

Ada Chat Transcription

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Kathleen Baril: First up, Dr. Phillip Zoladz, who's an associate professor of psychology. He's going to talk about his work from an NIH funded project. Let's see if I can get this right, that could help us understand why some people are more susceptible to traumatic memory formation and the development of post-traumatic stress disorder. And I'm going to let him take over.

Phillip Zoladz: Thank you Kathleen. So, I'm Phil Zoladz, can everyone hear me? Is this good? Okay. So today I'm going to be talking about emotional memory formation and how genetics might play a role in that. When I say emotional memory formation, I'm particularly talking about how stress influences memory. I've been studying stress and its role in memory formation for about the past fifteen years. So, the first question is why – why look at emotional memory formation? How is it relevant? And stress and stress memories play a role in everyday life.

We have sometimes very powerful memories that are produced from stressful experiences, like the terrorist attacks that occurred on 9/11. But, we also have times when stress can impair memory. So, you might have had a long day at work or it's around the holiday season, you went into the mall or something and then you come out, "where did I park my car?" That's what you can see here. We know that stress and emotion can both enhance or impair memory formation. The other reason that it's important to study it is because stress, and its effects on memories, is implicated in multiple psychological illnesses – such as post-traumatic stress disorder, major depression, and actually several others as well. With post-traumatic stress disorder, you actually have an interesting finding where, number one they have very powerful memories that have been produced from a stressful experience that they cannot get out of their heads. And that causes sleep disruption, it causes disruption in everyday life, and they also have memory impairment. Probably in part because of these traumatic memories that are constantly interfering with their attentional processes. With major depression, you have mainly memory impairments that you find. So, stress-related affects on cognition and memory-formation are prevalent in a lot of psychological disorders. That's one of the main reasons that I've been studying this.

Because we know that stress can enhance and impair memory, one big question that comes up is what mediates that difference? Why does stress sometimes enhance memory? Why does stress sometimes impair memory? Something that I've been looking at over the last ten years or so is what are the mechanisms for that? Specifically in the brain and physiological responses. So, that was not all supposed to jump up there at once like that. But, what we...I'm hoping that my...okay, I guess I'm going to have to pull it all up for the lines to come up. No? Okay. Why is it not...Something happened. Alright. There's supposed to be a bold white line that goes all the way across there in the middle. And that's supposed to signify baseline. What I'm trying to show here is, this graph is supposed to show on the y-axis the amount of learning and memory that happens. And on the x-axis, we have time. So we have stress onset and then we have seconds/minutes, and then minutes to hours after that. What we know now, and in part from some of the work we've done in my laboratory over the past five to six years is immediately after the stress onset, there is a major increase in arousal. And so, I think of heart rate, adrenaline

response. At that time, and that's that first blue rectangle there, there is a peak or an enhancement of learning that will occur. So, if you think about a stressful experience that you have, it's probably adaptive to have enhanced learning right around that time, so that you can remember what the stressor is, maybe what the threat is that could be threatening to survival. But, if you look over time, minutes to hours later, you'll see a drop below the baseline there. If learning occurs at that point, what we have found is that it is impaired. And this is not due to the arousal, this appears to be due primarily to – did it not come up? There it is – cortisol. Cortisol is what we commonly call a stress hormone. You see different physiological things, mechanisms that are associated with different effects of stress on learning and memory. Sorry that didn't pull up the correct way.

So, how do we study stress and memory in our lab? Clearly, we're not able to traumatize people, or overly stress them in the labs. So, we have to come up with a way to do that. And what we do is we bring participants in. Usually they're healthy undergraduate students from different classes around campus, and we expose them to some learning manipulation. It could be a list of words, it could be a classical conditioning task, really it's unlimited. We just have them learn something. And then, usually separated by 24 hours, we bring them back the next day. And we test their memory for that list of words, or whatever it is they learned. And then, we are going to stress them at some point. Before learning, before retrieval, it depends on what we're looking at. For our purposes today, I've been talking about stress right before learning. So, if we stress participants right before learning, we find that that enhances long term memory. What is the stress that we use? It's varied over the years. But, one of the main stressors that we use is something called the cold pressor test. I don't know if any of you have ever experienced an ice-cold water bath, a very very cold water bath, but we have a water that is kept at about zero degrees Celsius, and the participants have to put their hand in that for up to three minutes – and I think that some of my research assistants who are sitting out here could attest that that hurts. Right? It hurts a lot. Okay? It doesn't do any physical damage or tissue damage. I'd better get that on there. Okay? But it induces a nice physical and psychological stress response in participants. And so if we do that we would do that right before learning here for about three minutes and then have them learn something right afterwards. And see how that affects memory. And as I said, that enhances memory. If we separate the stressor by about 30 minutes, you actually find the opposite effect. You find that that leads to a memory impairment. Now, I'm simplifying this, there are many other factors that are involved – intensity of the stressor, individual differences, sex different, males versus females – there are many things that come into play with that. But this is the overarching theme in the general findings that we observe.

So, what does genetics – uh, there we go – what does genetics have to do with it? One of the things that we put in this national institute of health grant is that we believe that some individual differences that I just mentioned, particularly genetics, might influence this response. So, if you go back to that figure that I showed a couple of slides ago, instead of just having stress cause an immediate enhancement and then an impairment, we predict that there is genetic variability among individuals – certain genes that some people have and that others might not, or what we call polymorphisms, where they're different in some people – that might create a really big enhancement of learning and memory after stress or a really big impairment of learning and memory after stress. And so that's one of the things that we've been looking at, what particular genes might predict that kind of a response in individuals? If we could find out that this gene, 'x' for instance, causes a huge increase in learning and memory right after stress, that might

tell us that individual is more susceptible to traumatic memory formation. Because he or she is really going to produce a strong memory right after the stress onset.

You take your DNA, you combine it with a major stressful experience, that is stressing your brain, and what you theoretically might get is an even greater enhancement or greater impairment of memory as a result. And that might ultimately relate to the development of PTSD or major depression or others. So I'm going to give you an example of susceptibility factor that we have discovered in our work, and we have published on in the last few years. And this is the most complicated thing that you'll see all day, but I'm going to really simplify it. The ADRA2B deletion variant. Wow. Alright, so that is just a variant in your genetics that some people have. It's actually rather prevalent. Maybe up to 33% of Caucasians at least have this particular variant, whereas the others do not. Now, what does this variant predict? It's associated with more arousal. Particularly to emotional situations and stress. It's also, now this is another one, associated with increased amygdala activity. What is the amygdala? The amygdala is a brain area that's involved in arousal. So, when you are afraid. If it's late at night and you're walking to your car and you hear something, your amygdala's going off. So, when we're stressed the amygdala is going to be that alarm that's associated with arousal and people with this variant have a stronger alarm. So we predict if we stress them, you're going to freak them out. They're going to have a much greater response, which then might lead them to have greater affects on learning and memory.

So, our particular prediction with this specific genetic variant was, if we stress them right before learning, and they have this super arousal response, we might find that that enhances 24 hours, their memory for whatever they might learn. Because, if you remember, going back to that slide I showed you earlier, that first part, right after stress where you have enhancement of learning, that's because of arousal. And these people show a huge increase in arousal.

So, what have we discovered? I have just a couple graphs here. In this first figure, we're actually not looking at anything related to stress effects yet. If you just look at people with this deletion variant – which I'm calling a genetic variant – and we compare them to what I've put up there as normal – we call them wild type where they have the normal genotype. And if you look at memory that these individuals have for arousing words versus non-arousing words – arousing words would be like 'murder,' 'rape,' things like that, non-arousing like 'rice,' 'table.' People with this genetic variant, at baseline not even taking stress into consideration, have greater memory for arousing words than people without it. And you see no difference in the non-arousing words. What if we stress them? Here is the main finding. If you stress these individuals right before they learn, you find that the people who show an enhancement in memory are the ones that have this genetic variant. The ones that have this greater arousal response. And you can see that up there, that group on the far left had the genetic variant combined with stress is the only group to have that enhancement of memory.

What does this all mean? What else are we doing? We're also looking at how do these genetic variants, coupled with stress, how does that impact fear learning? For the most part we've been doing lists of words. But now we're actually creating a fear memory in participants and seeing how the genetic variants influence that. Because, people with PTSD, they don't just have a memory for words. They have a fear memory that is intruding. So we want to see how is that influenced? And that's the second study that these wonderful people are running right now. We've also submitted another grant that we're going to look at similar things, genetic influences, sex differences, and other factors on fear generalization. Because people who have PTSD, they ... think of someone who goes off to war and then

comes back to the US and they freak out when they hear a car backfire. They're generalizing their fear wave. So that's another thing that we're looking at as well.

And the importance of all this is ... the, uh, the sexy area of stress research, and a lot of research in general – had to get that in there – a lot of research in general is, who is more susceptible to certain illnesses. We see that in pharmacy, we see more susceptible to certain medications or ... we see that in psychology. If we can find out if these genetic variants predict someone to respond more to stress, that might tell us who's more likely to develop PTSD going off to war. And you don't send that person. Or you help them have treatment beforehand. So, I just want to acknowledge everyone who has been involved. So, some of these individuals in their blue box are all my undergraduate research assistants who are currently or who have helped on this grant. Boyd Rorabaugh obviously has collaborated in assaying cortisol levels in participants and other hormones. We've been collaborating with Emory University who are collaborators on this grant. And then the National Institute of Mental Health. And Dr. Rorabaugh is going to be talking about some other research we have collaborating on. And I just want to make sure that some of my other research assistants from his study that he'll be talking about were up there as well.

Thank you and I guess I can take questions if you have any?

Yep?

Audience question: I'm a bad scientist, so, how do you test for the genetic variant?

Phillip Zoladz: So for the genetic variant you can do it in various ways, but we collect a big nice hefty saliva sample from participants. And we send that off to a company that actually will do it for us, where they'll be able to look at the DNA and look at the sequence of the nucleic acids and all that fun stuff and see if it's different in certain individuals. They can give us the genotypes.

Yeah?

Audience question: I'm just wondering. What are the applications of this? For example, if I want my kid to do well at school, do I have to scare them before the exam?

Phillip Zoladz: Good question. There's actually been some research on that where they've taken people at universities and they've stressed them or aroused them right after a lecture and they show better memory. It is good to – like you can ask my students, when I'm in class sometimes, I'll act pretty humorous sometimes. At least I think it's humorous. I'll goof off a little. I'll try to create an emotional arousal in them to get to remember it. Because, yeah, anything that is tied to arousal will be enhanced in memory. I'm not saying you have to do that, but it can help.

Yeah?

Audience question: If someone was in the library here in the dark and is attacked somehow and then they see the individual face-to-face, right after. Are you saying that if they have the right gene they'll have a better memory of what that person looks like than if they don't?

Phillip Zoladz: Potentially yes. I say potentially because when you're stressed there are a number of things that happen. For instance, you have attentional focus, so we tend to remember certain things better than others. We don't always remember like the specific face or the color of the shirt, but we'll

remember a gist about the experience. Maybe, though, yeah. If some of these individuals have the particular, they could remember some of those details more. But, yeah, that would be the prediction. If I'm raped and I have a particular genotype I might be more likely to have a traumatic memory from that experience. Therefore, then, more intrusion from that memory and more PTSD symptoms.

Audience question: I have talked to people who were in the 1964 last earthquake. And some of them, it was so traumatic, you know there were people who died right beside them ... and their minds were so sharp as if it was, and you've heard people say you know "I remember just like it was yesterday" of some traumatic thing. If you could go back to those kind of people and see what gene they have and compare to someone who in a wreck and doesn't remember ... if maybe?

Phillip Zoladz – Yeah, there could be, uh ... and surprisingly enough the connection between genetics and traumatic memory formations has really not been studied as much up until the last 5 to 10 years. The other thing you mentioned there was important because some people don't remember as well. Some people have, like, a traumatic amnesia. Or something. And that might be related to that down slope where you have impaired memory. Some people might not have that enhancement and they just ... as soon as that traumatic experience happens they shift over and they don't, they can't learn anything. So they have PTSD but they can't remember why. But if we could go back and look at people like that, you could have a nice study on maybe existing data.