

You will find very valuable for the care of our patients that we're honored to serve. We hope that you engage with each other in the chat box. And with the speakers throughout the day. As you know, we have four fantastic plenary speakers, followed by a break for lunch, and then our workshops in the afternoon. I do have a couple of quick housekeeping items to go over. The afternoon workshops are from 1300 to 1630. And you've received a personalized email with the link that you signed up with a workshop you've signed up for.

Next week, you'll receive an email survey evaluation. And please fill that out because that's invaluable to future planning and funding of our annual substance use disorder symposium. So, we really are counting on you. Give us your ideas, give us your feedback, how we can make it better what you want to hear. In addition, you're going to have a CME survey evaluation. So please remember that these are two separate evaluations. One is for us. One is for CME, that CME evaluation, it takes about two to three weeks for you to get that once your credits have been assigned, then you receive an email to complete the CME survey, and you have to complete the survey to retrieve your CME. Now, if you're requesting CME CNE download from the files pod and return that sign in sheet to Troy Spencer, by the 28th of September. If you attend a full day, you'll need to both submit the CME sign in sheet for the am session and for the pm workshops because they're kind of broken out. If you're requesting, see us there's a specific CEU sign in sheet. download that from your files pod and return that to Karla. An overall Certificate of Completion is the only certificate available, and it will be emailed to you if you need one, please email Amy Osik for that, and enduring materials will be sent to the address that you indicated on your registration. So, look out for those enduring materials and put a lot of thought into that. And I think that you're going to find that useful as well. Information for this symposium, pain skills, all the other things that we do, please check out our website NCRPI, National Capital Region Pain Initiative, [ncrpi.org](http://ncrpi.org).

Finally, I want to thank our outstanding speakers for giving us their time and expertise today. Also, I want to thank our staff who really make this possible. And that's Amy Osik. Carla, Troy and A'Riel, from my team to Infinity Conference Group and Evolve Media our contract support. Most importantly, I want to thank you all for taking time away from your patients, your clinics, your families, to attend and engage with us today. Now, on to our keynote speaker, our first speaker, Dr. David George, who's going to speak with us today about the biological causes of domestic violence, PTSD and how they interact with substance use disorder. Dr. George is a senior scientist in NIAAA. He received his medical degree from Bowman Gray School of Medicine at Wake Forest, completed residency in internal medicine at Henry Ford in Detroit, and Psychiatry at Duke. He is board certified internal medicine and psychiatry, and His research interests include exploring new treatments for alcoholism and understanding the biological antecedents of domestic violence and PTSD. He is widely published with over 100 peer review articles and author of the book "The Untangled Mind Why We Behave the Way We Do". Dr. George is clinical professor at George Washington University School of Medicine as well. With that, Dr. George, I'm going to turn it over to you.

Well, thank you very much. It's such a pleasure to be here today. I have no conflicts of interest, and that the things that I'm expressing today are not related to NIH or to Walter Reed. We've already talked about the title, my learning objectives. My goal has always been to try to understand human behavior. And to me, the better we can understand it, the better we can help our patients. The other goal that I would have been that perhaps we would spark new ideas and create an interchange here between.

Can you hear me now? Yes, we hear you very well. Dr. George. Oh, okay. It said it was muted. Alright, so a long time ago, I was doing a protocol. I had got the patient to sign the consent. And as you know, things happen as I was walking out the door, he said to me, oh, by the way, doctor, sometimes I'm afraid I'm going to lose control, and hit my children. And this was a question that had never been asked before. I sort of fumbled around and exited the room. But it really was the seedbed for trying to think about human behavior and really is responsible for a large part of what I'm going to share today.

I thought I'd begin with this picture here. I was giving a talk in Uganda, to health care professionals. They're about PTSD. This is years ago, this is at the height of the Lord's Resistance Army, there was tremendous amount of trauma. And on the way home, I took this little, tiny aircraft landed in a dirt field here. And this is taken from the veranda of the room where I was staying. And it was the most beautiful place that I think I've ever seen. The sky was blue, it went on forever, off to your left with Mount Kilimanjaro. And you can't see it here doesn't do it justice. But there's Monkeys Jumping throughout these bushes off in the field or elephants to rafts in that water or hippopotamuses, zebras, I've never seen anything like it. And it was the most sort of relaxing surreal experience. At around 630 That night, we had a naturalist come and say listen, I want to take you out in this open-air vehicle to see the see the fields. And as we got into the truck, he looked directly at me and he said, under no circumstances do you ever get out of this vehicle, it is not safe. We were driving around and here was mama cheetah with her little cubs. And he made the comment he said, if she leaves them for more than five minutes, there's a good chance that they won't survive. And as it started to get dust, there was a tension that came in the air. And you saw all the animals start to get to come together to try to protect each other. And we see a lion who is chasing after its prey. And the naturalist said that lion has three times to chase the prey at maximum velocity. And after that they are compromised to be able to take care of themselves. You see the lion catch the prey has to drag it off under a tree. And there's 20 hyenas that are coming to try to get the food as well.

And so, in other words, what I came up with and its sort of solidified my thinking was to understand the nervous system, I think at its most primitive level. It's about survival. So basically, what you're seeing is you have a response to threat and the pursuit of reward. And now I've also moved my thinking beyond that. We'll talk about it a little bit at the end. And that is what is long term survival look like.

Anyways I'm a clinician so I want to talk a little bit about, you know, basing it on Mr. Wilson here. I thought we would start with him. This is a patient that I saw in my private practice. A long time ago, came in. And he said, well, Doc, he said, I've seen a bunch of shrinks. They've never done anything for me. I don't really think I need to be here, but my wife wants me to come. So anyway, I said, Okay, well, tell me a little bit about yourself as well. He says, you know, my boss, my job, I like my job. My boss. He's, he's a micromanager. He really turns me off. I just have to avoid him as much as I can. He said, as far as major issues in my, its money, we're always trying to say, okay, how can we make ends meet? And? Well, the biggest issue that we're dealing with right now is my daughter, she's 16. She's starting to get into trouble. She's been cutting herself. She's starting to some use some drugs. She's not always getting to school. And my wife and I, well, we just see things differently. She wants to get her sent off to some place and get her fixed. But we don't have the money.

Comes in a couple weeks later, and he says, well, things have been gone too well, Doc, he said, well, I lost my job. They were cutbacks. And I'm thinking to myself, well cut the axe, or did you get angry at your boss? He then recounts that was stopped off at the local watering hole, he always calls it the

watering hole and came home, and the house was dark. And he said I got nervous. And I said, Where's my wife? So, I call her on the cell phone. And he said, she's at the mall, and she's buying carpets for the house. I felt so disrespected. That Well, I just sat down, and I said, Listen, I'm just going to drink some here. wife comes home, she sees them. She makes some comment, like you're nothing but a drunk. He gets furious, tries to leave. And she blocks the door. She's, oh, no, you don't you're going to deal with me this time. And then things happen.

How can we understand Mr. Wilson, I guess is the question? And so, I thought what I would do is try to just give you the cursory here and this is not meant to be intimidating. I'm hopefully that by do a good enough job. You know, you can follow the science here that I'm trying to integrate. We have the cortex, the anterior cingulate, you can see that Thalamus, we're not gonna talk about the insula. But we talked about the thalamus that the structure there in the midbrain, then the amygdala we all heard about, and the hippocampus is for memories. And then you see the structure there on the bottom of the PAG, periaqueductal gray. And that is come to be my favorite little structure.

Most people probably haven't even heard of it. I know I never had until I started to, to deal with my research. And, you know, if you really question Okay, the importance of it, I think 1000 a picture's worth 1000 words. And this is a taken from an article that I wrote with the Institute Director, Dr. Koop and he put this into the paper. And basically, it shows all of these structures in the brain, and how they all integrate into that PAG, the periaqueductal gray, and that it has its inference going out from it as well. This is a structure that's located in the midbrain. It's only five millimeters by 10 millimeters. And the answer your part is described as active coping. And you have here fight and you have flight. We've all heard of that. You bet you didn't know really where they were coming from. And so, this is sort of the final common pathway for fight and flight right there in the PAG. In the more anterior portions, you have shutdown, and you have pain and predatory behavior. And what's interesting is, there's now you have the sympathetic system that's fight and flight and parasympathetic was shut down and pain.

I want to share with you now, the model that I've come up with over the years trying to understand, you know, how do we understand emotions and behaviors? So, what you have here is you have sensory stimuli that are coming into the brain and go to the thalamus. And I think it's something that, you know, we all sort of take for granted. But if you think about it, a loud noise, can signal a gun could signal, anything that could be of great danger to us. And so, all of our sensory stimuli chest pain, you know, is another one that would stimulate us. So, it's very important comes into the thalamus. And it's going to be processed in two directions, it's going to go to the cortex, and you're going to have multiple synapses. And it's very slow, but it's going to give you a very detailed approximation of your environment. The second thing that it's going to do is it's going to go to the amygdala. It's extremely fast, single synapse. And this is really important, this is outside of your conscious awareness. There's an article back in Scientific American in the 90s by [Indiscernible]. And so, he tries to figure out what is actually going on here. So, he portrays a man walking through the woods, and he sees a wiggly line, which would be the amygdala, and looks at it, and says, immediately, that's a snake. He then looks at it, and he says, no, it's a branch in that would be the cortex. And so, in other words, you have this fastest and you have this slow system, and they're constantly interacting with each other, to give you an appraisal of what that environment is. Now, let's assume that it's a snake. So, what's going to happen now is that the amygdala is going to come up to the cortex, and it's going to cut it off, because the cortex is too slow, and you need to react immediately. So, you're going to bypass the cortex now. And you're going to come over to the periaqueductal gray. As we said before, these are hard wired neurons, that if you go into that

structure, and you stimulate it, you're going to get in the anterior portion their fight, which is, to me in the cat is the Halloween cat. In there, the cat, you know, puffs up, its long stand sideways, tail is up, eyes are up, you know, mean hissing claws are out. It's defensive behavior to cats afraid. Then you have flight, just couple millimeters apart from there, you stimulate the cat tries to get away, just gets out of the picture. was around 2000 that I read, you went into another place, and you would get shut down, the animal would just sort of come into itself and say, just leave me alone. Then you have predatory behavior, predatory. And there you see the two different types of aggression. The fight is defensive, this is offensive. This is where the cat slinks down, tries to get the bird doesn't want anybody to know that it's there becomes very quiet. And then you have pain. Alright, so in other words, it's very difficult to have behavior without emotion. So, I'm saying that what happens here is anger is on a continuum from a little annoyed to an angry to I'm enraged to drive fight. I'm going to feel a little bit on easy, I may say anxious, fearful panic, it's going to drive flight. The thing that really interested me was this idea of shutdown.

Depression never made any sense to me, why would we have this ugly emotion. And the way I see it is depression is the emotion that's going to drive you into shutdown. And if you think about it, all of a sudden, now you do have a purpose for it. You know, you get the flu, and you can hardly move. You can hardly go from place to place. The body puts you in shutdown and I'm saying it's for healing, so that he would never stop you just keep right on going. You lose somebody very close to you. And you just go numb inside. Alright, so in other words, I was talking about depression. In driving shut down. And that, you know, to me it came alive when I saw that it had a purpose. The one that really interested me, and this is new for me in the last six months or so is what is the emotion that's associated with predatory where the cat sleeps down and tries to get the bird. And I've always thought of that as there was no emotion. And what hit me was, I think that what it is, is its empathy. And so, the nervous system withdraws empathy, and sort of facilitate that predatory behavior. And then you have pain. In pain, if you think about it is sort of an emotion as well, it says, don't do this, take your hand off the stove. As we look at that, there's nothing wrong with these emotions in these behaviors. It's where they occur, it's how you get to them. And so, I'm saying that you can have a connection between the cortex to the PAG, and it can be completely normal, for example, I step on your foot, and you're angry at me. Or it can go directly from the amygdala to the PAG. And that would be an emergency kind of situation, I beat you up, and I rob you, and you go into these emotions. Or if the connections between the cortex and the amygdala are not very good, then you get to a pathologically, and they're I'm angry or I'm depressed, for no particular reason. And that's the pathology. The other points that I would come out is that these are very, highly controlled behaviors and emotions. And the one that I'm going to point out here is that the connections between fight and predatory, they are very inhibitory to each other.

So, in other words, if I'm trying to slink down and get the bird, I don't want to start hissing. And if I'm trying to scare you away, I don't want to be quiet. This is going to become important as we go on in latter part of the talk. The last part of this thing is that the PAG, as we showed before, in that one picture, is it's really tightly connected now with the autonomic nervous system, the endocrine system, and I don't have it here, but the immune system, so that they're all coming together, and then gives rise to this body mind body connection. So, in other words, when you're anxious, you know, you it changes your breathing, it changes your gut etcetera. So that you see the whole thing coming together. So that's basically the model in which I have come to appreciate.

So, what I do now is we have a video that you can hopefully look on at another time. It's some it's only four and a half minutes. And in it is you see this person, his faces been distorted, and his voice is distorted for confidentiality. But to me, this was a very important thing in my career, trying to formulate my thinking on domestic violence. I saw an article back in the 60s, it's written by [Indiscernible] was the New England Journal of Medicine. And in it they described where they gave an infusion of point five molar sodium lactate to people with panic attacks. When they gave it over 20 minutes? That individual experienced a panic attack if he had panic disorder. And if they didn't, it was just they got a little bit anxious. So that in other words, this was an agent that could reproduce panic. What made me interested was panic has is one of its features, the feeling of out of control, what would happen if I gave it to my perpetrators of domestic violence? And so, in it, you'll see this condensed version of what took place. You have a man that's laying there and dead perfectly calm, nothing's going on. And we started infusion. At first it was an infusion of placebo. And I would ask him questions like Do you have any shortness of breath? Do you have any palpitations Do you feel fear? Do you feel anger. And at the end of the placebo, he had no reaction. We then gave him the sodium lactate. And it was an entirely different situation. At first, he said, well, I start to feel my heart pounding, I start to feel shortness of breath. And you can see his chest expanding. And even though it's hard to tell in the video, his voice changes, it gets much coarser, gets more louder, and you see his muscles start to tighten up. As the infusion goes on, he says, I think I better stop. I'm not sure when I'm about ready to do. And so, we stopped the infusion. And then he sort of gives a narrative afterwards in terms of what he experienced. He said, I started to get confused. Like, I didn't know my thought process like you were here. But you weren't there. And it felt like, I didn't know what I was going to discuss how first I felt like the police were after me and I had a desire to run. But then it was like it was too late to run. And I needed to fight. I said, well, is this anything like you've experienced before? Yes, this is what I've experienced, this is how I feel when I hit my girlfriend. What have I just done? And then I asked the question, well, what if you've been drinking? And he said, well, if I'd been drinking, I wouldn't have had the desire to run, I would have just fought. And so, in other words, what this did for me was, it moves me on to seeing a new way of looking at domestic violence. First of all, it was defensive behavior. It took me forever to see that it was defensive. Because you have this big guy, little woman, what's he afraid of, but it's traveling over those pathways of defensive behavior.

The second thing was, it reminded me then when I heard of defensive behavior of a study that I had heard when I was in medical school, and why I remembered I'll never know. But anyway, it was a study done by Bard, he was at Harvard in 1928. And what he did was he transected, the cat brain at various levels and looked at the behavior. And when it got to the high midbrain, everything that cat bumped into, it went into defensive rage, the Halloween tap. When he got to the low mid brain, there was no behavior. And so, in other words, the point is that defensive rage is coming from the midbrain, and it's being controlled by the cortex. And then, future studies went into dissecting the PAG. And seeing that that's the ultimate place that it's arising from, in the periaqueductal gray.

I did a study with PET scans with the perpetrators rests and looked at the connections between the cortex and the amygdala. In healthy controls, there's a tight correlation between those two structures. However, when we looked at it in the perpetrators, that connection was lost. And so, in other words, they had, you know, decrease the ability of that cortex to modulate the amygdala activity, and that the amygdala became activated inappropriately. And the way I see it is the individual. Normally the amygdala is designed to pick up enemy aircraft, but without the connections without a dampening. Now

it starts to react to birds into flies into gnats, and it becomes much more reactive. And that's basically what we see with perpetrators is everything bugs them.

This picture here is always interesting to me. One of the things that I'm trying to get at is that with domestic violence, and as the person becomes enraged, you have a change in cortical function. And you I talked about it in the video there as far as you know, I didn't know what I was going to do. I felt confused. I was in charge of my mind. And if you think about it in a war zone, you know, you start to go to black and white thinking, it's for survival. And so, in other words, these people, they go to black and white thinking, I'm so right, you're so wrong. And, you know, you see that with borderline personality, you see it in post-traumatic stress disorder, that with threat, I become right, you become wrong. As far as the cognition is concerned, just sort of broadening now I think this is really something that we see quite a bit now in our society. Let's say that, you know, you have two individuals, and I give them the task of saying, I want you to describe this elephant.

And so how can we talk about treatment? Well, I think the first thing you have to do is you have to remember that this is a defensive behavior. And so, my job is to become a long side of that person, not to be confrontational. And so how I have found it to be effective is invariably I listen to them, and I say, hey, listen, maybe, maybe this will help. This is how I sort of see things. And I'll get out my little paper and pencil, and I'll start to draw my diagram for them. And all of a sudden, it's not me, it's not them, it's the paper, they're seeing it, they're looking at it. And I would say, 95% of the time, the patient becomes engrossed in that diagram, and then start saying it, that's it, that's me. And then, you know, you've sort of gotten engaged in terms of trying to understand their behavior. Because I mean, this is very frustrating for them as well. I mean, they're constantly walking around dropping atomic bombs on anthills.

The next thing is medication. And I've done this study here with Prozac. And it's tremendously effective. And what it's going to do, it's not going after depression, but it's, it's doing two things, it's going to help that person to have an extra second to think, and they're not as angry. And it's extremely effective there. And then what you do is this is where it's helpful to go back and see the model, that amygdala is responding to sensory stimuli outside of your conscious awareness. Within say, 20 or 30 milliseconds there, I've already reacted. So that is why I think therapy sometimes is not as effective as we'd like it to be, is because the system is so fast. Which brings me to the next section.

All right, what do you do with therapy? And let me give you an example of a patient that I had. He went through our treatment program for alcoholism, he had a horrible problem with violence. And when he was sober, I recommended that he go to an Oxford house. And so anyway, he comes in, he's on the drug, and or he's on placebo, either one, or he says, Doc, are you taking no more of your blankety blank bill? They're not helping at all. So, we, we finished the study, we break the blind, he was on placebo. And so, I put him on Prozac. He comes back a couple weeks. And he says to me, he said, Doc, I'm at Oxford house. I almost killed my roommate. And my heart sank. I thought, oh, this therapy didn't work. And so, I said, well tell me what happened. He said, well, it was 530 in the morning, I had to get to work to go to the bathroom, and my roommate is in there. I knock on the door, and he ignores me. So, what did you do? He said, I didn't do anything. So, if you think about it, in the past, his choices were, I knocked the door down. I punched the guy out and say, Listen, the next time I knock on this door, you come to me that we've been fight flight is he would have gone back to his room, packed up his stuff and said, I'm out of here. I ain't putting up with this Oxford house stuff anymore. Or he would have gone back to bed,

pulled the covers over his head and just said, I'm not going to work today and gone into shutdown. But he didn't do any of those. And that to me is really where I see therapy is the place to kick in. fight flight and shutdown. Those were his go twos all his life. But now it's like how I interact with my roommate? to try to solve this problem. And so that's what I would see is the purpose of therapy there is, you know how to help you cope with these threats in life. There are two caveats. One is, if you're drinking, these meds are just not that effective, and you're still more likely to go off. And that's a major problem because 70% of perpetrators have an alcohol problem. The other one is conditioned fear. So, when I did the study with Prozac, I had spouses rate these individuals, and they rated them as .0001. Better. I mean, there was no question it helped it, I thought they were going to be coming in and saying, doctor, you're the most wonderful doctor in the world, you've helped our marriage or helped our situation, it never happened. And one of the things that I came to realize was conditioned fear. So just imagine you're the spouse, or the significant other, and you've been cursed, that you've been beat up, you've been punched, you've been choked. Uh, you got to be neutral around this individual know, you're going to have a bunch of conditioned fear. And so, in other words, that's that other part of that equation that takes place. And then what you see is, you see that amygdala interacting with the perpetrator's amygdala, he can pick up that anger, he can pick up that fear. And so, it still creates problems that need to be addressed.

Alright, so let's get on to another person here. And that's Mr. Smith. And I feel as though I'm preaching to the choir here, because this was a person that I took care of years ago, in our program, who had just come back from Iraq, and he said, my life is out of control. So, in other words, that's plugging back into that thing that we heard earlier, is feeling like, you know, I feel out of control. And he was experiencing extreme mood changes, alcohol was becoming a problem for him, his relationship with his family, he and his wife weren't getting along, he described a bunch of traumas that took place when he was in Iraq. And this was his third tour of duty. And the thing that really interested me was, all he wanted to do was to go back to the war. So that was a number of things that, you know, went through my mind when I evaluated him.

So basically, you know, we know the criteria for PTSD, you know, there's exposure to some horrific events, then it gets re-experienced, I tend to avoid things that are associated with it. I have a lot of negative thoughts. And one that I would like to put in here. And it's not necessarily war, obviously. But it's, you know, sexual abuse in this, to me is one of the major causes of PTSD that I see. And how does it affect people's thinking. And this is something that I want you to look for in your patients, they're not going to tell you it, but I sort of discovered it, you know, just casually one time the person mentioned, it is a personal sense of disgust. And I think that's nature's way of saying don't get involved in this sexual relation between your brother and your sister etcetera. But anyway, if it doesn't get dealt with them to discuss stays with that individual, and they always feel like they're damaged goods, and then you have arousal.

Okay, so, for me, okay, you've got these criteria. There's sort of, you know, very concrete, what does it look like in reality? And so, one of the questions I always ask people, when I'm looking at for PTSD is, you know, where do you sit when you go into a restaurant, and invariably, they'll say, I sit in the back with my back to the wall so that I can see everything going on. They're scanning their environment; they're always looking over their shoulders. They have disconnections between the cortex and the amygdala. I think that's the major thing that, you know, we talked about before. So, in other words, they are much more prone to fight to flee or to shut down. It all makes sense in a war zone. So, in other words, PTSD,

it's your last-ditch effort to survive. That makes sense. I'm an American. You're Iraqi. I trust you. You can kill me. I am wired Now. This is not just haphazard, it's wired. I can't trust and this negative self-image, you know, is there with the abuse and other things difficult to love. If you think about it, if I fall in love in a war zone, I'm in Lala land, I'm not thinking about war, I'm thinking about love. And so, in other words, that gets lost and the last one is no future. And this one came alive to me with these with this man, it's like, if I am thinking of going home for Thanksgiving, and having grandma's turkey dinner, I'm not thinking about yesterday when my buddy just got killed and so my brain now is wired, to see no future.

Change in PTSD. So, you know, as I, as I alluded to, with this gentleman, you know, he wanted to go back to war. And I remember saying to my son, you know, was the war that just, and that wasn't his rationale for going back. And so, you can also apply it to the other things that you see in your practice, like, you know, you see the woman that goes back into an abusive relationship, or they keep going back into those relationships. Why is that? And I mean, obviously, I don't really know, I'm just trying to piece it together with the things that I've seen. But if my brain is wired, not to trust you, if I'm always looking over my shoulder, and I'm in a loving, caring relationship, that becomes irrational to my brain, it's very upsetting. And so, in other words, even though I think people hate the relationship, at least, I can trust you as the way on Wired, and you aren't trustworthy. It makes sense. It's rational, even though I don't like it. So anyway, that's how I'm beginning to try to think that thing through. The second thing is when I've dealt with people, especially this is in marital types of relationships, if they're used to being in a very antagonistic thing, and they come into a healthy, loving relationship, it tends to be boring, because your sympathetic system is activated. And now you have to adjust to, okay, everything is just calm. And it's hard to make that adjustment. So, I've worked with people to try to work through these things and to get past sort of the raw emotions that drive them into bad situations.

I think the next thing you see is this mind body connection. And I think we all know this, but why is like early, like trauma correlates with addictions with anxiety, depression, suicide attempts, cardiovascular disease, cancer, COPD, diabetes. How does that work? So, this was a study that was done back in the 90s, he had mailed out about seven or 8000 letters to people and ask them, okay, did you have any early life traumas? And they rated maybe seven or eight of them? And then that what illnesses did they have? And if you think about it, if I am now sitting on the button of being wired to fight, or I'm sitting on the button, a fear, I have sympathetic system changed on I have the endocrine system changed, I'm ready to go to war. I stay there chronically; you start to see how that can affect time. Over time, it can affect your health.

What about early life, trauma and PTSD? Well, not everybody gets. So, you have to try to think that thing through. So, there's an interaction between stress genes and epigenetic changes. And you know, if you read that literature gone over to me, one of the things that it keeps coming back to is the cortical cortisol system. And here you can see changes in the epigenetics of methylation of the glucocorticoid receptor FKBP, which controls also helps to control cortisol is affected. You have changes in the prefrontal cortex, the hippocampus, the amygdala, they are all become smaller, and the default network so that you have these changes that take place.

I talk about a couple structures here and we'll be done. So, one of the things that's interested me is systems that turn things on and turn things off. And so, there's an interaction between the amygdala which is sort of your day Your place and the nucleus accumbens, which is approach. Nucleus accumbens is all involved with dopamine. And so, you have two systems here that are very important in it. The



kappa system suppresses dopamine released into the synapse, and you have the dopamine reuptake inhibitor that retakes up dopamine faster. So, in essence, what you have in PTSD is this synapse, it's got reduced dopamine. And so, in essence, those dopamine receptors that are there become super sensitive. And I think what happens is that when you drink, you get more release of dopamine, and it becomes a much more powerful response to that individual. And this interaction, they've done two studies with it. One, they did studies, I believe it was at Duke, where they had about 750 students, and they challenged them with a stressor and looked at the activation of the amygdala and the nucleus accumbens. And the individuals that activated more the amygdala, and less of the nucleus accumbens had more problems with drinking.

A second one, and this is interesting for PTSD. They did, people soldiers before and after war looked at and before and after, the ones that were the most likely to get PTSD had more amygdala activation than they did the nucleus accumbens. And there's another part that's interesting to me here. And I think this is something you can look for in your practice as well, in that is that we decrease dopamine, you start to get an Anhedonia. And I usually think of it as depression. But I think this is something different, it's sort of depression, partly, but it's also your ability to enjoy the ability to feel, you know, compensated. And I think that's another thing that drives it. You look at amygdala activation. And when you give it a threat, PTSD, it's much more likely to respond actively. If you look at neutral, the amygdala is more active. However, if you give it something pleasant, or new, it is less activated, again, suggesting that it's more prone to this. And Anhedonia in PTSD.

Alright, so that's one switching place that takes place. This is an interest of mine, I'm designing a protocol, hopefully, to look at a kappa antagonist that would, you know, facilitate dopamine release in the presence of PTSD, would that change their addiction would it change Anhedonia. Another one that's here, if you think about it is the connections between the cortex and the amygdala. And so, you have switches that take place in the cortex between the ventral medial prefrontal cortex in the anterior cingulate. And I got interested in its years ago, because there was a study done in around 2000. And they looked at people that were hungry, and they fed them chocolate in a PET scan. And then they kept feeding it and then looking at how it changed the cortical activation. And so, it's switched in the brain when they no longer wanted to eat the chocolate. And so, it becomes, you know, we see it all the time, I'm hungry, I eat, I stopped eating. And so, the ventromedial prefrontal cortex to the amygdala sort of turns off fear turns off reward, whereas the anterior cingulate turns it on. Can we switch this often on switch here? And that's another study that I'm trying to do is looking at the effects of electroconvulsive therapy on can it turn off the fear? Can it turn off the reward system and get some normality in these people's lives?

This next slide here, and that is looking at the default network. And I got interested in this, because when asked your patients, the alcoholics, where are you the most likely to drink? And my experience has been they say, when I'm doing nothing, they asked What were you the most likely to worry? And well, it's when I'm doing nothing. And so that brought me to this default Network. And this was about 20 years ago, it was described where, you know, normally you think of fMRI is where you move your foot, and you see the neurons move in the cortex you activate. Whereas they saw these other neurons that were firing, and they were doing nothing. And so, as I understand that this is a structure in your brain or not structure, but a whole network, where what you're doing is you're evaluating the past, you're evaluating the present, and then thinking about the future and trying to say, you know, how do I proceed. And so, you think about, well, if I am in a war zone, I am going to proceed and I didn't go to my

period up to Greg, I'm going to be more prone to fight to fear to anger, depression. Whereas I come home, and I say, Okay, I am safe now. Now I move into long term survival. And this is where I remember I made the comment where, you know, Ray of fight, inhibits predatory behavior, and vice versa, I started to see how the nervous system has these inhibitory pathways and also facilitatory pathways. So, if you think about it, now you have a cognitive process, where forgiveness turns off anger, and love turns off fear and thankfulness with turn off, shut down, and you have beauty, you have hope you have purpose, which start to take you into a future. And as I thought about it, I'm questioning whether or not PTSD is a switch that takes place here that blocks you from moving into those long-term survival things. And I'm in so you know, it, you know, it's hard for you ever to, to feel loved, it's hard to forgive, it's hard to feel, you know, a sense of peace. And thankfully, because I am stuck. And so, I'm saying, oh, can we remove that button there. And, yeah, when you when you think about this default network, I was just thinking that yesterday, the purpose of it is, I become very self-focused, it's all about me, it's about my survival. And I activate the salience network, which is, you know, picking up all of the things that are not safe around me. And if that's where I live, if I'm stuck with, say, PTSD, it's about me, and started thinking about addiction. And, I mean, how many people have you seen that they give up their family, they give up their job, they give up their health, because that alcohol becomes like food, and it says, I need to have this. It's, it becomes that central part, you look at heroin, it's like air I need. And so, it becomes that focus, to drive their own of their behavior. And then the last thing I always end with is the GPS system. And I think we all live here; you're going down the road. And that lady is always working. And she says, redirecting your path, you just missed your exit. And to me, that is the hope that we bring to our patients, as many times we see them, this exits, they are never going to be able to go on those exits again. But there's new exits coming up. And those roads can be beautiful in that they will be different, and to try to help them to find it. And with that, thank you. And I'm sorry for all the hassles that took place here. And I hope that this has been helpful.

Dr. George, thank you, this has been an absolutely phenomenal lecture. And we really appreciate you and everybody else, just, you know, staying in there with the metaphors that I use, how we you know, stay in there with our patients, even when we're having and they're having difficulties. So, we really appreciate that. So, we have multiple questions in the chat that unfortunately, we're not going to have enough time to, to get, but maybe if you would be so kind enough just to entertain a couple of thoughts from these. And perhaps we will email you our questions and then distribute those to the attendees as well if that would be okay with you. Sure. So just a couple of things. Some of the modalities that we're using here in the Military Health System, especially a Walter Reed, I'm wondering if you can comment on how they interplay with, you know, with this discussion that you gave us, mainly TMS, the use of ketamine for treatment resistant depression and pain, and also stellate ganglion block for PTSD? How do these three modalities kind of impact on what you've told us?

Um, you know, the one, I've done a lot of ECT's on sort of partial to it. And if you look at what is easy to do, I think the thing that amazed me when I studied it was that it increases the size of the cortex, the hippocampus, and the amygdala, and that is in maybe six to seven treatments. And then when they did studies in animals, they realized that what it did was it increased the arborization in these structures. So, you start to see how he could change that. And also, about the default network, that it changes the, the connectivity there. So that's what intrigued me about that. Now, I think, you know, TMS is, you know, I've tried to review it. In the past, when I was looking at ECT. There are some studies that it showed that it may be of some help, it's obviously probably trying to change in neural connections as well. Ketamine

would be another one is far as that's concerned, I don't know that much about stellate ganglion, which, you know, you're figuring that it's giving new feedback to that system, that's probably feeding back into the PAG, can it change? Can it get you off of some of those buttons that are pushed, I always like to think of as buttons, you know, I'm just sitting on my anger button or sitting on my fear button? So, I think, you know, those are things that, you know, obviously can be tried as well.

Fantastic. Well, we have a lot of trainees in the audience. And I know we have a lot more questions and we have would have a lot of interest in, in collaborating with you, hopefully on in future endeavors. Love to be part of this really groundbreaking work that you're you've been doing and that you were so kind to share with us today. So again, Dr. George, thank you so much. Thank you, I appreciate it.