premise was that if you have visual input with an avatar that combination can also potentially treat phantom pain. The bonus is that we can train people and teach their muscles to drive a next-generation prosthesis. The typical upper extremity prosthesis has three degrees of freedom for the bioelectric or the three-pronged hook. The new prosthesis has 17 degrees of freedom. The technology is so sophisticated that a subject can get feedback as to the hardness or softness of a ball based upon the sensors built into the prosthesis.

Finally, this work would not have been possible without an entire team of dedicated research assistants working with us over the last few years, as well as funding from the military, from the Dana Foundation, the Army, and the Navy.

Psychoemotional Issues and Treatment of Pain with Acupuncture

Robert L. Koffman, MD, MPH

Today we will discuss a different way of looking at pain — through the lens of integrative medicine. These are my views and do not reflect the views of the United States government or the Department of Defense. Today I will introduce you to battlefield acupuncture. There is currently a $5 million joint incentive fund to train virtually every one of you in the room to perform battlefield acupuncture. Later I will demonstrate battlefield acupuncture techniques on one of our corpsmen who has volunteered to participate for the treatment of his pain.

Complementary and alternative medicine is now referred to as integrative medicine. We use the word integrative because it uses every branch of medicine to approach patient care. As Dr. Wain mentioned this morning the relationship between the doctor and the patient is very important. Integrative medicine uses different techniques and different modalities to facilitate the relationship.

Acupuncture is part of a traditional Chinese medicine (TCM) system that is also considered an energy therapy. Seventy four percent of the American population desires a more natural approach to their healthcare. The problem is most people do not know what "natural" means. They know what they like and they want to have a natural approach, but the language is confusing in terms of what is natural and what is organic. Most Americans who have used alternative therapies say they would use it again. Because of the cost-benefit analysis the World Health Organization (WHO) has called for propagation of many of the Complementary Alternative Medicine (CAM) techniques.

Since 2002, acupuncture has become more popular largely because the media is pursuing integrative modalities. Why is this? The bottom line is we are 37th in the world in health outcomes. That is a deplorable statistic when you think that we spend twice as much on healthcare as other western nations. Part of a new approach may use complementary alternative methods. In fact, one of the alternative methods is the initiative from the Defense &

Veterans Center for Integrative Pain Management (DVCIPM) to demonstrate battlefield acupuncture.

Most of you in this room understand the difference between allopathic and holistic medicine. I believe that a Relative Value Units (RVU) system makes it difficult to be allopathic and proactive and preventive when you only have 20 minutes with a patient. The therapeutic relationship, whether you are a psychiatrist or an orthopedist, is the most important relationship that you can have with a patient. The relationship takes time to develop. At NICoE we have the time and this is one of the reasons that, irrespective of presentation and pain, our patients report significant improvements in pain with significantly reduced opioid use. I would rather know the person who has the disease than the disease the person has. Again, it is difficult to get to know a patient in 15 or 20 minutes.

I am going to talk specifically about TCM and medical acupuncture. The science of traditional Chinese medicine has been practiced for more than 3,000 years. It takes its charge from the idea that there is a life force or energy. Every culture considers that the life force or energy flows through channels, and when there is an obstruction or blockage of that flow disease results. As long as Qi, or one's natural energy, and blood enjoy harmonious flow, none of the hundreds of possible diseases will arise. Qi is the driving force. In the TCM world Qi stagnation is the cause of the psychiatric disorders that we see. Qi stagnation can be unblocked by a technique called cupping or by using a more traditional approach that uses needles. Medical acupuncture, which is what I have completed, is a 300-hour course from a licensed acupuncturist who has earned either a Masters or a Doctorate level of preparation in traditional Chinese medicine. People ask me why I embraced acupuncture as a psychiatrist. I learned acupuncture because of my interest in learning more about TCM. At its core, TCM resembles something much more like psychotherapy than it does a pursuit of a religion or a culture. Virtually everything can be treated with acupuncture. For example, Colonel Richard Niemtzow laid the groundwork for treatment of xerostomia, which is a condition of chronic dry mouth.

We are all familiar with the terms yin and yang. Within the tradition of Chinese medicine yin and yang are inseparable; they flow together and you cannot have yin without yang. There are various genders, anatomic surfaces, and seasons associated with it. In the traditional Chinese world the internal causes of diseases are due to obstruction or to problems with one of the seven affects: joy, anger, anxiety, thoughts, sorrow, fear, and fright. I will talk about fear and fright with regard to PTSD. The kidney is the organ in the traditional Chinese world that is associated with fear. Fear then spreads to all of the other organs. This belief is what guides us in an acupuncture approach to PTSD. The concept for acupuncture treatment of PTSD is treating the liver fire which probably makes no sense to anyone who has not studied TCM and acupuncture. It is interesting how poetic the description is. With liver fire rising you can understand that as a metaphor for someone's blood boiling mad.

When a patient has a TCM evaluation it is not approached from a Western perspective. The patient is asked how things smell, what they like to taste, or what seasons they are intolerant or tolerant of. The mind and body are inseparable. When patients ask me if acupuncture works and how it works, there are two ways to respond. One response is from the Western perspective and says, of your 365 acupoints or acupressure or acupuncture points in the body, 75% of them are co-located with neurovascular bundles. You can convince patients that there are anatomic reasons why acupuncture works, but the fact is that these acupoints were developed over 3,000 years ago before we even knew that neurovascular bundles existed. The other response involves the pain gate theory. The pain gate theory is probably the most accurate or most descriptive in terms of how acupuncture works. We know this because the analgesia resulting from acupuncture is reversible and we know that endorphins and endogenous opioids are involved.

Back pain is the single most common cause for use of analgesics in this country. If you can offer some different approaches for managing lower back pain, then you can potentially help stave the tide of some of the opioid abuse. Lower back pain has been studied in acupuncture perhaps more than any other condition. A study by Roland Staud shows less medication use, significantly less disability, and earlier return to work when patients with lower back pain are treated with acupuncture.

Pain and the brain is interesting. Age-related losses in gray matter are 0.5% per year for people suffering from chronic pain. Brain atrophy is 5-11% compared to healthy controls. Chronic pain is not just disabling and debilitating; it ages individuals and ages their brains, and it makes them more likely to develop anxiety and depressive disorders. One thing I have not heard presented today is the relationship of sleep to chronic pain. Integrative medicine may be one of the best ways to facilitate sleep. Individuals who have chronic insomnia, lasting longer than three months, have a three times greater likelihood of developing a DSM Axis 1 disorder whether it be major depression, anxiety, or substance abuse. What do you think the relationship between sleep and pain is? They are more than strange bedfellows.

I will talk a little bit about Colonel Charles Engel's study that is published through the Deployment Health Clinical Center (DHCC). Also, the Hollifield study in 2007 was probably the seminal article. In fact, that was the reason we were able to include acupuncture as a recommended modality in the CPG for the DOD/VA and for PTSD. Acupuncture did not provide an absolute reduction in PTSD CheckList (PCL) scores, but it was effective for improving sleep, anxiety, and pain. When compared with waitlist and CBT, participants in the acupuncture group had a comparable effect size both immediately and three months later. Colonel Engel's study had a similar beneficial effect looking at two groups. Participants were randomized to acupuncture and usual care. Four and eight weeks later the effect size was as demonstrated, 1.4 versus 1.6. It is remarkable to think that a five-element acupuncture treatment will produce the same effect size as CBT and the effect will be continuous for three months.

The VA recommendations state that there is insufficient evidence to recommend acupuncture as a first-line treatment. However, CAM approaches have facilitated the relaxation response. This is very important. There is probably no better way to develop a therapeutic relationship with your patient than to help them sleep; to make them feel better in order to give them a sense of decreased anxiety. Many individuals, as you know, are initially too anxious to be able to attend any evidence-based treatment.

Dragons. This is the treatment in the Chinese world for being possessed. Possession is usually the terror associated with trauma and is considered to be related to one of the seven emotions that becomes blocked. You diagnose it by lack of Shen. What is Shen? Shen is your spirit, or awareness or consciousness. You know the sparkle that babies have in their eyes? That is Shen. That is one of the things that a practitioner looks for. How much sparkle does somebody have in their eyes? I am sure that was not part of your medical training, but it is just as important as diagnostics that we use in Western medicine.

I am going to read an experience by one of my patients, a Special Forces warrior who basically had not stopped deploying since 9/11. He was self-medicating with alcohol, as we frequently see. He was depressed and his marriage was shaky. He also had considerable guilt, had experienced cumulative loss, and had feelings of detachment. I did internal and external dragons on this patient. Here is his experience with acupuncture:

> "The grief hit me before he left the room. On my way back the curtain is drawn, the room darkened and a wave of unfounded sadness and grief, it overtook me. I let it come. I didn't want to push it down. Tears fell. I felt my chin quiver as I gave into the grief and sadness. I still don't know or understand from where it came, only that it was there under the surface all along, myself too afraid to let it go. I have known it was there. I have never understood why. It still escapes me for some reason, but I slowly felt a calm settle as the tears stopped falling. A second-wave crashed the moment I thought of my daughter. Again, I do not understand the sadness, but I again found myself unable to stop crying. Is it sadness that I know? Is it that I must hurt her to heal myself? Is it grief for the hurt I have already inflicted? Is it grief in not believing I have shown my daughter how much I truly love her? I do not know. The meaning of the

> emotion and the reason for the tears escape me. Once the grief and sadness subsided, I noticed how I no longer needed to breathe. Quantity of time escaped me, but I counted one cycle and realized I was breathing maybe two or three breaths per minute. I did not feel hunger for air. Rather, I had to remind myself to breathe. It was then that I felt a lifting sensation like a string tied to my chest. I felt as though I was being pulled forward, my weight only slight. I sensed my consciousness several inches above my body. I would not describe it as an out of body experience, more of an awareness the two were connected. As the sensation reversed, still barely breathing, I became aware of how heavy my body was. I could not feel the length of my body pressing against the table. I noticed the heavy, but strong, slow beat of my heart too heavy to feel the weight centered over my chest. Captain Koffman entered the room to remove the needles. As each point was removed I could feel a tingling sensation in each of my extremities. The intensity of the experience did not escape me. Although I felt calm, heavy and relaxed, I tried to capture in my mind what had happened, but did not feel panicked to do so. I let go and trusted in the fact that the experience was real. I re-dressed and felt one more rush of grief as I washed my face in the nearby bathroom. Still, I don't understand the grief. Some of it is surrounded by my daughter, but I had the control to calm myself and head back outside. Several hours later, after dragons, I write this down. I still feel a weight over my heart, a knowledge it is there. It is not uncomfortable. It is like the sadness is balled around my heart; a lump to remind me it is there. The pinpoint source of grief, if there is one, still escapes me. I will continue to think."

This account was the genesis for an article that Dr. Joseph Helms and I wrote entitled, *Come For the Needles, Stay For The Therapy*. This was an individual with whom I had several productive sessions following dragons, talking about his grief and loss. This was not an individual who would, as you might imagine, be prone to hysteria.

The ear is a complete microsystem in and of itself. There is scalp acupuncture which is a microsystem, and the auricular system is actually a small homunculus. Somatotopically, every part of the body is represented in the ear.

Returning to the $5.4 million grant awarded through DVCIPM, with approval by the Health Executive Committee, acupuncture training across clinical settings creates a three-tiered approach. The first tier involves training almost everyone in battlefield acupuncture, which I will demonstrate. Battlefield acupuncture is a five-point technique and it is easily administered with very tiny needles. The technique takes two hours. Normally, one has to be a licensed, independent practitioner to learn battlefield acupuncture. Now, with DVCIPM's approach, the idea is to train everybody to first level Tier 1 so that anyone who encounters a patient in pain can immediately reduce their pain with the use of battlefield acupuncture. It is safe, easy, and effective, but it is not without some contraindications. About 80% of patients will respond. My experience is actually higher. What I cannot tell patients is how long their analgesia will last. There is some discomfort. Sometimes there is euphoria and lightheadedness.

In 2006, *Military Medicine* published a randomized trial of 87 active duty military personnel with the control group receiving only little band-aids over their ears. The experimental group received two of the five acupuncture needles and the little band-aid. Twenty five percent of the acupuncture group had about 23% reduction in pain before leaving the emergency department. Twenty four hours later with standard treatment, both groups were pretty much unchanged.

I will conclude with a demonstration of battlefield acupuncture on a staff member who was kind enough to volunteer. The dictum is clean hands, clean ears, and sterile needles. How many of you have been trained for battlefield acupuncture in here? Three? That is a good start. Our volunteer had surgery last March for a fractured fourth metacarpal. His hand was caught in a car door, and he also injured his fifth metacarpal. Since his open reduction he has had chronic pain in his right wrist.

[*Demonstration*]

DR. KOFFMAN: What level of pain are you having today?

VOLUNTEER: About a five.

DR. KOFFMAN: About a five. We use the scale (0–10) to begin the assessment.

VOLUNTEER: Dr. Koffman and I have already sat down and gone over risks, benefits, and consent.

DR. KOFFMAN: He has never had battlefield acupuncture before, therefore he does not know what to expect. The use of five points is in each ear. Each ear is not always required. Sometimes you have to use all of the needles, five in each ear, but sometimes you can get a response with just a few needles. The needles are inexpensive and the application is as simple as grabbing the ear and putting in the little needle. I am going to put in two needles at a time for the sake of brevity. Ordinarily the procedure, the protocol you will learn if you take the two-hour class, is to put in one needle at a time and walk the patient and see what his or her response is. The end point is either termination of pain, zero, or no more than a one, or the patient asking you to stop.

[*Inserts the first needle.*]

Please stand up and take several steps. I am following Colonel Niemtzow's protocol, and he feels that walking the patient helps circulate whatever is circulating whether it is good humors, endorphins, or endogenous opioids. How is the pain?

VOLUNTEER: Three, sir.

DR. KOFFMAN: It is down to a three?

VOLUNTEER: Yes, sir.

DR. KOFFMAN: Wow. Okay. For the sake of our demonstration, we will not stop until he either asks us to stop or he is down to a zero or a one. Ready for another needle?

VOLUNTEER: Yes, sir.

DR. KOFFMAN: I will put in two more. The first needle corresponded to the cingulate gyrus. The second needle is the point corresponding to the thalamus. Let me have you take a couple steps. We always walk with the patient because they invariably have vasovagal symptoms. Please flex your hand and see how it feels. Give me a number.

VOLUNTEER: It is about a one in my hand, sir. A two or a one. Whenever I close my hand, it is painful.

DR. KOFFMAN: I am going to break from the protocol just because this is a real instruction. I will end with Shen Men. Ordinarily this would be a stopping point with just the four needles. In fact, these are the four needles that Colonel Niemtzow did the Malcolm Grow study with. But I am going to continue because I always want to put a needle into Shen Men. Remember we talked about Swhen - Shen is your spirit. Shen Men, which is in the top of the ear here in the triangular fossa, is actually what Chinese medicine calls the Spirit Gate. It is probably the most common point in the entire body. I always put in Shen Men because I know that it will help us with anxiety for whatever reason. In fact, Shen Men is one of the points on the National Acupuncture Detoxification Association (NADA) protocol.

We are almost done, but I want to end with the two points that I know are going to help our volunteer sleep and help reduce any anxiety and liven his spirit. Interestingly enough when we were talking earlier, you told me that you are also having back pain. Please stand up and see how your back feels as well. The analgesia is not specific. It is just like it is for any pain.

VOLUNTEER: It is down to about a one right now.

DR. KOFFMAN: Thank you for volunteering. That is why there is currently a $5 million joint incentive fund to evaluate the utility of this particular technique for pain.

[*At this time a video,* Unimagined Bridges, *sponsored by the NADA, was shown.*] The purpose of the video was to show how acupuncture may help with detoxification. Most substance abuse programs are currently using the video. In fact, Yale University trains their psychiatric residents in the NADA protocol.

Speakers

Commander Russell B. Carr, MD

Dr. Russell Carr is Chief of the Psychiatry Department at Walter Reed National Military Medical Center. He is a board-certified psychiatrist and the only fully-trained psychoanalyst on active duty in DOD. He graduated from the University of North Carolina at Chapel Hill with a B.A. in Russian Language and Literature with Highest Honors, and then completed medical school at the University of Tennessee at Memphis. Dr. Carr completed his internship in Psychiatry at the Naval Medical Center Portsmouth. After five years as a General Medical Officer, Dr. Carr completed a psychiatry residency at the National Capital Consortium. He has served fifteen years of active duty in the Navy, including a deployment as a General Medical Officer in 2002 with the JFK Battle Group to the Persian Gulf in support of Operation Enduring Freedom and another deployment in 2008 to 2009 with an Army Combat Stress Control Unit to Mosul, Iraq. Leadership roles in the Navy have included: Medical Department Head aboard the USS SEATTLE as a GMO, Chief of Inpatient Psychiatry and Department Head of the Psychological Health-Traumatic Brain Injury Department at the National Naval Medical Center in Bethesda, and Service Chief for the integrated Adult Behavioral Health Clinic at Walter Reed.

In 2013, CDR Carr completed six years of training in adult psychoanalysis at the Institute of Contemporary Psychotherapy and Psychoanalysis (ICP&P) in Washington, DC. Dr. Carr was named a Laughlin Fellow of the American College of Psychiatrists in 2008 (which recognizes the top ten psychiatry residents in the country). He was selected in 2013 to testify before the Military Personnel Subcommittee of the House Armed Services Committee along with the three Surgeons General and Dr. Woodson on PTSD treatment in the military. Dr. Carr was requested by name by the Ugandan military to train their mental health providers on his published approaches to difficult-to-treat combat trauma.

Colonel Geoffrey G. Grammer, MD

Dr. Geoffrey Grammer is Chief, Department of Research at the National

Intrepid Center of Excellence (NICoE). He completed his Bachelor of Science in Biology at the Virginia Polytechnic Institute before beginning his training in medicine at the Uniformed Services University (USU) in Bethesda, Maryland, graduating in 1996. Subsequently, he completed residency in Internal Medicine and General Psychiatry at Walter Reed Army Medical Center, followed by a fellowship in Geriatric Psychiatry.

Dr. Grammer currently holds board certification in Psychiatry, Geriatric Psychiatry, and Behavioral Neurology and Neuropsychiatry. He is also currently an Assistant Professor of Psychiatry at his alma mater, USU.

Dr. Grammer has completed two deployments to Iraq, serving as the Medical Director for the 785th Combat Stress Control Company on his first deployment and as a psychiatrist at the Combat Support Hospital at COB Speicher on his second. He has also deployed to Afghanistan as a psychiatrist at the Combat Support Hospital in Bagram.

Dr. Grammer served as the Chief of Inpatient Psychiatric Services at Walter Reed National Military Medical Center, which covers the 28 bed General Psychiatry and 6 bed Neuropsychiatry wards for eight years.

Dr. Grammer's military awards include the Bronze Star Medal, Meritorious Service Medal, Army Commendation Medal (3rd Award), Army Achievement Medal (3rd Award), Iraq Campaign Medal (3 Stars), Afghanistan Campaign Medal, Global War on Terrorism Service Medal, NATO ISAF Medal, National Defense Service Medal (2nd Award), Army Service Ribbon, Army Superior Unit Award and Overseas Service Ribbon (3rd Award).

Lieutenant Colonel Scott R. Griffith, MD

Dr. Scott Griffith is Program Director, NCC Pain Management Fellowship, Pain Consultant to the Army Surgeon General, and Director, National Capital Region Pain Initiative, Walter Reed National Military Medical Center. As an Army physician, Dr. Griffith has been active in leadership, clinical and academic medicine, and pain research during the past decade. His contributions include leadership activities as the inaugural Pain Management Consultant to the Army Surgeon General and as the National Capital Consortium Pain Management Fellowship Director. Dr. Griffith was a member of the 2009 Army Pain Management Task Force and subsequent Pain Campaign Plan aimed at improving pain care for Army healthcare beneficiaries. He has twice deployed to Iraq in support of Operations Iraqi Freedom and New Dawn, providing anesthesia and interventional pain management care at Combat Support Hospitals. Dr. Griffith has supported and coauthored numerous research papers with a concentration on treatment of spinal pain and treatment of warriors. He remains active in clinical and academic medicine at his current assignment, Walter Reed National Military Medical Center.

Captain Robert L. Koffman, MD, MPH

Dr. Robert Koffman is the Senior Consultant for Integrative Medicine & Behavioral Health at the National Intrepid Center of Excellence in Bethesda, MD. With over 17 years of operational experience as a naval medical officer, Dr. Koffman's operational mental health expertise is unparalleled in Navy medicine.

Dr. Koffman holds a Doctor of Medicine degree from the University of Santo Tomas and a Masters in Public Health degree from the Harvard School of Public Health. He also has collaborated on numerous studies and projects, including the work of the Mental Health Assessment Teams (MHAT) and a landmark study on the psychiatric sequelae of combat duty in Iraq, and was the 2008 recipient of the Sears Award, presented to the leading Navy psychiatrist.

Prior to coming to the NICoE in 2010, Dr. Koffman served as a Navy collaborator and investigator to the Walter Reed Army Institute of Research, where he continues to provide input as the Navy's expert in operational psychiatry. Among his other previous positions, he was the Navy's Director for Psychological Health to the Navy Surgeon General where he directed the management of over $100 million in programs for psychological health and traumatic brain injury.

A subject matter expert in deployment health, Dr. Koffman has dedicated himself to improving the delivery of mental health care in operational settings. For more than two decades, he has provided behavioral health care services for service members in a multitude of operational settings, including standing-up Navy Medicine's first Combat and Operational Stress Control Consult position at the Navy's Bureau of Medicine and Surgery (BUMED), staffing one of the first Naval Combat Stress Centers in Operation Desert Storm, serving at Antarctica's McMurdo Station (Operation Deep Freeze), embarking aboard aircraft carriers and amphibious vessels, and most recently, several deployments to Iraq and Afghanistan.

Dr. Koffman is a passionate advocate for increasing access of non-stigmatizing psychological services. Following a 2010 deployment to Afghanistan where he headed up the first naval medical Behavioral Needs Health Assessment Team (BNHAS), Dr. Koffman and his Mobile Care Team conducted the first battlefield mental health assessment of more than one thousand combat deployed Sailors. Dr. Koffman returned to Bethesda in 2010 to serve as the inaugural Department Chief for Clinical Operations at the new National Intrepid Center of Excellence and was also a member of the blue ribbon panel that crafted the current Acute Stress Disorder (ASD) and Post Traumatic Stress Disorder (PTSD) Clinical Practice Guidelines. Among his treasured awards, Dr. Koffman was the 2013 recipient of the USSOCOM Patriot Award, presented to an individual or organization for significant and enduring support to USSOCOM'S wounded warriors.

Paul F. Pasquina, MD

Dr. Paul Pasquina, COL (R), USA is the inaugural Chair of the Department of Physical Medicine & Rehabilitation (PM&R) at the Uniformed Services University (USU) and the Director of the PM&R Residency Training Program at Walter Reed National Military Medical Center (WRNMMC). He is board certified in PM&R, Electrodiagnostic Medicine, and Pain Medicine. Dr. Pasquina is a graduate of the United States Military Academy at West Point and USU. He completed a fellowship in primary care sports medicine from USU and Georgetown University. Dr. Pasquina's current research efforts are focused on exploring new technologies to enhance the recovery, rehabilitation, and reintegration of combat casualties, particularly those with traumatic brain injury and extremity trauma. This work is primarily focused through his work as the Director of the Center for Rehabilitation Sciences Research (www.CRSR.org) and Co-Principle Investigator for Rehabilitation within the Center for Neuroscience and Regenerative Medicine (www.usuhs.mil/cnrm/).

Prior to his retirement from active military service, Dr. Pasquina served as the Chief of the Department of Orthopedics and Rehabilitation at Walter Reed Army Medical Center, the National Naval Medical Center and the Walter Reed National Military Medical Center, which also included the Amputee and Traumatic Brain Injury Services. He has served as the PM&R specialty consultant to the Army Surgeon General; Senior Officer in Charge of the Ortiz Level II Military Treatment Facility, International Zone, Baghdad, Iraq; and a Secretarial appointee for the U.S. Department of Veterans Affairs' Advisory Committee on Prosthetics and Special Disabilities Programs. He continues to serve as a consultant to the Defense Advanced Research Projects Agency (DARPA), U.S. Army's Medical Research and Material Command (MRMC), Food & Drug Administration (FDA), and University of Pittsburgh School of Health and Rehabilitation Sciences as a member of their Board of Visitors.

Dr. Pasquina has received multiple military awards, as well as awards for teaching and mentorship, including the U.S. Army's "A" Proficiency Designation for academic excellence, the Order of Military Medical Merit, the Legion of Merit with two oak leaf clusters, da Vinci Lifetime Achievement Award, Partners in Progress Heroes of Military Medicine Award, Lewis Aspey Mologne Award, Alfred Mann Foundation Scientist of Year Award, Distinguished Clinician Award from the American Academy of Physical Medicine & Rehabilitation, and Honorary Fellow of the Rehabilitation Engineering and Assistive Technology Society of North America (RESNA).

Dr. Pasquina has authored multiple book chapters, journal articles, and policy papers. His work as the co-editor of the *Textbook of Military Medicine: Care of the Combat Amputee* was recognized with the First Place award for Technical Text from the Washington Book Publishers Association in

2010. Dr. Pasquina continues to serve on the Editorial Board of the *Journal of Rehabilitation Research & Development*.

Christopher Spevak, MD, MPH, JD

Dr. Christopher Spevak is Professor of Anesthesiology at Georgetown University Medical Center in Washington, DC. He received his MD degree from Northeastern Ohio University College of Medicine in Rootstown, OH. He attended the University of Michigan School of Public Health in Ann Arbor, MI, where he completed a Master of Public Health (MPH) degree in Health Management and Policy. He was a resident in the Department of Anesthesiology at the Cleveland Clinic Foundation in Cleveland, OH, and the Children's Hospital of Pittsburgh in Pittsburgh, PA. He serves as a Physician/Clinical Investigator at the Walter Reed National Military Medical Center Defense and Veterans Pain Management Initiative in Washington, DC. In addition, he is a member of several professional societies including the American Society of Anesthesiologists, Supreme Court of the United States Bar, District of Columbia and Florida Bar, American Health Lawyers Association and American Bar Association. He was also Past-President of the Medical Society of the District of Columbia.

David L. Thomas, PhD

Dr. David Thomas is Deputy Director, Division of Clinical and Behavioral Research, National Institute of Drug Abuse (NIDA) and a founding member of the National Institutes of Health (NIH) Pain Consortium. After 12 years as a pain and opioid researcher, in 1995 Dr. Thomas joined the National Institute on Drug Abuse (NIDA) where he has managed much of NIDA's pain and opioid research efforts. He currently is chair of the NIDA Prescription Opioids and Pain workgroup, which fosters pain and opioid research and education. He is also a member of the Department of Health and Human Services Behavioral Health Coordination Committee Prescription Opioids Subcommittee, Emerging Opioid Overdose Strategic Group, National Pain Strategy working group on Provider Education, and the Interagency Pain Research Coordination Committee. Dr. Thomas is the lead on the NIH Pain Consortium Centers of Excellence in Pain Education which promotes pain education in medical, dental, nursing, pharmacy, and other professional schools. Dr. Thomas attended Stockton State College in Pomona, NJ and graduated with a degree in Psychology in 1981. He received his MA in Experimental Psychology from the University of Hartford in 1986 and his PhD from the American University in Washington, DC.

Colonel Jack W. Tsao, MD

Dr. Jack Tsao is the Director of Traumatic Brain Injury (TBI) Programs for the US Navy Bureau of Medicine and Surgery, Professor of Neurology at the Uniformed Services University, and Fellow of the American Academy of Neurology. Dr. Tsao received his undergraduate and medical degrees from Harvard University, a master's degree from the University of Cambridge, England, and doctorate from the University of Oxford, England. He completed his neurology residency at the University of California, San Francisco and was then stationed at Naval Hospital Jacksonville, where he was neurology department head. While there, Dr. Tsao completed a behavioral neurology fellowship at the University of Florida. Dr. Tsao is actively involved in developing and managing Navy and Marine Corps TBI policy and programs, including methods for detecting and preventing TBI in service members and telemedicine programs for neurological and TBI patient care. His clinical research is focused on treatments for phantom limb pain in amputees, for which he was recently awarded the 2014 United States Navy Hero of Military Medicine by the Center for Public-Private Partnerships at the Henry M. Jackson Foundation for the Advancement of Military Medicine. Dr. Tsao is also past chairman of both the Government Services Section and the Practice Committee Telemedicine Work Group of the American Academy of Neurology.

Harold J. Wain, PhD

Dr. Harold Wain is Chief of the Psychiatry Consultation Liaison Service at Walter Reed National Military Medical Center. He is also a Professor in the Department of Psychiatry at the Uniformed Services University, Bethesda, Maryland. Previously, Dr. Wain was Director of the Psychiatry Consultation Liaison Service and the Director of the Psychosomatic Clinic. Dr. Wain was also Chief of the Psychology Service at Walter Reed Army Medical Center.

Dr. Wain completed his clinical training at Walter Reed Army Medical Center. He has published and lectured extensively both nationally and internationally in the areas of psychosomatic medicine, hypnosis, somatoform spectrum disorders, trauma, pain, and consultation liaison psychiatry.

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