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Memory is such an everyday thing that we almost take it for granted. We all remember what we had for breakfast this morning or what we did last weekend. It's only when memory starts to fail that we appreciate just how amazing it is and how much we allow our past experiences to define us.

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But memory is not always a good thing. As the American poet and clergyman John Lancaster Spalding once said, "As memory may be a paradise from which we cannot be driven, it may also be a hell from which we cannot escape." Many of us experience chapters of our lives that we would prefer to never have happened. It is estimated that nearly 90 percent of us will experience some sort of traumatic event during our lifetimes. Many of us will suffer acutely following these events and then recover, maybe even become better people because of those experiences. But some events are so extreme that many -- up to half of those who survive sexual violence, for example -- will go on to develop post-traumatic stress disorder, or PTSD.

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PTSD is a debilitating mental health condition characterized by symptoms such as intense fear and anxiety and flashbacks of the traumatic event. These symptoms have a huge impact on a person's quality of life and are often triggered by particular situations or cues in that person's environment. The responses to those cues may have been adaptive when they were first learned -- fear and diving for cover in a war zone, for example -- but in PTSD, they continue to control behavior when it's no longer appropriate. If a combat veteran returns home and is diving for cover when he or she hears a car backfiring or can't leave their own home because of intense anxiety, then the responses to those cues, those memories, have become what we would refer to as maladaptive. In this way, we can think of PTSD as being a disorder of maladaptive memory.

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Now, I should stop myself here, because I'm talking about memory as if it's a single thing. It isn't. There are many different types of memory, and these depend upon different circuits and regions within the brain. As you can see, there are two major distinctions in our types of memory. There are those memories that we're consciously aware of, where we know we know and that we can pass on in words. This would include memories for facts and events. Because we can declare these memories, we refer to these as declarative memories.

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The other type of memory is non-declarative. These are memories where we often don't have conscious access to the content of those memories and that we can't pass on in words. The classic example of a non-declarative memory is the motor skill for riding a bike. Now, this being Cambridge, the odds are that you can ride a bike. You know what you're doing on two wheels. But if I asked you to write me a list of instructions that would teach me how to ride a bike, as my four-year-old son did when we bought him a bike for his last birthday, you would really struggle to do that. How should you sit on the bike so you're balanced? How fast do you need to pedal so you're stable? If a gust of wind comes at you, which muscles should you tense and by how much so that you don't get blown off? I'll be staggered if you can give the answers to those questions. But if you can ride a bike, you do have the answers, you're just not consciously aware of them.

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Getting back to PTSD, another type of non-declarative memory is emotional memory. Now, this has a specific meaning in psychology and refers to our ability to learn about cues in our environment and their emotional and motivational significance. What do I mean by that? Well, think of a cue like the smell of baking bread, or a more abstract cue like a 20-pound note. Because these cues have been pegged with good things in the past, we like them and we approach them. Other cues, like the buzzing of a wasp, elicit very negative emotions and quite dramatic avoidance behavior in some people.

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Now, I hate wasps. I can tell you that fact. But what I can't give you are the non-declarative emotional memories for how I react when there's a wasp nearby. I can't give you the racing heart, the sweaty palms, that sense of rising panic. I can describe them to you, but I can't give them to you. Now, importantly, from the perspective of PTSD, stress has very different effects on declarative and non-declarative memories and the brain circuits and regions supporting them. Emotional memory is supported by a small almond-shaped structure called the amygdala and its connections. Declarative memory, especially the what, where and when of event memory, is supported by a seahorse-shaped region of the brain called the hippocampus.

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The extreme levels of stress experienced during trauma have very different effects on these two structures. As you can see, as you increase a person's level of stress from not stressful to slightly stressful, the hippocampus, acting to support the event memory, increases in its activity and works better to support the storage of that declarative memory. But as you increase to moderately stressful, intensely stressful and then extremely stressful, as would be found in trauma, the hippocampus effectively shuts down. This means that under the high levels of stress hormones

that are experienced during trauma, we are not storing the details, the specific details of what, where and when.

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Now, while stress is doing that to the hippocampus, look at what it does to the amygdala, that structure important for the emotional, non-declarative memory. Its activity gets stronger and stronger. So what this leaves us with in PTSD is an overly strong emotional -- in this case fear -- memory that is not tied to a specific time or place, because the hippocampus is not storing what, where and when. In this way, these cues can control behavior when it's no longer appropriate, and that's how they become maladaptive. So if we know that PTSD is due to maladaptive memories, can we use that knowledge to improve treatment outcomes for patients with PTSD?

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A radical new approach being developed to treat post-traumatic stress disorder aims to destroy those maladaptive emotional memories that underlie the disorder. This approach has only been considered a possibility because of the profound changes in our understanding of memory in recent years. Traditionally, it was thought that making a memory was like writing in a notebook in pen: once the ink had dried, you couldn't change the information. It was thought that all those structural changes that happen in the brain to support the storage of memory were finished within about six hours, and after that, they were permanent. This is known as the consolidation view.

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However, more recent research suggests that making a memory is actually more like writing in a word processor. We initially make the memory and then we save it or store it. But under the right conditions, we can edit that memory. This reconsolidation view suggests that those structural changes that happen in the brain to support memory can be undone, even for old memories.

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Now, this editing process isn't happening all the time. It only happens under very specific conditions of memory retrieval. So let's consider memory retrieval as being recalling the memory or, like, opening the file. Quite often, we are simply retrieving the memory. We're opening the file as read-only. But under the right conditions, we can open that file in edit mode, and then we can change the information. In theory, we could delete the content of that file, and when we press save, that is how the file -- the memory -- persists. Not only does this reconsolidation view allow us to account for some of the quirks of memory, like how we all sometimes misremember the past, it also gives us a way to destroy those maladaptive fear memories that underlie PTSD. All

we would need would be two things: a way of making the memory unstable -- opening that file in edit mode -- and a way to delete the information.

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We've made the most progress with working out how to delete the information. It was found fairly early on that a drug widely prescribed to control blood pressure in humans -- a beta-blocker called Propranolol -- could be used to prevent the reconsolidation of fear memories in rats. If Propranolol was given while the memory was in edit mode, rats behaved as if they were no longer afraid of a frightening trigger cue. It was as if they had never learned to be afraid of that cue. And this was with a drug that was safe for use in humans. Now, not long after that, it was shown that Propranolol could destroy fear memories in humans as well, but critically, it only works if the memory is in edit mode.

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Now, that study was with healthy human volunteers, but it's important because it shows that the rat findings can be extended to humans and ultimately, to human patients. And with humans, you can test whether destroying the non-declarative emotional memory does anything to the declarative event memory. And this is really interesting. Even though people who were given Propranolol while the memory was in edit mode were no longer afraid of that frightening trigger cue, they could still describe the relationship between the cue and the frightening outcome. It was as if they knew they should be afraid, and yet they weren't. This suggests that Propranolol can selectively target the non-declarative emotional memory but leave the declarative event memory intact. But critically, Propranolol can only have any effect on the memory if it's in edit mode.

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So how do we make a memory unstable? How do we get it into edit mode? Well, my own lab has done quite a lot of work on this. We know that it depends on introducing some but not too much new information to be incorporated into the memory. We know about the different chemicals the brain uses to signal that a memory should be updated and the file edited. Now, our work is mostly in rats, but other labs have found the same factors allow memories to be edited in humans, even maladaptive memories like those underlying PTSD. In fact, a number of labs in several different countries have begun small-scale clinical trials of these memory-destroying treatments for PTSD and have found really promising results.

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Now, these studies need replication on a larger scale, but they show the promise of these memory-destroying treatments for PTSD. Maybe trauma memories do not need to be the hell from which we cannot escape.

12:06

Now, although this memory-destroying approach holds great promise, that's not to say that it's straightforward or without controversy. Is it ethical to destroy memories? What about things like eyewitness testimony? What if you can't give someone Propranolol because it would interfere with other medicines that they're taking?

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Well, with respect to ethics and eyewitness testimony, I would say the important point to remember is the finding from that human study. Because Propranolol is only acting on the non-declarative emotional memory, it seems unlikely that it would affect eyewitness testimony, which is based on declarative memory. Essentially, what these memory-destroying treatments are aiming to do is to reduce the emotional memory, not get rid of the trauma memory altogether. This should make the responses of those with PTSD more like those who have been through trauma and not developed PTSD than people who have never experienced trauma in the first place. I think that most people would find that more ethically acceptable than a treatment that aimed to create some sort of spotless mind.

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What about Propranolol? You can't give Propranolol to everyone, and not everyone wants to take drugs to treat mental health conditions. Well, here Tetris could be useful. Yes, Tetris. Working with clinical collaborators, we've been looking at whether behavioral interventions can also interfere with the reconsolidation of memories. Now, how would that work?

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Well, we know that it's basically impossible to do two tasks at the same time if they both depend on the same brain region for processing. Think trying to sing along to the radio while you're trying to compose an email. The processing for one interferes with the other. Well, it's the same when you retrieve a memory, especially in edit mode. If we take a highly visual symptom like flashbacks in PTSD and get people to recall the memory in edit mode and then get them to do a highly engaging visual task like playing Tetris, it should be possible to introduce so much interfering information into that memory that it essentially becomes meaningless. That's the

theory, and it's supported by data from healthy human volunteers. Now, our volunteers watched highly unpleasant films -- so, think eye surgery, road traffic safety adverts, Scorsese's "The Big Shave." These trauma films produce something like flashbacks in healthy volunteers for about a week after viewing them. We found that getting people to recall those memories, the worst moments of those unpleasant films, and playing Tetris at the same time, massively reduced the frequency of the flashbacks. And again: the memory had to be in edit mode for that to work.

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Now, my collaborators have since taken this to clinical populations. They've tested this in survivors of road traffic accidents and mothers who've had emergency Caesarean sections, both types of trauma that frequently lead to PTSD, and they found really promising reductions in symptoms in both of those clinical cases.

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So although there is still much to learn and procedures to optimize, these memory-destroying treatments hold great promise for the treatment of mental health disorders like PTSD. Maybe trauma memories do not need to be a hell from which we cannot escape.

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I believe that this approach should allow those who want to to turn the page on chapters of their lives that they would prefer to never have experienced, and so improve our mental health.

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Thank you.

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(Applause)