Moderator: Hello and welcome to today's webinar, Current Perspectives on Trauma, Memories, Substance Use, and Treatment. This webinar is paid for by McLean Hospital, a top-ranked freestanding psychiatric hospital, a leader in psychiatric care, research, and education, and the largest psychiatric teaching hospital of Harvard Medical School. Some important points before we get started. Dr. Robin Gay and Dr. Rocco A. Iannucci, the presenters for today's webinar, have working relationships with McLean Hospital.

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Next, this program does not offer CE. However, we will email everyone watching live today a certificate of attendance. Certificates will only be issued to those who watch for a minimum of 45 minutes. A recording of this presentation will be emailed to everyone in two weeks' time. The recording will include the presentation slides. During our time together, you will be on mute. You can communicate with us using the Q&A box located on your webinar screen. If you have a question for our presenters, type them in using the Q&A box located on your webinar screen.

A link to the presentation slides will be posted in the chat box of your webinar screen. If you miss them, don't worry. We will email them to you with the recording. Now, let me introduce our presenters. First, Dr. Robin Gay. Dr. Gay is the Director of Psychological Services at Fernside, a McLean Hospital Signature Addiction Recovery Program that specializes in treatment of substance use disorders and co-occurring conditions. Dr. Gay completed her PhD in Clinical Psychology in New York City at the New School for Social Research, and her pre-doctoral internship at Mount Sinai Medical Center in Manhattan. Her clinical interests include the effects of substance use disorders on cognitive functioning in relation to treatment outcomes.

Dr. Rocco A. Iannucci. Dr. Iannucci began his psychiatric career at Massachusetts General Hospital and McLean Hospital where he served as the chief resident in addiction psychiatry and as assistant director of psychiatric residency training. In 2008, he entered a practice at the Berkshire Medical Center, serving as medical director of inpatient psychiatric and addiction treatment. At Berkshire Medical Center he concentrated on improving the lives of patients with substance abuse issues including developing protocols for the treatment of alcohol withdrawal and of pregnant women with opioid dependence. In 2011, he earned Most Patient-Centered Physician Award. Welcome, Dr. Gay and Dr. Iannucci.

Dr. Gay: Thank you, it's a pleasure to be here. Welcome to this webinar. I want to introduce the subject that I'll be discussing today briefly. Many of us have experience working with patients who have had trauma and some who may also have difficulty with remembering some aspects of the trauma or conversely may have intrusive memories regarding the trauma. I'm going to begin with a brief discussion of the neurobiological processes for both physical trauma and then emotional trauma.

Then I will shift to focusing more exclusively on emotional trauma and memory. Following this, I'll discuss how alcohol misuse is often associated with trauma and the negative effects of alcohol on both memory and treatment. For example, alcohol use increases the risk of so many types of traumas. For example, car accidents, other types of physical injury, domestic violence, and sexual trauma. As we know, acute alcohol intoxication can impair memory.

Furthermore, for many, many people who've suffered a trauma, alcohol use may be used to cope with the trauma and therefore negatively impact treatment and recovery. Finally, I'm going to conclude with discussing some potential effects of early trauma on brain development and potential increased risk for both alcohol use disorders and physical brain changes as well as changes in cognitive functioning that may predispose individuals to be more likely to develop PTSD later in life if they've experienced a trauma.

For example, early trauma experiences may foster brain functioning and the HPA axis, the Hypothalamic-Pituitary-Adrenal axis, leading to both increased rates of alcohol use, trauma experiences, and potential increased rates of PTSD. Finally, I'll discuss briefly the evidence-based treatments for trauma and the potential of adding CRT, which is cognitive remediation therapy as an adjunct to treatment. Welcome, everyone.

Memory and trauma overview. To start out, what is the neurobiology of trauma memories? How does the biological process to psychological trauma affect memory? Well, I'm going to begin with talking about TBI which is physical trauma. We know that when someone has an injury, if the injury is severe enough, it can result in what we call post-traumatic amnesia. During post-traumatic amnesia, what we call PTA, the person is not able to recall things if the injury is severe enough.

During the acute phase of the trauma for the period at which PTA lasts, so period of anterior grade memory problems so after the injury until PTA heals, they may have problems with memory as well as sometimes a brief period right before the trauma. We like to think of it as a DVD recorder, and during this period you take out the DVD when the brain is going through an injury, and it may be due to a neurochemical storm, and since the DVD recorder, or the disc is not in the recorder, the brain cannot recall these memories because they're not encoded.

However, trauma, PTSD, and alcohol all can have a negative and synergistic impact on memory that affects treatment. Normal memories, as opposed to physical trauma memories or emotional trauma memories, undergo a process of consolidation and become part of episodic memory. What we understand about memory consolidation is that it's a process where temporarily memories are vulnerable to not being encoded. They are then transferred into long-term memory.

This research on memory consolidation came from an understanding of the hippocampus. In patients where the hippocampus was damaged, the memories were not well encoded or able to be encoded. It was first proposed by Muller and Pilzecker, and it accounts for the effect of how memories may not be encoded. Basically, normal memories undergo consolidation and become part of episodic memory, but this process may be disrupted in types of trauma.

Can you advance this slide, please? What happens during a psychological trauma? We discussed physical trauma and what happens, and there may be a biological process for some people that happens that can impair memories for physical trauma. One theory is that the amygdala, which is part of the limbic system responds and detects a threat. When this happens, the Hypothalamic-Pituitary-Adrenal axis which we call the HPA axis, is activated, sending a signal to the pituitary glands then the adrenal glands to release hormones to prepare the individual best to survive. We know this as the well-known fight, flee, or freeze response.

Additionally, one thing that can complicate memories during a trauma is attentional focus. People may hyper-focus on a certain aspect of the experience and not attend to other aspects of the experience, thereby, if they're not attending to it, it will not be well encoded. Advance the slide, please. Thank you. During the trauma, when the amygdala is activated, the theory is that the hippocampal function may be hampered during this experience.

As we discussed, hippocampus is where memory for events are stored in contextual format, chronological format, where they're in this vulnerable space before they're transferred to long-term memory, and they undergo consolidation. In this way, trauma memories may have strong retrieval cues that are fear-based relating to contextual details such as what day it occurred and certain information, however, may not be well encoded, which is the domain of the hippocampus. In this way, some information may be sensory, and some information may not be well encoded. Again, that's the contextual information regarding specific details, regarding what time it occurred, or other sequencing information. Please advance slide. Thank you.

Trauma memories, therefore, may occur in the form of sensory information such as perceptions, sounds, images, or smells. One theory, according to Chris Brewin is that the memories are often fragmented. They may be fragmented in time, they may consist of sensory information, the images and smells, and be linked to physiological fear responses. The prevailing thought in this model is that trauma memories are stored both as images and in a narrative format, and this is called dual representation. In this way, they're partially stored as autobiographical memory, yet they may not easily be verbalized. They may be fragmented in lack context, which can impact treatment. Advance slide, please. Additionally, not only can the trauma experience have an impact on memory and PTSD, however, also is known to have an impact on memory if the individual goes on to develop PTSD. As we know, gaps in declarative memory, which is basically just recall, can be and is one of the diagnostic criteria for traumatic stress disorder. Criterion D in the DSM states that individuals must have two or more of seven different symptoms in this domain, and one of which is inability to remember key features or an important aspect of the trauma.

PTSD may involve both unwanted intrusive memories as well as gaps in recall regarding important details, including autobiographical memory. Brewin notes, who's one theorist, PTSD sufferers may be perfectly able to provide a general account to others of what happened to them that is rehearsed and coherent but omits details of the worst moments of the trauma.

Again, please note they may also have intrusive memories of the worst moments of the trauma, so there's this dysregulation in memory that can happen for some patients. Advance slide, please. Compounding this whole picture is alcohol, so how does alcohol relate to PTSD and trauma? Just to go over a few statistics to give an idea, the National Center for PTSD found that alcohol use is associated with an increased risk of PTSD. Alcohol problems are more prevalent in people who've experienced traumas. Substance problems and the risk for individuals is much greater for people who are high on the ACE's score. Now the ACE's is an Adverse Childhood Events study, which was done by Kaiser Permanente and the CDC, looking at early experiences of childhood abuse and neglect and following these individuals over a period of time to see what the health outcomes as well as psychological outcomes were.

What they found was that there was a high rate. One of the highest rates of factors is that they had problems with or likelihood of abusing alcohol. Up to 75% of people who've experienced abuse or violence report problems with drinking. Additionally, up to a third of people who've experienced a severe physical illness or an accident or physical disaster such as natural disaster or hurricane, report problems with PTSD. Even higher is the rate or potentially higher among Vietnam vets. For example, Vietnam vets entering treatment for PTSD were found to have problems with alcohol at a rate of 60% to 80%. As we know, alcohol use negatively impacts PTSD treatment course and treatment outcomes. Next slide, please. Thank you.

Therefore, understanding how alcohol use and trauma effected memory can be helpful in developing better methods to treat PTSD. One study found that veterans of 9/11 who both had problems with alcohol use and combat exposure, they were found to have negative impacts on their visual working memory. If this is the case that it affects cognition, what is the importance or potential benefit of adding cognitive remediation training?

We have found that cognitive remediation according to the literature, may improve PTSD symptoms. Cognitive remediation training may also improve memory impairment resulting from alcohol use, which we know impacts memory. Alcohol affects both memory and executive functioning, and alcohol misuse or abuse is associated with an increased risk of early-onset dementia. Other research also appears to support the continued or adjunctive use of CRT, Cognitive Remediation Training for people with PTSD, or alcohol abuse. Next slide, please.

The effects of PTSD and trauma on memory, just to talk more about them, veterans with PTSD and trauma exposure were found to have changes in their hippocampal volume, and persistent trauma may also result in brain changes for areas responsible for both memory and executive functioning. Now I do want to make it clear that most of these studies are looking at cognitive performance on neuropsychological or other cognitive tests. They're not stating that globally people have impairments in their day-to-day functioning. They're looking at more small impairments. It's still nonetheless important to look at these to see how this type of impairment may lead to a treatment modal of cognitive mediation therapy, or what people can do to help people function better if we can find any way to any of better avenues for treatment.

Alterations in the myelination of axons, which is the connection between axons, which helps them communicate. It's also been found that they are either thicker or thinner in people who've experienced trauma. The nucleus accumbens, which is the reward center of the brain, has been found to be changed as well as changes to the corpus callosum, which is the band of nerve fibers that connect the right and left hemisphere. Additionally, patients were found to have decreased hippocampal volume and increased amygdala volume. Therefore persistent trauma can result in brain changes responsible for memory and executive functions as well as other functions.

Furthermore, childhood trauma neglect can result in changes to the HPA access, making people have a greater startle response, greater physiological response to fear. Additionally, other research shows that there may be with some individuals decreased performance on short-term memory tasks, working memory, and episodic memory. Next slide, please.

Some of the research is looking at whether memory impairment may increase the risk for later development of PTSD, and there seems to be a very complex relationship between memory and PTSD, and people with prior memory deficits may have a higher incidence of developing PTSD. Again, we're talking about small and minute studies and effects on studies. This is not something saying people are globally impaired in any way or have more significant impairments, but they have found declarative memory impairment may be a risk factor for PTSD rather than a result fact, result of the trauma, so you may have the impairment first in a subtle form, and maybe the impairment even starts from early childhood experiences of neglect and abuse. This is something that needs to be explored further.

What they did find is that there were impairments on verbal list learning tasks such as the CVLT and the RAVLT as well as the ability to remember story, which is narrative memory and paired associates where you pair one word with another. Although do note this is debated in some studies. However, other studies have shown that the severity of PTSD symptoms predicts level of cognitive decline in older patients. This really points to the need to treat PTSD symptoms, not only to help the individual function better and to help their psychological well-being, but to maintain brain health. Again, there's this discussion of how early trauma may lead to vulnerabilities in the brain as well as the HPA access that could potentially for some individuals make PTSD more likely. Next slide, please.

Finally, I'm going to discuss some of the CRT treatments for PTSD and alcohol use disorder. What they found is that cognitive mediation training has been used to treat alcohol use disorder and also PTSD. Individuals-- and I'll get into what cognitive mediation training is a little bit later, but individuals with PTSD have cognitive deficits in multiple domains, and executive functioning obviously have worse outcomes. It's another way of just really helping our patients and adding a type of treatment that doesn't seem to have many or any negative side effects and may be beneficial.

Anyway, but the domains that are mostly affected are declarative memory, short-term memory, attention, and executive functioning according to a 2015 study. Also, cognitive remediation therapy has been used for patients who have substance use disorder and was found to be helpful for improving working memory, processing

speed, and executive functionings, and correlated to treatment improvements in substance use disorder, even in patients that were not found to have cognitive impairments, which is actually quite interesting. Next slide, please. To discuss the treatments a little bit, mainly what's of course, the main focus and importance is to help the individual feel comfortable with what they do and do not recall, helping to provide psychoeducation about memory, to destigmatize what they do and don't recall and to help them feel comfortable with their own experience. Evidence-based treatments mainly focus on-- the main ones are CPT, which is cognitive processing therapy, PE, prolonged exposure, and CT, which is cognitive therapy, which is a bit from CBT. To discuss CPT, which is a type of therapy that focuses on reinterpreting one's beliefs about the trauma and challenging beliefs about the trauma that may not be helpful, and that may be negative to the person's well-being.

Usually, it occurs over the course of 12 sessions. What they found is very much like CBT challenging the unhelpful beliefs helps lessen the symptoms of PTSD and improve functioning. PE is a little bit different and that is a type of therapy that helps patients accept feelings, images, and memories related to the trauma and mainly focuses on helping them avoiding the trauma memories and feelings and thoughts related to it to help extinguish the fear response. PE has four main parts. One is education about PTSD and PE, two is breathing retraining, and three is in vivo exposure and then four is imaginal exposure.

They develop hierarchy of which situations are most avoided, they try to help the individual go to certain situations or environments that may trigger memories and to be able to tolerate these memories, and then also imaginal exposure is where they start talking about the trauma in therapy often that's recorded, there's tape recordings of the experience of trauma, they discuss it and then listen to it over and over again. Again, it's to help them not avoid trauma and lessen the anxiety and experience related to the feelings, thoughts, and memories.

CT for PTSD, cognitive therapy came from CBT but as a type of CBT that focuses solely on PTSD. It focuses on elaboration of autobiographical memory, to help give a different meaning to trauma and lessen the severity of symptoms. All in all, we do want to focus on non-judgmental compassion, providing psychoeducation, and challenging unhelpful cognitions about the event, especially when memory impairment is implicated.

Additionally, we want to look at whether CRT, cognitive remediation therapy could be beneficial for some patients. What specifically is CRT? Basically, it focuses on proving neurocognitive functioning and targets cognitive domains that may benefit from improvement in functioning, domains such as attention, memory, processing speed, and executive functioning. It often consists of drill and practice exercises and activities that may be done on a computer. It can also consist of metacognitive remediation, which means awareness about one's cognition, and memory and when they may have problems and when they are doing better, and also social awareness.

To summarize, this presentation started with a focus on neurobiological processes involved in TBI and psychological trauma and how memory may be affected. Then the material I presented focused on how alcohol use is often associated with trauma and impacts treatment. This was followed by a discussion of memory disruption and

PTSD. Finally, this talk concluded with a presentation on how early trauma may cause changes in the HPA axis, as well as alterations on cognitive performance and specific domains that may potentially lead to an increased vulnerability of developing PTSD.

I concluded with a brief discussion on evidence-based treatments for PTSD and the possible benefit of considering on a case-by-case basis if CRT may be helpful. I want to thank you all for attending and now I'm going to switch over the talk to Dr. Rocco Iannucci.

Dr. Rocco: Thank you, Dr. Gay. I'm just waiting to get-- Well, I'll start but I'm hoping to get control of the slides. Great. I think I have them now. My name is Rocco Iannucci. I really appreciate all the folks who are listening to the stream, as well as anyone who's listening to this in the future on a recording. I'm an addiction psychiatrist where I have the pleasure of working with Dr. Gay at McLean Fernside, and primarily focusing on people with substance use disorders, as well as with co-occurring conditions like PTSD and primarily doing clinical work, not research.

I'm trying to advance my slide, not quite advancing yet. Yes, I can't get it to-- Yes, it's okay, I got control now. Great. I'm going to start, I just want to say what I'm not going to talk about first, much at least, is what used to be called Korsakoff syndrome, it's now called alcohol-induced amnestic congratulatory neurocognitive disorder. It's too long a name to really talk about, I would say, but in seriousness, the presentations were fairly dramatic. This was a syndrome based on vitamin B1 deficiency, where people just couldn't form new memories, and they would confabulate or make up stories, apparently, to fill in the gaps.

Dramatic presentations, but really rare, I'm going to rather focus on some of the things that we see all the time, which are patients who have experienced alcohol-induced blackouts and then patients who have more subtle longer-term memory or executive dysfunction that's caused by their use of alcohol. I'll make the case for our-- the fact that these patients whether we're recognizing or not are in our population all the time.

I don't think this is on slideshow, is it? Because it doesn't seem to be doing the animations. Well, I think the slides will work okay, anyway. Alcohol-induced blackout, I want to make the distinction between passing out and blackout, people do not lose consciousness during an alcohol-induced blackout. Rather, what happens is, they have loss of memory for events that occur during a drinking episode, there's amnesia that takes place. Events either are not recalled at all in which case we call it en block blackout or people can have fragmentary blackouts where things are fuzzy, details are not remembered, particularly the contextual clues are not remembered well, those are sometimes colloquially called brown-outs or gray-outs, and these are quite prevalent.

Surveys of college students report 50% prevalence of blackouts, and if you look at young people, depending on how far you look back when you ask them, 30% to 50% is pretty standard. These are very common, we used to think of it as something that was a marker of severe alcohol use disorder but in fact, it's not, it's quite prevalent.

There are risk factors for its occurrence, probably some genetics to it, that's a little hard to tease out because it's difficult to separate the genetics of blackout from the genetics of alcohol use disorder itself. We do know that when there is a high alcohol level, things along the level of 0.2 to 0.3 grams per deciliter. It occurs when it takes place rapidly through rapid increase, that's what sets the stage for a blackout. That is the set of circumstances that we see oftentimes with binge drinking, which is another quite common behavior, particularly among young adults. Definitions vary of binge drinking, the NIH official definition is a pattern of drinking that leads to a blood alcohol concentration of 0.08 grams per deciliter, and that generally amounts to four to five drinks for two-hour period, depending on the gender, the size of the person. Some definitions of binge drinking, just talk about four or more or five or more drinks.

There's situations in which binge drinking is likely to occur, that involve a rapid increase in alcohol level and those situations are therefore also a risk factor for blackouts and those are things like drinking games, like what people sometimes described as pre-partying, maybe drinking at home before going to a bar or a party, drinking hard alcohol, preferentially doing shots, rapidly drinking on an empty stomach, and then people who drink for positive aspects to drink to feel good rather than people who say, "I'm drinking to get a little relief or to manage my anxiety," they're more likely to have a blackout as well. Alcohol use disorder, as well as binge drinking and blackouts, are associated with sustained deficits and executive function including memory problems. This is important for some of the reasons that Dr. Gay already alluded to. Executive function deficits, predict worse outcomes with treatment for alcohol use disorder, and they predict treatment dropout. There also may be a relationship between this dysfunction and post-traumatic stress disorder in that you may have an increased risk for developing post-traumatic stress disorder based on, in the presence of neurocognitive dysfunction. Binge drinking itself and blackouts can make the person more vulnerable to accidents, to injury, and to even being victimized. It can really set the stage for high risk for developing post-traumatic stress disorder.

Thinking about what we know of neurobiological mechanisms for blackout, I'm going to reflect back on some of the things that Dr. Gay already talked about, which is the process of how memories are formed. We think that the information first has to get in, sensory information has to come in, and then it's consolidated into a memory that's stored. There's an encoding process, there's a storage process, and then we retrieve the memory when we want to recall it or when it comes back to us, whether we want to recall it or not. Aspects of this are inhibited acutely by alcohol. In particular, we think consolidating the memory with contextual cues and moving it into a longer-term memory.

That's because of the alcohol effects on certain regions of the brain, including the hippocampus, which is the memory area where things are put into, as Dr. Gay said, a sequence with contextual clues as well as frontal regions. We know from functional neuroimaging that there are alterations in brain chemistry, including signs of oxidative stress and GABA neurotransmission abnormalities in blackout states.

What do we do with this information? I'm primarily a clinician. I do like to know what's going on with my patients and to understand it but I also want to know what can I actually do with this? Well, one piece of information I think it's helpful to know is that

a history of blackout in patients is actually associated with an increased likelihood of benefit from personalized normative feedback. Personalized normative feedback essentially involves getting information from an individual about their drinking patterns and also getting information from them, oftentimes on what they think their peers drink. What do they think the patterns of their peers are so that it can be compared to actual data about their peers. Typically, we find that young people overestimate how much peers may drink and do other things, but in this case, I'm focusing on alcohol.

You provide them that that feedback, and then also education around safer drinking limits. It's been found that people with history of blackouts are actually more likely to benefit from that feedback. It provides an opportunity. If the person is open to that, if they're concerned about blackouts, we can talk to them certainly about stopping alcohol if they have an alcohol use disorder or a reason to stop but also about trying to manage. A lot of young people aren't going to be ready, willing, or maybe it's not appropriate for them to stop fully. They can be educated on modifying some of the behavioral risks of having a blackout. Not drinking hard alcohol or doing shots or drinking-- Very palatable drinks sometimes lead people to drink more quickly.

It should be noted though, that in some surveys there is a group of college students who drink with the intention of having a blackout. They go out planning to get intoxicated, have a blackout. It's part of the plan. This really has to be dealt with on an individual level, working with people to try to figure out their goals and try to organize around that.

I'm going to move now from short-term effects, acute effects of alcohol, to thinking a little bit more about the longer-term effects of alcohol. This slide is meant to illustrate some cognitive processes that are affected by alcohol use and also to bring the point across that the processes by which we reflect back, we remember things. There is some overlap in some of the brain functions that let us do those things with those that let us think forward, look forward, anticipate what may happen and make decisions. I'm going to talk a little bit about some of the terms on this slide and just how there's a symmetry to them because these are all things that are affected by alcohol use in the moderate to longer term.

I'll start with Episodic Past Thinking because that's really episodic memory, a form of memory. That's one we're familiar with. This is recalling something that happened. The order of the events, the context where it happened, who was there, pulling an episode back and reflecting on that. Well, we can think about episodic future thinking as the symmetrical in the future version of that kind of a thinking. We ask people to do this, certainly in substance use treatment.

A lot of times we'll ask them to do something with patients call playing the video forward. If you have that first drink, then what happens? Then what happens? Then what happens? To walk them through to get to the point of understanding longer term consequences. You can see how if alcohol and PTSD would affect the mechanisms involved in this, it's going to make it a little bit harder for them to look forward and to make choices that may be helpful for them in their lives.

Working memory I have on here because it's in the middle, it's fundamental to a lot of these other functions, we think. Also it's very immediate. It's a right here and now. I'm going to come back to working memory in a moment. It's neither in the future nor in the past. It's very much in the present kind of a function.

Then temporal discounting I want to say something about quickly because it's something else that seems to be abnormal with substance use disorders possibly at baseline, but definitely worsening with substance use and perhaps improving with periods of absence. Temporal discounting refers to the fact that we put a premium on things that are more immediate compared to things that happen in the future. If someone were to offer you $100 today versus $100 tomorrow, you'd probably take $100 today. What if it were 100 today, 101 tomorrow, 200 tomorrow, 1,000 tomorrow? There is some sort of a calculation that our brains do where we value things that happen sooner than later.

What happens with substance use disorders is that curves tends to be steep. There's a relative overvaluation of immediate rewards compared to later rewards. All these things are naturally targets for helping people get better with substance use disorders. There's a symmetry to temporal discounting where it's the same thing in the past. More remote events don't have as strong a balance for us as more recent things. You see that when people get into recovery and start to forget maybe the pain that they went through beforehand.

Just reflecting again that there are problems caused by alcohol, with memory, with executive function and with working memory, which I'm going to expand on a little bit more because it seems to be so central to some of these other things. Just to illustrate the way I think about working memory, we're holding small amounts of information in ready access so you can almost think about I'm holding something here in order to be able to do something with it. You hold those things. It's a very immediate form of memory and you could see how this capacity would be central to some of these other functions.

It oftentimes when we think about working memory, we implicitly include other executive skills such as concentration that are needed to be able to engage working memory in the first place. People have working memory deficits with substance use disorders. What can we do about that? Well, we have two directions we could go in. We can either try to improve their cognitive function or we could try to accommodate their current level of cognitive function in our treatments. But to think about doing that, it helps to reflect on the educational literature.

In education you could think about how working memory capacities increase for young people as first grader, fifth grader, high school student, there's going to be different curricula that are designed for the different working memory capacities and over time it improves on its own with age and maturation. With people with substance use disorders, there have been efforts to try to target these things, to improve them without having a natural healing, which I'll mention something about natural healing that happens as well.

My last few slides I do want to say these are more to tell a story. This is not a systematic review of all the data that's available on these interventions, but it's

something that I found exciting. I'm trying to just kind of give you a little bit of a view of these and where they might hold some promise for the future and help us understand our patients today, I think at least but I'm not prescribing these as something we should do with all of our patients.

That being said, there have been some clinical trials of working memory training with people with different substance use disorders and with somewhat varying results. The eventual goal would be to be able to enhance working memory and then have that effect, have that transferred to these other more complicated tasks like delayed discounting, being able to delay gratification, and then that's subsequently helping people to be able to stay away from the substance. That's what's looked for. We're seeing bits and pieces that look promising. For instance, with people who had opioid use disorder treated with methadone, working memory, training seem to enhance working memory and that translated into better drug use outcomes. So that's pretty exciting. The working memory training is essentially, for example, memorizing a string of digits and increasing the number of digits that you'd have to be able to reflect back on and training someone over time in that. Methamphetamine and cocaine use disorders, both stimulant use disorders. There did seem to be a translation from enhancing working memory to actually improving or flattening out that delayed discounting curve so that people would have a better capacity to delay gratification. These are not consistent results.

There's one more study, again, not being systematic, but I will mention a study with alcohol use disorder where there were a few different interventions, many different arms, but what essentially the take home point was it looked like with a group of people with alcohol use disorder, if they had working memory training and if they were engaged in episodic future thinking, so sort of play the video forward, then what happens, then what happens, then what happens to really engage that part of thinking as well. Then they did actually have improvements in in delayed discounting in the group of people that had the biggest deficits.

The consistency maybe we just have to do enough, maybe we have to learn how to better do this and to select our patients for the ones who need it the most. The final point though on here is that executive function does improve with cessation of substance use. Much like the child where we just have to let them get older and mature, their working memory gets better. A lot of aspects of executive function get better if we can just help people not use the substance. I want to wrap up, the psychiatrist-- I'm going to talk about medications, we can't help it.

There are a few medications indicated by the Food and Drug Administration for PTSD and for alcohol use disorder, and there's no reason not to use these. There's others that have been looked at for co-occurring alcohol use disorder and PTSD with mixed results. To summarize, I'll just say they tend to work for the disorder for which they were originally developed. Naltrexone tends to help with alcohol use disorder, sertraline with PTSD in the patients who have both. There's more to that story. Maybe it'll come out in questions, but just for the sake of brevity.

Getting back to the topic of learning and memory, though, some of these medications seem to have a beneficial effect on aspects of executive function, so that's helpful potentially. If you think about the action of disulfur, so disulfiram is an

aldehyde dehydrogenase inhibitor. It causes people to accumulate noxious metabolites of alcohol. When that happens, they get sick. This is the medicine Antabuse, they drink, they get sick, so what happens? They don't drink. People don't need to actually have the experience and engage their episodic past thinking and remember and learn and not use alcohol.

If they know they're on disulfiram they just don't drink it in the first place so they engage episodic future thinking. Clearly, even with medications, there's times when those executive function problems they apply for people in these situations. I would say the next step, and this is much more investigational, it's a trivial statement to say that the whole point of psychotherapy or a big point of psychotherapy, certainly to connect with people, but also to rework some memories and relationships and learn associations. It's a part of what happens in psychotherapy.

More recently, and I think it's thought-provoking, have been these efforts to use medications to enhance psychotherapy. Some of these medications that I have listed, they've been used on their own without psychotherapy, but there have also been trials to look at these medications, which are thought to take advantage of the memory process of retrieval because when we pull the memory back out and we access it, when we put it back away, it can get changed in that process. It has a relative period of instability. I think of it as putting a new edition of pulling a textbook off the shelf and what you return to the shelf is the new edition, the updated edition of that same textbook.

This is how our memories can work as well. The idea is to take advantage of that inherent instability of the memory and maybe make it more flexible still with medications. Each of these medications, I won't go into details, but it affects the process of reconsolidation. Putting the memory back together to put it back on the shelf in such a way that it may offer opportunities when combined with psychotherapies that pull memories back out or have people access previously learned associations. Those things can be either weakened or the relationship to them can be weakened or maybe even new associations can be formed. This is investigational. I'm not doing this with any patients at this time, but I'm very interested in seeing where this takes the field especially the collaboration and the synergy between medications and psychotherapy.

Just to summarize to very bullet points, alcohol use has a major impact on executive function acutely and can chronically as well have a more subtle effect. It's important to look for and just know that it's there. It helps me to understand and be patient with my patients just to know that their brains aren't entirely working the way they would find it most helpful for their brains to work.

Asking about blackouts may provide therapeutic opportunities because you may find areas of motivation for patients if they have had blackouts. Then we may find some new avenues to help our patients through working on training executive function and memory, combining psychopharmacology with psychotherapy in potentially more novel ways. Then thinking about, is our treatment matching our patients' capacities?

I think about that as you're not necessarily developing a new treatment for every class of working memory problem or episodic memory problem, but more getting

feedback directly and individually from our patients as to what their treatment experience is, is it working for them and then then trying to make those modifications as is appropriate for our patients. I will just move quickly through. There's a bunch of sources, I think these will be provided to you, but I really thank you all very much for your attention and for the opportunity to speak to you today. Thanks.

[silence]

Moderator: All right. Thank you to both of our presenters. We'll now start our Q&A session. I could take one question here. "Hi, Professor Iannucci. During your clinical work, do you also take clients that's sex or love-addicted or mostly just substance and alcohol abuse? Thank you."

Dr. Rocco: Yes. I guess that's a practice question. I work at McLean Fernside, so we're happy to talk to people about whatever they have, I guess from the more maybe of broad interest. Yes, would be the short answer. Love-addicted can mean a lot of different things. I would say some things, certainly sexual behaviors can have the compulsive out of control pattern substance use disorders also show.

There's also relational behaviors that are based more on relation that do light up some similar areas of the brain. We get reward in relationships as well. Easy enough to reach out to us at McLean and at Fernside available on the web. What we do is we screen people, we would talk to them if it was a complicated situation just to see if we thought we could be helpful.

Moderator: Thank you. Another question we have here is, "Dr. Gay, do you see EMDR as one of the evidence-based treatments for PTSD?"

Dr. Gay: I'll refer to the literature on that. What I did pull up was an APA guide. It could have been outdated, but EMDR wasn't listed on the reference that I was looking at in preparing the slides. If it is evidence-based and recommended, I have absolutely no qualms with that. I'll refer to the research. It was just what I was doing in my search.

Dr. Rocco: Maybe I can chime in too. There are a couple of trials that look like they're not published yet on EMDR with PTSD and alcohol use disorder. Obviously, in preparation for this, I looked again and I see protocols right now. It looks like we're going to have a better answer to that question pretty soon.

Moderator: Wonderful. Next, we have questions for both of you. "How reliable are repressed memories?"

Dr. Gay: That is something that's a huge area of debate, and I wanted to actually talk more about the neurocognitive effects of trauma and so forth because the literature on this, as we know, goes back pretty much the 1990s and what was referred to as the memory wars and the work by Beth Loftus showing that we can implant memories in people. Unfortunately, therapists can talk to patients in such a way that they, in her studies, believed that something happened, which didn't. Her classic study on someone being lost in a mall as a child, and about 30% of people recall that memory is actually happening.

I would say, in treatment, I focus on helping the individual cope with their experience of trauma and in the therapy not ongoing into any questions or detail on the validity of the memories. I keep that to more of the legal domains or domains outside of the treatment that I do. As we know that it's just there's so much research or debate in that area that it is something I didn't focus on for that reason in this talk. Reliable or not, it's just that there's a lot out there. There's a lot of controversy.

Dr. Rocco: Yes. I think I would say the same thing. I think patients are the best source of information on their own experiences. Clinically, we're not, I think in a position where we need to question that a lot. I think we're best served by listening to our patients and just being careful about what we're bringing in, how we're providing our own interpretations of things. I think we're best off just listening to patients. They can tell us their experience. I'm purely a clinician. I don't get involved in the legal sense of things. At least not in that kind of a way. I don't find I struggle with what the patients say because they're just relating their experience to me.

Dr. Gay: Sometimes there can be other processes involved that do not include repression of memories, but rather reinterpretation of events and a process of what we would call normal forgetting, even for trauma memories. What I'm referring to is that sometimes patients can look at or experience something as a child through the child's mind and forget it. Especially things that may have been a form of abuse.

They may have been told that it was their fault or that they-- whatever that to not look at it as abuse. Then later through the adult's mind when they're an adult, maybe their child has some experience, they can reexamine what they experienced as a child and through this process of not thinking about it, think about it in a different way, where then it comes to light that what they experienced actually was trauma. It's different than repression but rather reinterpretation of something. Because we can-- actually, the research does seem to show we can forget things even of a traumatic nature. Not always, but sometimes, if that's helpful.

Moderator: Thank you. Have you ever applied gestalt therapy?

Dr. Rocco: I'm not a gestalt therapist.

Dr. Gay: I'd say in the sense of doing some share work sometimes, but it's not a main focus of my treatment.

Moderator: How would you reflect on how these brain changes impact adolescent substance users?

Dr. Gay: I worry, and I want to let Dr. Iannucci answer too, if he wants to, but I do worry, especially as the brain is developing during adolescence, we know the myelin of axons is still continuing well up into early adulthood. The brain is still developing and it's so crucial, I believe for brain health to not use substances, especially in a developing brain. I know that's one of the periods where people use substances the most. I just think it can have long-term impacts and I think providing psychoeducation on how dangerous it can be.

Dr. Rocco: Yes, I think that's the concern is that there may be lasting problems. There are some studies where it looks like what happens is you get-- basically you have a pause in development and then some things start to return again to where they might have been. It interrupts some of the capacities, development of some of the capacities. The trouble is there's so many important things happening in adolescents that even a delay is a problem that can have long-lasting implications. It's a major worry.

We do know that exposure to substances, you can draw a graph that the earlier they age that people are exposed to substances at all, the more likely they are to develop substance use disorders. It's obviously affecting the brain in a different kind of a way. There is that lasting risk for many people that perhaps there's some people that would not have developed a substance use disorder if they were the first drink was actually at age 21 and not at age 14. Even, waiting till 25 seems like a pipe dream in American culture. In some ways makes the most sense from a developmental neurobiology perspective.

Moderator: Thank you. We have time for maybe one or two more questions here. "Could you say something about the neurobiology of vigilance and the effects of vigilance on memory and executive?"

Dr. Rocco: Was that vigilance?

Moderator: Vigilance.

Dr. Gay: Are you referring to vigilance as hyper-focus or hyperarousal or attention? I'm not sure about the question, but I know that people can be hypersensitive to certain sounds, events, or situations if they've experienced a trauma. It also, we know attention regulates often what's really encoded. If someone's not vigilant or attending to something, it won't be encoded into memory all that well. If that's helpful.

Moderator: All right.

Dr. Gay: People with PDST may be more vigilant, hyper aroused, they may have an exaggerated startled response. If you're more vigilant to certain threats in your environment, you're going to be more likely to detect those threats even when they may not be there.

Dr. Rocco: Yes. If it's hypervigilance, that is definitely associated with people trying to self-medicate, to use substances to try to get a little relief because it can be pretty uncomfortable to be on edge all the time like that.

Dr. Gay: All right. Absolutely.

Moderator: I got our last question for today. "Can you comment on the effects of heavy marijuana youth on memory and cognitive functioning?" There are a few questions revolving around the topic of marijuana.

Dr. Gay: Yes. It doesn't help memory [laughs], it doesn't help attention.

Dr. Rocco: No. Yes. One of the challenges, I guess, we see very frequently, especially with younger people is you find folks who have ADHD and they do have ADHD and they will tell you and I believe them, that marijuana makes them feel better. It makes them function worse. It's very much a challenge. I think that has to do with, it relates to the temporal discounting. When I smoke right after I smoke or vape or whatever, I feel better. That has a strong valence. I know what that does, as opposed to, can you keep track of your grades for the semester and see what they're over a longer period of time? It is a little harder for people to have those things feel real longer-term things.

I think a lot of us are-- I'm very concerned about marijuana and it's not that everyone gets dependent on it, but that it's got other problems that it causes. Certainly, we're worried about its connection with potential psychosis for a small group of people, but an important group of people who can get quite ill. Then I know one of our former colleagues, Kevin Hill, he says, even though it's a small percentage of people who get addicted to marijuana, a small percentage of a big number with many more people using cannabis is a big number. It is something we're worried about.

Moderator: All right. Thank you so much for joining us, Dr. Gay and Dr. Iannucci, and thank you to all of our [crosstalk]

Dr. Rocco: Real pleasure.

Dr. Gay: It was an absolute pleasure. Thank you.

Moderator: We'd also like to thank McLean Hospital for making this webinar possible. A recording of this presentation will be emailed to everyone in two weeks' time. The recording will include the presentation slides as soon as the webinar has ended. A short survey will appear on your screen. Please take the survey and give us your feedback. We thank you for your attention and hope you have a great day.

[00:59:35] [END OF AUDIO]