Erasing Memories:

A Solution for Emotional Trauma?

Can erasing memories become a realistic and practical solution for victims plagued by traumatic memories?

Emily Low

The ability to erase memories might appear closer to the realm of science fiction than reality. However, erasing memories is a very real possibility in the present. For the past few decades, scientists have been working to understand memories and emotions in order to remove traumatic memories Such an accomplishment would help relieve the suffering of those with posttraumatic stress disorder, addiction, or a variety of other conditions in which memory playsh a key role. To explore the possible applications of erasing memories, a brief mechanism of memory formation will be presented, followed by an overview of some of the research currently being done on this topic.

Some of the most vivid memories that people hold are based on a single, meaningful event. Often, the profound meaning these memories have comes from the emotions associated with them. Recollection of the memory sends a clear flash of images through the mind, accompanied by an onslaught of feelings. What is playing in the brain, then, is perceived to be more like the event happening again before one's eyes, rather than something that already occurred in the past, creating a much stronger experience of the memory. Scientists sometimes refer to these recollections as "flashbulb memories" (Reisberg and Hertel 2003). Despite the clarity these memories hold for the person recalling them, however, scientists note that a caveat exists. The associated emotions can function to focus a memory at a specific center so that certain details are recalled with distinction. On the other hand, this narrowing of attention to just one aspect of the memory often distorts the memory of what occurred outside of this center (Reisberg and Hertel 2003). The consequence of recalling one object or instance better than the surroundings that place the memory in context might perhaps cause an already emotional recollection to be even more jarring.

The profound effect emotional memories have on a person forms the basis for why one might want to erase particularly traumatic memories. Memories and emotions have been found to be directly correlated to each other: the organs that are at least partially responsible for both memory and emotion lie in close proximity in the brain. The amygdala mediates emotion, while the hippocampus plays a key role in memory formation, and both are nestled between the two hemispheres of the brain (Glannon 2006). Removal of either one of these organs results in a change in the respective function. For example, if the hippocampus is removed, a patient may still remember older memories that were experienced before the operation, but be incapable of creating any new memories (Dowling 2004). This implies that, at least in a rough sense, it is possible to prevent the creation of a memory.

An important question stems from this implication. If memories can be prevented from being formed, is it possible to manipulate the brain so that memories are forgotten?

Memories, while arguably necessary for defining a person's consciousness as a human being, can sometimes have negative effects on people who have traumatic long-term memories. For example, sufferers of posttraumatic stress disorder or addiction associate certain memories with strong emotions that may impact their ability to go through everyday life. To cure disorders like these, scientists have entertained the idea of erasing the traumatic memories that cause them. However, erasing memories of any kind is not simple. Completing the task of understanding the way long-term memories operate is a prerequisite for such an undertaking.

"Memories and emotions have been found to be directly correlated to each other: the organs that are at least partially responsible for both memory and emotion lie in close proximity in the brain."

At a molecular level, the formation of long-term memories occurs at connections between neural cells,

called synapses. The construction of these synapses is dependent on two events: the initial consolidation of the memory, followed by the recollection of the memory (Sacktor 2008). Collectively, the mechanism underlying this phenomenon is referred to as long-term potentiation (LTP). The response to an external stimulus during the event itself allows for the formation of the synapse that creates the memory. Subsequent stimuli that prompt recall of that memory maintain the synapse so that information can be passed between neurons, even years after the experience itself. This is the fundamental idea behind long-term memories. As long as the connection between the cells remains, the pathway for memory retrieval exists and allows for the memory to be recalled (Dowling 2004).

Interestingly, the stimuli that prompt the memory to resurface do not need to be as strong as the initial one that formed the memory. In fact, even a comparatively weak stimulus may be enough to reactivate the memory (Dowling 2004). This stimulus comes in the form of chemical messengers known as neurotransmitters. When LTP occurs in the brain, these messengers are released into the synaptic cleft that exists between one neuron and another. The chemical messengers diffuse across the cleft and bind to receptors on the recipient cell. This binding causes ions from outside the cell to flow inside, activating a vast array of molecules, one of which is known as calmodulin. Calmodulin is thought to increase the response of the post-synaptic cell to future stimuli (Dowling 2004). While the mechanism for calmodulin's activities are unknown, this implies that calmodulin may account for why even subsequent weak triggers can cause a recollection of a memory and strengthen the synapse. When this synapse is strong, the connection required for the recollection of a long-term memory has been formed.

Since synapses are continually being formed as we collect new memories and solidified as we create long term memories, the human brain is constantly undergoing anatomical changes (Sacktor 2008). For example, proteins interact with receptors on brain cells to cause branches to grow or retract, creating and removing synapses as memories are formed or forgotten. This process of strengthening, weakening, and silencing synaptic activity is referred to neuromodulation (Dowling 2004). The fact that this occurs has lead some scientists to believe that established memories are not as static as they were once believed to be. The act of recalling memories might not just strengthen a synapse, but alter it as well in a dynamic process termed reconsolidation (Miller 2010). Since the brain naturally alters and prunes its connectivity this way, artificial alteration may be possible by a similar process. Scientists are targeting such approaches like creating and removing synapses to erase long term memories.

Since the formation of synapses is initially responsible for the existence of long-term memories, preventing their formation would be a logical approach to prevent the establishment of these memories. In a situation where a person has just been subjected to a traumatic situation, preventing the impression from the event from establishing itself in the brain would effectively erase the memory. From this angle, scientists have gained some understanding of how inhibiting molecules with roles in memory establishment may halt the formation of long term memories.

> "If memories can be prevented from being formed, is it possible to manipulate the brain so that memories are forgotten?"

One of the molecules that has been found to function in long-term memory formation is called brain-derived neurotrophic factor, or BDNF. Initial studies by Yamada and Nabeshima at Kanazawa University and the Nagoya University Graduate School of Medicine demonstrated that BDNF is necessary in rats for spatial memory acquisition, as well as memory retention and recall. When non-functional forms of the neurotrophic factor were implanted in rats in place of the functioning factors, rats that had been taught various tasks experienced impaired spatial memory for the task they had learned, presumably because no functioning BDNF was available to form memories about the tasks they had been taught. In addition, BDNF was found to activate another protein kinase, referred to as mitogen-activated protein kinase, or MAPK. MAPK has been implicated in the acquisition of fear-related memories (Yamada and Nabeshima 2003). Since BDNF not only appears to be a key player in memory formation but also emotion association, further investigation into the mechanism of BDNF could be important in emotional memory research, not only to erase memories, but also to aid in the understanding of why traumatic memories evoke such vivid emotional responses.

Furthermore, research in 2009 by Slipczuk et al., at the Universidad de Buenos Aires in Argentina demonstrated that BDNF functions in a molecular process called the BDNF/mTOR pathway, which appears to be at least partially responsible for the effects noted by Yamada and Nabeshima. In this pathway, BDNF activates mTOR, a protein kinase previously implicated in synaptic plasticity, which controls levels of a signaling molecule, GluRI. This last molecule has been found to be necessary to

consolidate memories (Slipczuk et al. 2009). The ability to change levels of GluRI could have an important effect on whether or not a memory is formed.

In order to investigate the effects of manipulated levels of GluRI, the scientists varied the levels of factors that controlled GluRI. In experiments on memory formation and retention in rats, the pathway could be disrupted by controlling the function of mTOR. Rather than altering levels of BDNF to control mTOR function, however, the researchers mimicked decreased levels of BDNF by using another molecule that can inhibit mTOR function, called rapamycin. Injections of rapamycin in crucial time windows associated with LTP resulted in a deficit in long-term memory formation in rats. If lowered levels of mTOR function can prevent effective long-term memory formation, then controlling the amount of BDNF, which activates mTOR, could have the same effect as rapamycin (Slipczuk et al. 2009). For this reason, BDNF may be a tool for understanding the mechanisms of long-term memory formation and maintenance, in the quest for a realistic procedure with which to erase memories.

However, as a consequence of the human brain being so malleable, or plastic, the formation of a synapse is not all that is necessary to have a long-term memory. The synapse must somehow be maintained so that the memory can be retrieved, months or even years after the actual event itself. Understanding the mechanisms that form and maintain these long-term synapses has been the focus of several researchers who have been seeking ways to manipulate the process of memory-making. If one can understand how these synapses are maintained, then one might be able to reverse the process to effectively erase memories.

With this as a major goal of research, Todd Sacktor and others at the SUNY Downstate Medical Center in New York have been investigating one of the mechanisms implicated in maintaining LTP and long-term memories (Yong 2010). Protein kinases were first associated with long-term memory formation by Dr. James Schwartz in the late 1980's, and research in recent decades has further elucidated the functions of these proteins. One in particular, the activated protein kinase referred to as PKMzeta, has been found to function in the brain by maintaining LTP so that a memory can be stored (Sacktor 2008).

> "Who chooses to whom the treatment is administered?"

In a series of experiments, PKMzeta was examined in the context of spatial long-term memory in mice. Mice were placed on a shock platform and would learn to avoid the area that they associated with the shock by utilizing the spatial markers in the surrounding environment. The following day, the mice were injected with a selective kinase inhibitor, ZIP, which would, at least theoretically, inhibit the function of PKMzeta, and placed back on the platform. Whereas the control mice remembered the zone in which they were shocked and avoided it, the mice injected with ZIP explored the platform as they had the first time and experienced the same shock. Since ZIP could be administered even after mice demonstrated memory for the learned task, it was not interfering with memory formation but with retention. Interestingly, the mice could still relearn to avoid the zone and maintain the short-term memory to stay away from the shock region. In addition, further experiments demonstrated that even after the half life of PKMzeta and ZIP had passed and the molecules were degraded, the memory did not resurface. Hence, ZIP was not interfering with memory recall, either. This implies that ZIP can interfere with LTP to prevent the maintenance of a synapse so that a previously established memory is erased (Sacktor 2008).

Figure 1. The loss of a memory: the memory of the girl playing with the teddy bear has faded away and only the teddy bear is remembered.

PKMzeta has been found at many parts of the brain that store different types of memory. For example, the hippocampus, which stores informational memory, and the amygdala, which stores emotional memory, have both been found to contain functional levels of the molecule. For this reason, PKMzeta is being targeted as a molecule that might be used to erase memories associated with emotions. Research on these molecules could eventually help scientists gain an understanding of how they might be used to erase memories associated with addiction or pain (Yong, 2010).

Understanding exactly how these complex interactions work in the brain is crucial to being able to safely manipulate memories one day. The research

listed above is only a small part of the larger scope of projects that are being and still need to be conducted. Concerns over the ethical implications of manipulating memories are substantial, and many of them hinge on the claim that too little is known about the way these mechanisms work to be able to successfully erase memories. For example, scientists know that LTP is not just present in the hippocampus and amygdala, but also in other regions of the brain (Dowling 2004). Consequentially, disrupting LTP could quite possibly affect other brain functions, creating undesirable, and as of now, undocumented side effects. For example, preventing a person's brain from creating one memory may result in the inability to make memories for the rest of his or her life. This disability to remember anything beyond a certain point in life can prevent a person from recognizing where his or her existence lies in time. In addition, these experiments have largely been performed on animals with which humans cannot explicitly communicate. Consequentially, whether or not other memories unrelated to the task have been erased is something that scientists do not yet know. For these reasons and others, people are cautious about erasing memories to help those who suffer from unpleasant long-term memories.

In addition, considering how to apply the ability to erase memories is necessary. Who chooses to whom the treatment is administered? After all, one might reason that if a traumatic event has just occurred, it is not quite possible to judge whether a short-term or long-term memory will be formed, or whether it will be dulled over time. On the other hand, if treatment is not provided soon enough, it may be too late to help the victim (Glannon 2006). A careful judgment of who requires treatment and when is ethically important, and this matter must also be addressed before the erasing of memories becomes an accepted practice.

Memories form a crucial part of who we, as human beings with a sense of the soul, are. Erasing them is not a feat to be taken lightly. To achieve such an ability, a lot of effort has already been put into research, and more effort is sure to follow. In addition, careful consideration must be invested in order to figure out when it can be used. Decades ago, the ability to make a person forget forever would have been tantamount to magic. Today, the possibility is within reach, making the ability to judge the applications and limitations of altering human memory vital and important.

References

Dowling, John. 2004. Great Brain Debate: Is it Nature or Nurture? Washington, DC: National Academies Press. http://site.ebrary.com/lib/berkeley/docDetail.action?docID=10071479&p00=great%20brain%20debate.

Glannon, Walter. 2006. Bioethics and the Brain. New York: Oxford University Press. http://site.ebrary.com/lib/berkeley/docDetail.action?docID=10283673&p00=bioethics%20brain.

Miller, Greg. 2010. "How Our Brains Make Memories." Smithsonian Magazine, May. Accessed October 14, 2010. http://www.smithsonianmag.com/science-nature/How-Our-Brains-Make-Memories.html

Reisberg, Daniel and Friderike Heuer. 2003. "Memory for Emotional Events", in Memory and Emotion, edited by Daniel Reisberg and Paula Hertel. New York: Oxford University Press. http://site.ebrary.com/lib/berkeley/docDetail.action?docID=10085293&p00=memory%20emotion.

Sacktor, Todd Charlton. 2008. "PKMzeta, LTP Maintenance, and the Dynamic Molecular Biology of Memory Storage." Progress in Brain Research 169: 27-40. Accessed October 14, 2010. doi:10.1016/S0079-6123(07)00002-7.

Slipczuk L, Bekinschtein P, Katche C, Cammarota M, Izquierdo I, et al. 2009. "BDNF Activates mTOR to Regulate GluR1 Expression Required for Memory Formation." PLoS ONE. 4(6): e6007. Accessed November 9, 2010. doi:10.1371/journal.pone.0006007.

Yamada, Kiyofumi and Toshitaka Nabeshima. 2003. "Brain Derived Neurotrophic Factor/TrkB Signalling in Memory Processes." Journal of Pharmacological Sciences 91: 261-270. Accessed November 9, 2010. http://www.jstage.jst.go.jp/article/jphs/91/4/91_267/_article/-char/en.

Yong, Ed. 2010. "The Memory Molecules: Interview with Todd Sacktor (and a feature in Eureka)". Not Exactly Rocket Science, January 7. Accessed October 14, 2010. http://blogs.discovermagazine.com/notrocketscience/2010/01/07/the-memory-molecules-interview-with-todd-sacktor-and-a-feature-in-eureka/.

Image Sources

www.cgtextures.com
http://mayang.com/textures