MEMORY MODIFICATIONS AND ETHICAL IMPLICATIONS

Ross Michael Reul, Jr.

Plan II Honors Program
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Laura L. Colgin, Ph.D.
Department of Neuroscience
Supervising Professor

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Rebecca A. Wilcox, Ph.D.
Honors & Scholarships, College of Natural Sciences
Second Reader

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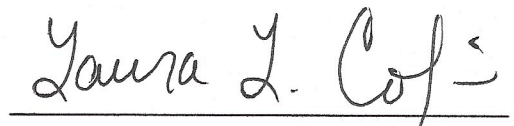

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ABSTRACT

Author: Ross Michael Reul, Jr.

Title: Memory Modifications and Ethical Implications

Supervising Professors: Laura L. Colgin, Ph.D. and Rebecca A. Wilcox, Ph.D.

Memory is a complex mental phenomenon that connects us to our past. It allows us to learn and better navigate our world on a day-to-day basis, but more importantly, it helps us to form an idea of who we are as a person, a sense of self, or an identity. Still, we forget most of what we perceive at any moment, and even that which we do remember is extremely fallible. The complexity of memories is that they are stored in the brain in such a way that they are vulnerable to new information and constantly reformed through a process known as reconsolidation. While this happens naturally in the brain, there are methods of promoting memory reconsolidation such that specific memories can be modified, suppressed, or enhanced. Three such instances of memory modification are false memories, molecular memory modifications, and direct stimulation of memory storing neurons. False memories are a psychological method of implanting false childhood memories in test subjects through suggestible discourse, while molecular memory modifications involve a similar process with the aid or manipulation of molecules known to have a role in the reconsolidation process. This paper reviews the current literature on memory modifications and memory neuroscience before a review of the current ethical debate on memory research and modification. It then puts forth an ethical framework for how to proceed with human memory research as neuroscientists and psychologists develop increasingly precise methods of influencing the natural functions of the human brain.

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Introduction

Memory is an essential aspect of the human experience. Our memory acts as a survival adaptation in that we remember negative or harmful experiences and avoid them in future situations. It stores aspects of our daily perceptions and links them to sensory and emotional cues. In this way memory also plays a role in our moral development, tying feelings of regret or satisfaction to past actions. Our memory is also intrinsically tied to our personal identity and sense of self. It connects our present self to our past experiences, while allowing us to imagine future scenarios.

For many centuries, philosophers and writers have commented on the inadequacies and frailties of the human memory. From Augustine in his *Confessions* to Descartes in his *Meditations* to modern autobiographers, those writing about their lives and experiences have expressed the idea that their memory of past events is not infallible, but rather limited and untrustworthy. Recently, vulnerabilities in memory have become a focus of psychological and neuroscientific research. As neuroscientists continue to understand the underlying mechanisms of the mind, novel methods of artificially exploiting brain functions tend to follow. The same is true for memories, and recent findings regarding the processes of memory formation, storage, and retrieval have opened up possibilities for memory interventions, wherein memories may be purposefully altered, suppressed, or enhanced. To better understand memory modifications and the ethical considerations related to their use in humans, I begin with an explanation of the neuroscience behind memory formation and recall. I then address the significant research on false memories, a purely psychological method of altering, and even implanting, memories in test subjects, that has provided

substantial insights into the nature of modified memories and their behavioral consequences. I next discuss various methods of molecular memory modification, whereby particular memories are activated while pharmacological interventions are used to enhance or suppress the targeted memory. I finish with experimental memory modification technologies involving light or electric stimulation of the brain and how to proceed with the possible integration of memory modifying techniques into medical or judicial practice in an ethically sound manner.

Memory Formation and Reconsolidation

Memory is a complex mental process, and there are many different types of memory. The initial stage of memory, called sensory memory, is the automatic response to perceptual stimuli that degrades very quickly when we are not attended toward the stimulus. The initial sensory input memory then enters short-term memory, or working memory, which involves holding a small set of information, usually 5-9 things, in mind for a short period of time, usually no more than a minute (Bear, Connors, & Paradiso, 2016). Short-term memories allow us to perform day-to-day tasks such as holding a conversation, but they are also quickly degraded when attention is distracted.

While sensory memory and short-term memory involve many unconscious processes, long-term storage of memories involves more conscious processing. Long-term memory is further divided into procedural, semantic, and episodic memory (Bear et al., 2016). Procedural memories often involve what may be called "muscle memory" and are involved in our ability to perform actions such as throwing a baseball. Semantic memory is memory for facts. Episodic memory is memory for autobiographical details of past experiences. Aspects of memories that make it into long-term memory can be stored indefinitely.

Each memory about our life was perceived by our senses, sent to our short-term memory where it underwent unconscious processes such as object recognition, then sent to our long-term memory for more conscious processing, before being archived somewhere in our mind. Each sensory perception that we take in is sent to the brain through a series of neurons, or nerve cells. Neurons send electrical signals called action potentials that propagate to the spinal cord and specific brain regions. Neurons in the brain

then receive and process the incoming electrical signals through their own connections. Memories are, therefore, products of electrical signals sent throughout different regions of the brain.

While the brain regions involved in many nervous functions such as speech and motor control had been located in the brain, up until the mid 1950s memory was regarded as a mental task that was not specific to any region (Squire & Wixted, 2011). Then Dr. William Scoville, a neurosurgeon, treated a patient known as H.M. for uncontrollable seizures by bilateral resection of his hippocampus. Following the surgery, H.M. was cured of his seizures, and his I.Q. improved by 8 points; however, he had lost all capacity for short-term memory. A psychological examination was given to the 29-year-old 19 months after the surgery on April 26, 1955, and a "memory defect was immediately apparent. The patient gave the date as March, 1953, and his age as 27.... this patient appears to have complete loss of memory for events subsequent to [his surgery]... but early memories are seemingly normal and there is no impairment of personality or general intelligence" (Scoville & Milner, 1957).

Other studies have shown that patients with hippocampal damage still retain memories for places from their past. A patient known as E.P. suffered bilateral hippocampal lesions as well as damage to some medial temporal lobe regions after suffering from herpes simplex encephalitis. The results of studies on E.P. showed that he could not answer questions about his current neighborhood based on his memory. E.P. was then asked about his childhood neighborhood. He was first asked to provide a “familiar navigation,” a route from his home to a familiar landmark, such as a school. He was then asked to provide an “alternative route” to the same destination, imagining the familiar route was blocked in

some way. Finally, he was asked to describe a "novel navigation," a route between two other landmarks from his childhood neighborhood. Given these prompts, he was able to provide information about his childhood neighborhood that was correct to a degree that was consistent with control subjects (Squire & Teng, 1999).

Consolidation is the process of stabilization of memories in the brain. Psychological studies performed on H.M. and E.P. showed that the hippocampus was required for consolidation of short-term memories into long-term memories, as H.M. could no longer form long-term memories for any event following his surgery. They also showed that after consolidation, long-term memories were no longer solely encoded in the hippocampus, as E.P. had memories of places that had been consolidated into his long-term memory prior to his hippocampal lesions.

To understand memory formation and recall, it is also necessary to understand Hebb's postulate about the synaptic plasticity of neurons. In response to stimuli, cell assemblies are activated and reverberate activity through reciprocal connections until the stimulus is removed. Two neurons that fire at the same time form connections and strengthen each other. As memories are consolidated, nerve cells are connected together and strengthened in a network known as a memory trace, or engram.

There are two models of memory consolidation. One model, known as "the dual trace model," claims that there are multiple memory traces, or physical neural networks encoding a memory, with short-term memory traces in the hippocampus and long-term memory traces in the neocortex. The other model, known as "the consolidation model," purports that memories are consolidated between the hippocampus and neocortex, but that the memory trace in the hippocampus is temporary (Dudai, 2011). Consolidation of

the memory into long-term makes it resistant to degradation. The two models are interrelated in that "both hypotheses embrace a universal unifying concept in biology: Living entities develop and grow" (Dudai, 2011).

Memory engrams act like electrical circuits in the sense that activation of a partial set of the network is enough to activate the entire engram. Possibly, activation of just one or a few neurons involved in a memory engram is enough to activate the entire physical trace for that memory. This provides a mechanism for memory retrieval. Thus, a particular smell that is perceived might be reminiscent of a certain flower that brings back an entire memory of playing outside at a childhood home one summer.

Just as development and growth involve physical changes in an organism, so does memory. As referenced in the introduction, "that memory involves enduring physical changes in the organism has been proposed, using era-dependent metaphors, since antiquity" (Dudai, 2011). When a memory engram is activated, that engram is not only remembered but also subject to reconstruction. This reconstruction of activated memories is a process known as reconsolidation, and it is the basis for many types of memory modification.

In 1968, an animal study was published that showed that interfering with brain processes using electroconvulsive shock stimulation therapy following the reactivation of a memory led to suppression of that memory (Misanin, Miller, & Lewis, 1968). Electroconvulsive shock stimulation (ECT) involves passing an electric current through the brain to induce a seizure. At this time, ECT was commonly known to cause retrograde amnesia of recently learned experiences by interfering with the consolidation process. Although the authors do not mention the term *reconsolidation*, the researchers were

intending to find out if ECT could result in retrograde amnesia long after the learning experience. Rats were fear conditioned with an 80-db white noise followed by a 3-second foot shock. 24 hours after the fear conditioning, one group of rats was given a brief presentation of the conditioned stimulus followed by ECT, while another group was given only ECT. Based on their fear responses, the rats that were presented with the conditioned stimulus showed memory loss of the fear conditioning, while the rats that received only ECT showed no memory loss (Misanin et al., 1968). This experiment was one of the first to show that activation of previously consolidated memory traces left those traces subject to disturbance. It would be many years before scientists understood that reactivated memories enter an unstable state until they are reconsolidated and that any memory intervention employed during this period of time could affect the memory.

In the 2000s, similar animal experiments were performed that suggested that reactivation of memory engrams induces a transient period of instability for the activated memory (Schwabe, Nader, & Pruessner, 2014). By this time, the process of new memory consolidation into long-term memory was better understood. It was understood that until consolidation into long-term memory, new memories are labile. It was also understood that protein synthesis in neurons is required for consolidation. A group of researchers, referring to the results of the electroconvulsive shock experiments of the 1960s, wanted to know if retrieved or reactivated memories required a reconsolidation process to become stable again (Nader, Schafe, & Le Doux, 2000). They fear conditioned rats with 30-second tones followed by 1-second foot shocks. Some of the rats underwent memory reactivation either 24 hours or 14 days after conditioning. They injected some of the rats' lateral and basal nuclei of the amygdala, a region believed to be the site of fear memory storage, with

anisomycin. Anisomycin is an inhibitor of protein synthesis and had been previously shown to prevent the consolidation of new memories. The results showed that regardless of whether reactivation was performed 1 or 14 days after conditioning, infusion of anisomycin following reactivation produced amnesia on later tests, and that without memory reactivation, anisomycin had no effect on the fear memory(Nader, et al., 2000). Also, if anisomycin was injected six hours after reactivation, there was no memory loss. These results are consistent with previous studies that suggest a time-sensitive period of memory instability following reactivation. By showing that stabilizing of the retrieved memory is dependent on one of the same processes involved in the consolidation of new memories, namely de novo protein synthesis, the results also suggested that reactivated memories go through a period of reconsolidation before stabilization.

While these studies showed that conditioned fear memories in rats could be erased or suppressed by disrupting the reconsolidation process, it was not certain that the same results would be found for human patients. Propranolol is a beta-blocker often used to treat high blood pressure and other cardiovascular conditions. It was also found that "propranolol selectively acts on the β-adrenergic receptors in the amygdala during emotional information processing in humans" (Kindt, Soeter, &Vervliet, 2009). β-adrenergic receptor activation has been known to have a role in protein synthesis, especially in the process of long-term potentiation of memory. Thus, it was believed that propranolol could disrupt protein synthesis in the amygdala. Given that the amygdala is the main storage location for emotional and especially fear memories, propranolol administration during reactivation of a fear memory should disrupt the reconsolidation process and result in the loss of amygdalar memory for a specific fear response. With this

in mind, researchers fear conditioned a group of human test subjects. Fear responses were measured by eye blink startle reflex in response to loud noises and pictures of spiders. They noted that those subjects who were fear conditioned towards the stimuli had stronger eye blink responses as compared to a control group. They separated fear-conditioned subjects into groups similar to the rat studies. One group received 40 mg propranolol with memory reactivation, one group received a double-blind placebo with memory reactivation, and one group received 40 mg propranolol without memory reactivation. The results showed a substantial decrease in fear response for the group that received propranolol with memory reactivation, as compared to the other groups, which showed little to no change in fear response (Kindt et al., 2009). Thus, even in human fear memories, reactivation of a memory is required to return the memory back to a pre-consolidation-like labile state, during which it is subject to disruption before it is reconsolidated and restabilized.

This suggests that propranolol did indeed disrupt the reconsolidation of the fear memory in the amygdala. Importantly, the subjects did not lose episodic memory for the fear conditioning. This is not surprising given that propranolol is specific to receptors in the amygdala, and the episodic memory trace is likely stored in the hippocampus or neocortex. The amygdala likely only stores the memory trace for the emotional fear response to the conditioned stimuli. The amygdala may be the reason that highly emotional memories, positive or negative, are so well remembered. The basolateral amygdala is associated with the emotional content of our memories, but it has also been shown to play a key role in modulating memory consolidation through stress hormones and other neuromodulatory influences (McGaugh, 2004). Thus, while disrupting the

reconsolidation of a memory in the amygdala may not erase the corresponding episodic memory traces in other brain regions, it also may suppress the memories as a whole by blocking the amygdala's influence on reconsolidation in those regions, and it certainly may take away the emotions that make the memory particularly strong to begin with.

The studies detailed above have focused on fear conditioning, for which the measure of the memory had been fear response. While these studies were crucial to understanding the process of memory reactivation and reconsolidation, they might only apply to fear memories in the amygdala as measured by unconscious responses to stimuli. Some experimenters wanted to know if the same reactivation-dependent modifications to memory could be accomplished in humans for episodic memories. Although previous studies focused only on erasing or suppressing the reactivated memories, reactivation opens a time-sensitive window for all types of modifications - strengthening, altering, or weakening - depending on the type of manipulation that accompanies the reactivation of the memory.

In order to test whether or not the same principles of reconsolidation applied to human episodic memories, researchers tested 36 university students (Hupbach, Gomez, Hardt, & Nadel, 2007). They were broken up into three groups of 12 and told they would need to memorize different lists of objects on different days of the study. On the first day of the study, experimenters pulled random objects (such as a balloon, crayon, flower, key, or sock) out of a bag and placed them into a blue basket. The basket was then hidden, and the subjects were asked to recall all of the items in the basket. This task was repeated four times or until the test subject recalled at least 17 of the 20 items correctly. Following day 1

there were no differences between groups on the average number of trials taken to reach 17 remembered items or four trials.

On day 2, one group of 12, the reminder group, was shown the empty blue basket from day 1 by the same experimenter and asked, "Do you remember this basket and what we did with it?" They were not asked to recall any of the items, because the researchers were focused on the effects of an incidental reminder rather than an explicit reminder (i.e. asking the subjects to describe the process but not the actual items). For another group of 12, the no-reminder group, there was no reminder at all of day 1. Individuals in these two groups were then presented with 20 objects and given 30 seconds to memorize them. The learning process differed from day 1 as to not incidentally remind the participants of the events of day 1. Again, participants repeated the memorization task four times or until at least 17 objects were remembered correctly. There was again no difference between the two groups on the average number of trials to reach 17 remembered items or four trials. The third group of 12, the control group, did not participate in day 2.

On the third and final day of the study, the experimenter asked all participants to recall all the objects they could from day 1. Once they could not name any more objects, they were given a break where the experimenter would engage them in an unrelated conversation before asking them to recall the day 1 objects again. All participants repeated this recall a total of four times.

The results of the study showed the mean percentage of objects correctly recalled from day 1 as well as the mean percentage of intrusions from day 2 objects that were recalled as day 1 objects during testing on day 3. The reminder group had a 36.3% recall for list 1 items and 23.8% intrusions. This was compared to 45.0% recall and 4.9%

intrusions for the no-reminder group and 49.5% recall with 0.5% intrusions for the control group that did not participate in day 2. There was no statistically significant difference in the total number of objects recalled from day 1; however, there was a significant difference between the reminder and no-reminder groups on the number of intrusions from the day 2 list. There was not a significant difference between the no-reminder group and the control group on number of intrusions from the day 2 list (Hupbach et al., 2007). Thus, the researchers showed that reactivation of episodic memories results in a similar process to fear memory reactivation, whereby the memory becomes labile and subject to modification until it can be reconsolidated. In the study, the participants who were given an incidental reminder of the first day's list of objects incorporated more of the day 2 objects into their memory for the day 1 objects. This level of incorporation of new information was only seen in the group that had recently reactivated the memory of day 1 before learning new information.

From an evolutionary point of view, it is not entirely clear why reconsolidation exists. At first, it might seem that we would be better off if our memories remained stable after the first consolidation from short-term to long-term memory. Given that we do not exactly know the biological reason for reconsolidation of memories, it may even be true that the instability of reactivated memories is a biological shortcoming. More likely are three popular proposals for more adaptive purposes for the labilization-reconsolidation process. The first proposal is that memory reconsolidation is beneficial due to the nature of our ever-changing environments. Memory updating (or the integration of new information into the background of different memories) allows us to adapt to new environments and store new information while connecting it with relevant past information. As Yadin Dudai

stated, "updating outside the time window of reconsolidation may further facilitate fast incorporation of new experience into existing associative knowledge schemas in the absence of superfluous activation of indirect associations" (Dudai, 2011). Another proposal holds that the labilization-reconsolidation process is crucial for the strengthening of the original memory. In one such study, memory strengthening has been shown to occur as a result of the reactivation and reconsolidation of memories rather than their retrieval alone. Further, the same study showed that the effects of strengthening were not present until after reconsolidation has occurred and the memory is restabilized (Forcato, Rodriguez, & Pedreira, 2011). One last proposed benefit for the reconsolidation process is that, at least for episodic memories, the reconsolidation process is actually good for our imaginations. The malleability of memories adds to the creativity of our imaginations, for "too rigid a memory may lead to poor imagination, one that plays scenarios of the future that are only similar to the past" (Dudai, 2011). It is conceivable that updating our past experiences with new information from the present will allow us to better imagine the future, because without the context of the present, past memories may become irrelevant.

When activated, memory engrams lose the stability that they gained through the original consolidation process. While in this susceptible state, neurons encoding the original memory can interact with neurons coding new events and information, and connections can be made and strengthened between the neurons. The connections between the original engram neurons can also be weakened, strengthened, or associated with new and different episodic memories or emotional states. Thus, activating memory traces make the memory susceptible to new information and influence. This reconsolidation of long-term memories provides a neuroscientific model for the

inadequacies of our memory and susceptibility to misinformation. It also provides a plausible explanation for how memories of past events can be altered, suppressed, or enhanced by activating a memory trace and providing an individual with conflicting information or emotions with the aid of suggestible discourse or molecular targeting, or even direct neuron stimulation technologies.

While the studies mentioned above have provided significant information about the role and process of memory reactivation and reconsolidation, they apply only to memories that have been conditioned in test subjects in a lab setting. What about long-standing episodic memories? Do autobiographical and personally relevant memories undergo the same process of reconsolidation following their reactivation? If so, manipulating such memories could have wide-ranging therapeutic and judicial uses as well as a range of ethical implications that do not apply to lab conditioned memories.

False Memory Research

One method of modifying past memories is the implantation of false memories. The process generally involves having test subjects think deeply about childhood environments or events and feeding them false information alongside other true stories from their childhood. These experiments were not initially performed in light of the neuroscience research on memory reactivation and reconsolidation, but rather as psychological examples of the fallibility of the human memory. Regardless, the methodology of false memory implantation involves activation of memory engrams from an individuals' distant past followed by the presentation of new information; therefore, I argue that the same reactivation-reconsolidation process is at work in the following false memory studies.

Elizabeth Loftus and Jacqueline Pickrell first explored the formation of false memories in 1995 (Loftus & Pickrell, 1995). Knowing that memories of past events were subject to interference by later experiences, they sought to prove that a memory, partial or complete, of an event that never occurred could be implanted in the mind of a test subject. In order to do so they came up with what has come to be known as the "lost in a shopping mall technique." In the first case of a successful false memory implantation, Loftus and Pickrell fed four stories of past events to a fourteen-year-old test subject named Chris. With the help of family members, they constructed stories of three true events from Chris' childhood and one false event wherein Chris was lost in a shopping mall in his childhood home of Spokane, Washington. According to the story, Chris was found crying by an elderly man after losing his parents. Over five days, Chris was asked to write out details of all four events while instructed to write "I don't remember" for any details that he was unable to recall. Over the five days, Chris remembered more and more about the event that never

occurred, including details about the elderly man being “really cool” and about being scolded by his mother. Rating his memories of the four events weeks later, Chris gave a rating of 8 out of 11 for the clarity of his memory for being lost in the mall, the second highest rating out of the four events. When later told that one of the memories was false, Chris guessed one of the true memories as the event that never actually occurred (Loftus & Pickrell, 1995).

Loftus and Pickrell then used the “lost in a shopping mall technique” on 24 test subjects. Student researchers recruited the subjects and a relative of each subject who had detailed knowledge of the subjects’ childhood experiences. Subjects were under the assumption that they were participating in a study on “the kinds of things you may be able to remember from your childhood.” The subjects’ relatives provided accounts of events from the subjects’ childhood, and the subject received a booklet with four short stories of events from their past, including three true events and one false story about being lost in a shopping mall, crying, and being rescued by an elderly person. Following the completion of the booklet and two follow-up interviews, 68% of the true events were remembered compared to 25% of the false memories. False memories were also remembered with a lower level of clarity, but of note, the clarity rating of the memories increased between the first and second interviews (Loftus & Pickrell, 1995). This increase in clarity may be the result of increasing connectivity between details of the false experience and true details and memories from the subjects' childhood shopping mall.

The findings of the first false memory study are remarkable not for establishing some percentage of people that can be made to believe false memories, but rather for providing what Loftus calls “existence proof for the phenomenon of false memory

formation" (Loftus & Pickrell, 1995). Prior to false memory formation research, Loftus had spent years studying memory and its association with eyewitness testimony. Her research on the misinformation effect investigated whether eyewitness' memories could be altered by exposure to incorrect information during questioning. The formation of a false memory for a completely fabricated event, however, paved the way for a larger debate involving issues beyond the misinformation effect and including realms of psychotherapy, criminal testimony and confessions, and medicine.

Follow-up studies showed similar rates of remembering for increasingly unlikely false childhood events. Ira Hyman and colleagues implanted memories of an overnight hospitalization or a birthday party with pizza and a clown in 20% of subjects (Hyman, Husband, & Billings, 1995). They then increased the pressure on subjects to recall a false memory of spilling a punch bowl on the parents of the bride at a wedding. In separate studies, 25-27% of the subjects claimed to remember spilling the punch bowl, some relaying details of the appearance and clothing of individuals at the wedding (Hyman et al., 1995).

Another interesting set of studies investigated the role of advertising in false memories. A fake advertisement was created suggesting an autobiographical memory in which the subjects had shaken hands with Bugs Bunny as a child at a Disney resort (Braun, Ellis, & Loftus, 2002). Well before testing, participants answered a life-events inventory questionnaire that contained a question asking them if they had ever shook hands with a cartoon character at a theme park. They were asked to respond with a number from 1 to 10, 1 being "definitely did not happen" and 10 being "definitely did happen". The researchers removed participants who rated the question as 1-5 on the initial test. On a test

after presentation of the ad, 78% of the participants who saw the Bugs Bunny ad responded with a higher confidence level on the same question for the life-events inventory. Also, when asked to write about their memory of their childhood Disney experience, participants who were shown the Bugs Bunny ad reported better clarity, emotional content, centrality to their childhood, and importance to their childhood, as compared to a control condition. Additionally, 16% of participants who were shown the ad reported to remember shaking hands with Bugs Bunny during a childhood visit to Disney (Braun et al., 2002).

In a follow-up study in Elizabeth Loftus' lab, researchers were able to get 25-35% of test subjects to remember meeting Bugs Bunny at Disneyland as a child after showing them fake advertisements with suggestible autobiographical material. Even more astounding, of those who claimed to remember meeting Bugs Bunny, "62% remembered shaking his hand and 46% remembered hugging him. A few people remembered touching his ears or tail. One person remembered that he was holding a carrot" (Loftus, 2003). Not only does this research provide evidence for the ability of advertising to change peoples' memories, but more importantly, it gives an example of the implantation of a completely impossible false memory. The researchers know with out a doubt that the advertisements led to a false memory rather than retrieval of a true memory because Bugs Bunny is a Warner Bros. character who would have never been present at a Disney resort.

Later experiments looked to determine which parts of the standard false memory implantation process were most critical to adoption of false memories. Alan Scoboria and his colleagues identified five components of false memory formation studies: “(1) a false event is presented; (2) a number of true events obtained from family members are

presented; (3) participants are told that all of the events occurred per their family; (4) participants are told that retrieval is possible; and (5) participants engage in a purported memory retrieval procedure, such as guided imagery and/ or context reinstatement, over repeated trials" (Scoboria, Wysman, & Otgaar, 2012). In separate studies to isolate individual components, Scoboria and his colleagues concluded that attributing the false event suggestions to parents resulted in stronger false memories. This is likely due to subjects having a perception that the information is from a trustworthy source, and thus, they should remember it and might even put more pressure on themselves to remember details. They also found that including true events alongside the false event in studies might enhance the false event suggestion because the subjects know that a credible source was consulted (Scoboria et al., 2012). Again, this suggestibility likely results in more pressure for the subject to remember details of all events, including the false memory. It is important to note that components (1) and (2) from the above scheme happen concurrently. Another important component of false memory studies that is not mentioned by Scoboria and colleagues is that the false event is personalized to the test subject using information provided by family members, such as specific people or places from their childhood. This incorporation of personally relevant people or places may serve to increase believability of the account from the beginning, but more importantly, it may reactivate memory engrams associated with those details. This would allow the information of the false event to be stored and connected with these activated memory traces, leading to a false memory that feels as true as any of the other true events relayed to the participant.

While these studies did not seek out to determine what types of individuals are susceptible to false memory acceptance, there were some correlations between personality

traits and false memory acceptance in the data. Individuals who had issues with memory, attention, and awareness, based on the Dissociative Experiences Scale, were found to remember false memories more. Also, individuals who were seen to have vivid mental imagery, based on the Creative Imagination Scale, tended to adopt false memories (Loftus, 1997). Regarding those individuals who have memory, attention, or awareness issues, this result is not surprising. They may have less trust in their own memories from the beginning, and thus, they would tend to rely on information from others more often to supplement their memory. They also would be less attentive or aware of signals that would normally alert others that something is not true, again resulting in a heightened trust for what they are told by others. For the individuals with a heightened capacity for vivid mental imagery, their tendency to adopt false memories at a greater rate may be more due to the reactivation-reconsolidation process for long-term memories. If they are able to more vividly imagine past events and cues, they are likely activating more of their distant memory engrams and associating those memories to a greater extent with the misleading suggested information provided by the experimenter.

False memory researchers also tested the role of sleep deprivation in false memory implantation. In one experiment, participants were first given a passage about a plane crash in Pennsylvania on September 11, 2001. They were told repeatedly that footage of the crash was widely distributed and asked if they had seen the footage. They were then shown a series of photographs depicting a man breaking into a car or a woman confronting a thief. They were later given narratives that included misinformation about the photo sets. The results of the study showed that subjects who had less sleep the night before were associated with increased false memories, and test subjects who “reported 5 or fewer

hours of sleep the night before the experiment were more likely to report that they had witnessed a news event that they did not actually see…. There was also a trend for these participants to incorporate more misleading information into their memory for visual materials" (Frenda, Patihis, Loftus, Lewis, & Fenn, 2014). Their second experiment addressed the role of sleep deprivation at different stages of the misinformation procedure: encoding, misinformation, and test. The results again showed that the sleep-deprived group was more susceptible to false memories, but that the effect was only evident when participants were sleep-deprived at all stages of the misinformation procedure (Frenda et al., 2014). The results of the sleep deprivation study may also be due to the diminishing effects that sleep deprivation has on memory, attention, and awareness.

Having "existence proof" of false memory implantation in humans as well as a plausible neurological model for their formation, the role of false memories in an individual's life must be addressed. Daniel Bernstein performed two experiments to examine whether or not false memories can have long-term effects (Bernstein, Laney, Morris & Loftus, 2005). In one experiment, 237 participants filled out a Food Preferences Questionaire. They were then given a falsified profile of their early childhood food experiences, which they were told was individualized and based on their responses. One third of the participants' profiles said they had gotten sick after eating hard-boiled eggs, one third were told they had gotten sick after eating dill pickles, and the rest of the participants made up the control group. The participants in the pickle group reported increased confidence that they had grown ill from eating dill pickles, and they reported higher avoidance scores with regard to pickles than others in an imaginary barbeque scenario test, but only the increased confidence was statistically significant (Bernstein et

al., 2005). In the second experiment, 180 participants filled out an identical questionnaire and received similar falsified feedback. Half were placed in the pickle feedback group and half in the egg feedback group. They then filled out further questionnaires to determine their belief in the false information about the childhood food experiment and their intent to avoid certain foods going forward. The results showed that those who falsely believed the food event were associated with increased avoidance of the particular food as well as closely related foods. Bernstein also notes that some individuals provided detailed information of the false memory (Bernstein et al., 2005). These detailed accounts were significant because those who provided very specific and detailed recollections of a bad experience with either food had previously denied ever having such experiences in the original questionnaire.

A similar experiment was performed linking false memories about alcohol to changes in alcohol preferences (Clifasefi, Bernstein, Mantonakis, & Loftus, 2013). Using a similar model to the food-preference study, the researchers suggested to some of the participants through a falsified individualized food and drink profile that they had gotten sick from either rum or vodka in their early teenage years. Non-control participants were asked to remember events surrounding the false autobiographical episode before completing exit questionnaires. The results showed that the individuals who received a false alcohol suggestion were more confident that the event had occurred as compared with the control group. The same group also showed a comparatively lower preference toward the suggested alcohol (Clifasefi et al., 2013). The food and alcohol studies show that adoption of false autobiographical memories can affect future behavior.

False memory implantation proves that an individuals' autobiographical memory can be manipulated through misinformation alone. There are, of course, boundary conditions for the reliability, types, and extent to which test subjects adopt false memories. In most studies, only 20-30% of participants claimed to have a memory for the false event. False memory studies are also limited to incorporation of new information into a subjects' memory. Entirely false past events can be implanted in a subjects' memory, or real past experiences can be reconsolidated with false details. But rather than enhancing or suppressing specific memories, false memory research only provides evidence that our memories are subject to new ideas at later times. In order to enhance or suppress specific memories of past events through reactivation and reconsolidation, other methods must be explored.

Molecular Memory Modification

Molecular memory interventions have shown promising results as methods for targeted and specific enhancement or suppression of established memories. Molecular memory modifications involve manipulating molecules known to be involved in the formation, consolidation, or reconsolidation of memory. By inhibiting or upregulating certain molecules that are critical for proper function of these memory processes, new or past memories can be altered in a very specific manner. It has already been shown that amnesic techniques and molecules disrupt the reconsolidation of memories in animal models. Here we focus on molecular memory interventions that have been proposed for human use and treatment.

The most commonly cited method of molecular memory modification is the oral administration of propranolol. As was described before, propranolol is a drug commonly used for cardiovascular conditions, but it also has a selective effect on the amygdala. In the study described before, propranolol was shown to have a dampening effect on the emotional fear memory for a conditioned fear response (Kindt, Soeter, &Vervliet, 2009). Here I will discuss the use of propranolol to modify non-conditioned emotional memories, that is, memories of past experiences of emotional significance that were not induced in a lab setting.

Stress disorders are a particular type of anxiety disorder caused by traumatic experiences. Post-traumatic stress disorder (PTSD) is a particularly severe form of stress disorder. According to the National Institute of Mental Health, symptoms of PTSD include nightmares and flashbacks, difficulty concentrating or falling asleep, avoidance of people or other things related to the trauma, extreme responses to being startled, emotional

numbness, loss of enjoyment, anger, and guilt (National Institute of Mental Health, 2016). PTSD can be a debilitating disorder that takes a toll on one's day-to-day relationships, sense of self, and peace of mind.

Just as with any other memory, traumatic memories undergo consolidation from short-term to long-term memory, however, especially traumatic memories have considerable emotional content behind them and trigger the release of adrenaline and other stress hormones. The influence of the amygdala and the increased levels of noradrenaline result in the overconsolidation of the traumatic memory engram (Henry, Fishman, & Youngner, 2007). Thus, the root of post-traumatic stress disorder is an overconsolidated, and therefore easily brought up and not easily forgotten, traumatic memory.

It is believed that propranolol, because it is a beta- blocker, could be useful in blocking the effects of noradrenaline during the consolidation of traumatic memories, preventing them from becoming overconsolidated (Henry et al., 2007). In fact, propranolol has already shown promising results for decreasing the instance of PTSD development in real-life trauma patients. In clinical trials wherein emergency room trauma patients were given either propranolol treatments or placebo (Pitman et al., 2001) or given the choice of taking propranolol or not (Vaiva et al., 2003), those patients who were treated with propranolol soon after traumatic experiences had much lower rates of developing PTSD. Although these results are promising for the use of propranolol as a preventative measure against the development of PTSD, it can often be hard to predict what types of events will result in an individual developing PTSD. Disrupting the initial consolidation of traumatic memories is a time-sensitive measure. A more universally applicable memory treatment

for PTSD would have to be able to affect memories for events that happened months prior, before the symptoms began to manifest and diagnosis was possible.

Knowing that interventions during the reconsolidation phase of a recently reactivated memory can have an effect on previously consolidated memories, a group of researchers set out to determine whether propranolol used during reconsolidation would indeed have a dampening effect on the traumatic memory of PTSD patients (Brunet et al., 2008). The study involved 19 individuals with chronic PTSD. They were asked to describe the traumatic event that caused their PTSD in order to reactivate the memory. A personalized script was made for each patient's experience by the experimenters. The patients were then given either 40 mg short-acting propranolol followed hours later with a 60 mg dose of long-acting propranolol or a placebo at both instances. 9 patients received propranolol treatments, while 10 received the placebo. One week later, subjects were called back in for testing. Baseline measurements were made for heart rate, skin conductance, and left corrugator electromyogram. Subjects were then asked to listen to their personalized scripts while imagining their traumatic experience, and the same measurements were made. The results showed that the physiological response to the mental imagery was significantly smaller for those individuals in the propranolol treatment group the week prior, as compared with those who received the placebo (Brunet et al., 2008). Follow-up studies by Brunet and colleagues used six treatment sessions rather than one, leading to more significant results about the clinical potential and the effect on PTSD symptoms (Brunet et al., 2011). Because propranolol is specific to the amygdala, it should not have an effect on the episodic memory trace for PTSD patients' traumatic memories, but it may be effective in diminishing some of the emotional pain and reactions to that

memory. These preliminary studies are promising for the efficacy of propranolol as a treatment for the physiological effects and symptoms of PTSD.

Propranolol has also been used in studies testing its effects on other types of memories. Drug reward memories are one such type of memory that undergoes reconsolidation after reactivation. In one translational study, the effects of propranolol during reconsolidation of nicotine- associated memories in rats and humans were investigated (Xue et al., 2017). For the rat study, rats were subjected to a nicotine-associated unconditioned stimulus before they were injected with propranolol. In the human study, memories were reactivated with an unconditioned stimulus and propranolol or placebo was administered orally. In both the rat and human studies, the results suggest that propranolol administration alongside reactivation and reconsolidation of nicotine-associated memories "may be a promising method for decreasing nicotine craving. Additionally, to the degree that the results from the rat models generalize to drug addiction among people, the potential value of the procedure should be tested for the prevention of relapse to smoking" (Xue et al., 2017).

Another study investigated whether or not the same type of post-retrieval propranolol administration would have an effect on craving and cue reactivity for cocaine addicts (Saladin et al., 2013). 50 cocaine-dependent individuals at an in-patient facility participated in the study. All were given cocaine cue exposure to reactivate cocaine-associated memories. Immediately after the cue exposure, 26 were given 40 mg propranolol and 24 were given a placebo. 24 hours later, they underwent another round of cocaine cue exposure. Cravings, heart rate, skin conductance, and blood pressure were measured before, during, and after both cue exposure sessions. The results showed that the

propranolol group had a greater reduction in cravings and physiological markers 24 hours after the post-retrieval propranolol treatment as compared to the placebo group (Saladin et al., 2013). The researchers found no evidence of treatment effects at a follow-up a week later, but given the 24 hour results and keeping in mind the Brunet et al. studies with PTSD, there is promising evidence that further studies that employ more than one treatment could have therapeutic effects that persist over time.

Propranolol has been shown time and time again to have a suppressing effect on emotional memories. Whereas propranolol has an inhibitory effect on the reconsolidation process, other molecules known to be involved in reconsolidation may enhance the process. It is known that in traumatic memory consolidation and reconsolidation, stress hormones can lead to the overconsolidation of memories. In a study investigating the effects of cortisol administration during reconsolidation of a conditioned fear memory, cortisol was shown to enhance the reactivated memories (Drexler, Merz, Hamacher-Dang, Tegenthoff, & Wolf, 2015). This type of experiment provides a model for how memories could be specifically targeted through reactivation and enhanced with pharmaceutical interventions. While this type of effect would be considered less than ideal for patients with PTSD or drug addicts with drug- associated memories, such memory modifications could be of use in scenarios such as eyewitness testimony.

Another study sought to determine the effect of stressors during reconsolidation of human declarative (episodic) memories (Larrosa et al., 2017). Participants were asked to memorize cues and responses. Experimenters used a cold pressor stress treatment (CPS) as a stressor, and saliva tests showed that CPS led to raised cortisol levels. The results showed that applying stressors before reactivation of declarative memories led to short

and long-term decreases in memory expression for the declarative memories (Larrosa et al., 2017). Other studies have shown that stressors during reconsolidation can have enhancing or impairing effects on the memories that are reactivated. As more information is gathered, the administration of stress hormones during reactivation of memories could become a minimally invasive method for precisely enhancing or suppressing various types of memories.

Another molecule called protein kinase M-zeta (PKMζ) has been shown to have a role in maintaining long-term memories in the brain by way of long-term potentiation(Hui & Fisher, 2015). Long-term potentiation, or LTP, refers to the strengthening of neural synapses involved in learning and memory and can last for months or longer after initial learning. PKMζ is a natural protein encoded by the PRKCZ gene. The brain must continually produce PKMζ in order to preserve long-term memory, as it is slowly degraded over time. "By manipulating [PKMζ production] in rodents, researchers have been able to both erase and enhance memory under laboratory conditions," because PKMζ can be either inhibited or upregulated depending on the desired effect (Hui & Fisher, 2015). Interventions with PKMζ during the reconsolidation process could lead to extremely specific memory alterations in either direction. Also, in contrast to propranolol and cortisol, " PKMζ appears to be common to all memories regardless of whether they are declarative (ie, explicit and conscious, such as facts) or procedural (ie, implicit and unconscious, such as muscle memory)" (Hui & Fisher, 2015). Thus, a molecule such as PKMζ could be a universal target for the erasure, enhancement, and modification of all types of memories.

One of the first experiments in manipulating the role of PKMζ involved erasure of long-term memory associations (Shema, Sacktor, & Dudai, 2007). The researchers

understood that PKMζ must be persistently phosphorylated to maintain long-term potentiation of memories. They chose to manipulate this process in the rat insular cortex, a region of the brain containing the gustatory cortex. The target for their memory intervention was the rat taste memory process. They conditioned a taste aversion for saccharin in rats. Three days later, they began infusing an inhibitor of PKMζ, myristoylated zeta-pseudosubstrate inhibitory peptide, or ZIP, into the rats' insular cortex. Rats receiving ZIP administrations were infused 3, 7, or 25 days following the initial conditioned taste aversion. Aversion was later measured through a pre-established aversion index. All three ZIP groups differed significantly from the control group in taste aversion, (Shema et al., 2007) and ZIP infusions into the IC appeared to selectively erase the conditioned taste aversion memory. Interestingly, there was no significant difference between the three ZIP groups on taste aversion index, (Shema et al., 2007) implying that ZIP effectiveness is not extremely time sensitive. Another important finding came from a follow-up study by the same researchers, in which they reactivated the memory trace prior to ZIP infusion. While similar results were obtained with reactivation of the taste aversion prior to ZIP infusion, "no reactivation is needed to render the trace susceptible to ZIP" (Shema et al., 2007). This finding seems limited to ZIP and its effects on PKMζ production, as other classical amnesic agents do not have an effect on long-term conditioned taste aversion unless the memory is reactivated prior to administration. This may have important implications for the specificity of PKMζ inhibitors such as ZIP, because it would seem that a reactivation-dependent system would be more accurate for targeted memories. With no necessity for or specificity towards cue-reactivated memory traces, it would appear that ZIP infusions are limited in specificity to the spatial brain area that they are infused into, meaning they could

easily miss their memory target or have effects on unintended memories.

A very similar experiment with PKMζ was performed to test the effects of overexpression of the protein on long-term memory (Shema et al., 2011). The experimenters designed lentiviruses that expressed PKMζ and infused them into the insular cortex of rats that had been taste aversion conditioned. They used green fluorescent protein (GFP) as a marker to assure transformation, and "overexpression of the PKMζ protein [in the insular cortex] was evident" (Shema et al., 2011). Memory for the conditioned taste aversion was significantly enhanced for those rats infected with PKMζ expressing lentiviruses, as compared to other rats infected with lentiviruses expressing a dominant negative (mutated, inactive form) of PKMζ and those expressing only GFP (control). Also, the results showed that the extent of "memory enhancement was positively correlated with the extent of $LV_{PKM\zeta}$ infection in the [insular cortex]" (Shema et al., 2011). This experiment showed how the upregulation of PKMζ could effectively enhance long-term memories. More research should be performed and novel methods of causing overexpression of PKMζ should be explored, as viral vectors are not an ideal technique for possible intervention in humans.

While PKMζ seems like a promising target for molecular memory interventions, J.L. Kwapis and F.J. Helmstetter have raised caveats (Kwapis & Helmstetter, 2013). While ZIP was believed to bind solely to PKMζ, there is evidence that ZIP targets other PKC isoforms in the brain that may have an effect on its role in memory maintenance. Also, there have been conflicting findings on the universality of PKMζ for memory maintenance, as some studies suggest that PKMζ does not maintain some specific types of memories in different regions of the brain. Finally, although the memory erasure study described above (Shema

et al., 2007) suggested that reactivation is not required for ZIP to effectively erase targeted memories, other work has been done that makes a case for the necessity of reactivation with ZIP infusion. Still, the findings of these studies "do not conclusively rule out the possibility that PKMζ normally acts to maintain memory" (Kwapis & Helmstetter, 2013). I would argue that the inconsistency with findings about PKMζ serves not to diminish its role in the maintenance of memory, but rather, serves as a testament to the complexity of memory systems and the inability to simplify such processes to the effect of single molecules.

Multitudes of molecules and drugs have been shown to affect the memory process throughout the years. In light of the relatively recent research on the neuroscience of reconsolidation, many of these drugs may be reconsidered as possible memory interventions during the reconsolidation process. Examples include scopolamine and benzodiazepines. Scopolamine is an anticholinergic drug that affects the neurotransmitter acetylcholine, and it "impairs aspects of initial memory acquisition (e.g. encoding and consolidation) and spontaneous memory retrieval" (Caine, Weingartner, Ludlow, Cudahy, & Wehry, 1981). Benzodiazepines are a class of psychoactive drugs the enhance gamma-aminobutyric acid (GABA) receptors in the brain, and "all benzodiazepines can be shown to cause anterograde amnesia" (King, 1992). These types of molecules and other molecules with known roles in memory formation, consolidation, maintenance, and reconsolidation must be investigated as possible interventions for safer and better-targeted molecular memory modifications.

Because the physical processes and mechanisms of reconsolidation are still largely unknown, there is considerable room for advancement with molecular interventions.

Knowing that protein synthesis is required for reconsolidation, the next step in finding effective, targeted, and reliable molecular interventions is to identify specific transcription factors, kinases, and other proteins and enzymes involved in the process and explore their role. There is still much to be learned because "studies of reconsolidation have taken the manipulations that are known to affect consolidation as a starting point, and examined their effects on reconsolidation" (Tronson & Taylor, 2007). While these processes are very similar, they are not entirely the same. Thus, not all molecules known to affect consolidation will have the same effects during reconsolidation, and there are likely mechanisms and molecules involved in reconsolidation that have no role in consolidation. As more is understood about the molecular processes involved in memory, it is also important to look at technologies that have the capability to influence memory in a less invasive manner than molecular manipulations.

Memory and Neuromodulation Technologies

Neuromodulation technologies are technologies that can alter nerve activity through various means of stimulation. As advances in neuroscience continue to lead towards a more refined understanding of brain functions and processes, neuromodulation technologies become more targeted and useful. For example, technologies such as brain-computer interfaces have progressed from EEG control of cursors on a computer screen to brain-implant technologies such as BrainGate, which have allowed paralyzed patients to move robot arms with enough precision to grab a bottle and take a sip of coffee (Robson & Davenport, 2014). Neuromodulation technologies affecting memory have been used since the late 1930s, beginning with the use of electroconvulsive shock therapy (ECT) for patients experiencing schizophrenia and depression (Impastato, 1960). Although still used today in some cases of severe depression, the use of ECT is under a significant amount of controversy. There are few other neuromodulation technologies directed toward human memory in practice today, but there have been plenty of instances of promising technologies developed for laboratory use. It is not beyond the scope of reason that as our understanding of memory processes continues to develop, more neuromodulation technologies with the power to enhance, suppress, or alter human memories will come into practice.

As has been already discussed, electroconvulsive shock therapy was employed as a method of inducing retrograde amnesia in rats in one of the first studies to identify a reconsolidation process for long-term memories (Misanin et al., 1968). A 2014 study on the effects of ECT on depressed human patients found similar results, namely that ECT applied during reconsolidation of an emotional episodic memory resulted in a decrease in the

reactivated memory (Kroes et al., 2014). 42 patients with unipolar depression participated in the clinical study and were randomly assigned to three groups. All patients were asked to learn two emotionally aversive slideshow stories. One week later, the patients were shown a partial version of the first slide of one of the slideshows in order to cue reactivation of that story. Patients in groups A and B were then anesthetized and underwent ECT immediately following reactivation of the first story. Group C patients were in the control group and did not receive ECT. Group B patients were tested on the two stories about 90 minutes after reactivation and ECT, while group A and C patients were tested on the stories 24 hours after reactivation and ECT. The results showed disruption of the memory for the reactivated story in group A. For the non-reactivated story, memory performance was comparable in groups A and B, and group B showed no difference in performance between the reactivated and non-reactivated story. Group C had better memory performance on the reactivated story than the non-reactivated story (Kroes et al., 2014). These results provide many insights into the potential of ECT and reconsolidation. First, ECT resulted in disruption of the reactivated memory but not the non-reactivated memory for group A, suggesting that ECT in and of itself does not result in general memory disruption and reactivation is necessary. Secondly, ECT did not result in a change in memory performance for a reactivated memory when tested 90 minutes after the therapy (group B), suggesting that reconsolidation of the reactivated memory must be completed before results are observed. Lastly, group C, who did not undergo ECT, had improved memory performance for the reactivated memory, suggesting that memory reconsolidation is beneficial when no manipulation is involved in the process. Unfortunately, because ECT is such a controversial neuromodulation technique, there are limited applications for

human use and other neuromodulation technologies should be considered.

One such neuromodulation technology with a wide range of uses in humans is transcranial direct current stimulation (tDCS). tDCS is a non-invasive neuromodulation technique that involves placing an anode and cathode over the scalp in order to pass a weak electric current through the brain. This region-specific technique can either enhance neuronal firing through anodal stimulation or dampen neuronal firing in the region through cathodal firing. Various studies have shown promising results of both forms of tDCS in processes such as initial memory consolidation and working-memory function (Javadi & Cheng, 2013). Few studies have examined the effects of tDCS on long-term memory reconsolidation in humans.

A 2013 study examined the effects of different types of tDCS stimulation during memory reconsolidation (Javadi & Cheng, 2013). The experiment involved 30 participants who were separated into a reconsolidation group and a control group. Participants underwent an encoding session where they were presented with words and asked to imagine and memorize them. After a three-hour "consolidation" window, participants in the reconsolidation group received tDCS stimulation for 20 minutes while performing an old-new word recognition task. Participants in the control group received tDCS stimulation while playing computer games unassociated with the words. Participants were then given a five-hour "reconsolidation" window. Then both sets of participants performed the old-new word recognition task. The experiment was performed over three days employing anodal, cathodal, or sham stimulation on different days. The results showed an increase in performance for the reconsolidation group with anodal stimulation compared to that of the control group. However, there was not a significant decrease in performance for the

reconsolidation group on the cathode stimulation day. The researchers suggest that it may be easier to enhance memory reconsolidation using anodal tDCS than it is to disrupt the reconsolidation process with cathodal tDCS (Javadi & Cheng, 2013). While the researchers failed to show how tDCS might dampen the reconsolidation process in the same manner that it had for previous studies on other memory processes, they did provide evidence that it is possible to influence human memory with anodal tDCS.

Another very similar study showed promising results for the lasting effects of tDCS on episodic memory in older adults (Manenti et al., 2017). In this study, 22 subjects learned a list of words and were separated into tDCS and control groups. 24 hours later, participants were given a contextual reminder of the words learned while the experimental group received tDCS over the lateral prefrontal cortex. They tested memory performance 48 hours and 30 days after the contextual reminder, and in both cases, the experimental group had higher performance than the placebo group. The researchers suggested that tDCS might have a potential use in the prevention of old-age memory disorders such as Alzheimer's (Manenti et al., 2017).

Another significant study showed that tDCS had enhancing effects on conditioned fear memories in humans (Mungee et al., 2014). 74 individuals underwent fear conditioning involving low-intensity wrist shocks. Skin conductance responses were measured throughout the process. One day later, all participants were reminded of the fear conditioning with a single presentation of the stimulus and shock. The experimental group then received anodal tDCS over the lateral prefrontal cortex while the control group received sham stimulation. On the following day, fear responses were measured in response to stimuli, and the results showed increased fear response after memory retrieval

with tDCS anodal stimulation as compared to the control (Mungee et al., 2014). An important follow-up study for these results would need to examine the effects of cathodal tDCS stimulation for fear memories, because a non-invasive dampening procedure could be of use for dampening reconsolidation of traumatic or addiction-associated memories.

Transcranial magnetic stimulation (TMS) is another method for inducing neuromodulation of specific brain regions in a non-invasive manner. TMS involves the use of a magnetic field rather than electric currents for stimulation of neurons. Depending on the coils used in treatment, TMS can be used for stimulation from 1-4cm below the scalp.

Isserles and colleagues explored the use of deep transcranial magnetic stimulation (DTMS) of the medial prefrontal cortex in patients with PTSD who were resistant to standard treatment methods (Isserles et al., 2013). 30 resistant PTSD patients were randomly assigned to three treatment groups. Group A received DTMS after exposure to a traumatic experience imagery script. Group B received DTMS after exposure to a positive experience imagery script. Group C received sham DTMS after exposure to a traumatic experience imagery script. Each group received 12 treatments over four weeks. Weekly psychiatric status evaluations and assessments were performed using various clinical PTSD and depression scales. The results showed that DTMS stimulation of the medial prefrontal cortex could be effective in treating resistant PTSD patients (Isserles et al., 2013). This study showed that TMS can be an effective therapy for PTSD patients, but it did not provide a mechanism for the therapeutic effect. Further studies on PTSD patients should be performed with appropriate experimental conditions and controls to determine if TMS stimulation had a dampening effect on the reconsolidation of the traumatic memory or if it had an enhancing effect on an extinction process for the memory.

Other studies have looked into the effects of TMS on other memory processes. In one such experiment, TMS was shown to improve working memory in healthy individuals, expanding on data of the same effects in schizophrenic and depressive patients (Bagherzadeh, Khorrami, Zarrindast, Shariat, & Pantazis, 2016). TMS applied to the primary motor cortex during reactivation of a specific motor memory suggested that TMS had dampening effects on the reconsolidation process for existing motor memories following reactivation (Censor, Dimyan, & Cohen, 2010). Thus, TMS interventions could be therapeutic for memory enhancement for individuals with working memory disorders or for memory suppression with reactivation of unhealthy memories.

tDCS, TMS, and other non-invasive brain stimulation technologies are especially useful because, as opposed to neuroimaging techniques such as fMRI, which can only provide correlational data, these brain stimulation techniques provide a causal link between neural processing in specific brain regions and memory function in those areas. Also, tDCS and TMS only affect stimulation for about an hour after treatments, but especially for memory processes, they can "induce long-lasting effects... [and] can be also used as adjuvant strategies for the rehabilitation of neurobiological deficits and the treatment of psychiatric disorders" (Sandrini, Cohen, & Censor, 2015). Unfortunately, due to the nature of the stimulation techniques, there is potential for remote effects of treatment in untargeted brain regions. Still, these non-invasive techniques can provide much more immediate results and targeted effects compared to behavioral or pharmacological interventions.

There are many other types of memory directed neuromodulation technologies that are not currently feasible for use on humans. Nonetheless, they have helped provide causal

data for the role of various systems in memory function through animal models. They have also helped peak the interest of the popular media into the capacity for memory modification techniques and their future in the field of memory research.

Optogenetics is a rapidly evolving biological technique for stimulating targeted cells with the use of light. While electrical, magnetic, and pharmacological methods lack the type of specificity for controlling individual neurons in the brain, transforming cells to have a light-dependent switch for activation can result in a level of spatial specificity previously unimagined as well as activation of cells with greater speed. In regards to memory, one optogenetic study became widely popular in 2013. Steve Ramirez and colleagues created an experiment to show that false memories could be implanted by activating certain neurons in memory-engram regions (Ramirez et al., 2013). Knowing that the hippocampus plays a critical role in memory formation and consolidation, the researchers identified cells in the dentate gyrus (DG) of the mouse hippocampus that coded contextual memories, or memories for particular environments. They used transgenic mice whose dentate gyrus (DG, a region of the hippocampus) neurons were labeled to express channelrhodopsin-2, a light-sensitive ion channel. When cells expressing channelrhodopsin-2 are exposed to blue light, the ion channels are opened and sodium ions enter the cell, inducing an action potential in the transformed cells. On day one of the experiment, a mouse was placed in box A, and the DG neurons that responded to the context of box A were identified and transformed with viral vectors to express channelrhodopsin-2. The next day, the mouse was placed in box B, where a different set of DG neurons would fire in response to the new context. The researchers then simultaneously shocked the mouse, while activating the channelrhodopsin-2 expressing cells from context A. On day 3, the mouse was placed back

in box A and showed a fear response, though the mouse had never been shocked in box A. To show that a generalized fear memory had not been developed, the mouse was next placed in a new context, box C, where it did not demonstrate a fear response (Ramirez et al., 2013). The study provides an animal model for which false and real memories can be studied down to the level of a specific memory engram, and showed an interaction between a genuine and false memory in the cells. Although no specific memory engrams have been identified during human false memory experiments, Ramirez and his colleagues provided a solid model for how false memories in humans may be caused by the same type of interaction between concurrent activation of memory engrams from the retrieval of genuine memories and association with new information through reconsolidation.

Ethical Debate

Neuroethics is a relatively new concept focused on the ethical dilemmas involved in our increasing understanding of and ability to control and manipulate brain functions and processes. Neuroethicists therefore seek to delineate how to proceed when neuroscientific advancements yield questions about the impact of such information, if and how it should be used, and who has the right to develop and administer the products and methods that follow. While within the field of bioethics, neuroethics is especially important because it deals with issues of the brain, and changes made within the brain have wide-ranging consequences impacting the mind.

Because memory is an essential component of our learning, moral development, sense of narrative and personal identity, and overall survival, the neuroethics of memory is an especially complicated subfield. Accordingly, there is considerable room for debate about if and the extent to which we should allow certain techniques and technologies that have the ability to modify human memories. In this paper, I have described various means of enhancing, suppressing, or otherwise altering human memories that are currently used for research. I have also described memory modification techniques not currently deemed safe for human experimentation. This research into memory interventions has provided significant findings about the nature of memory as a whole as well as the physical mechanisms of consolidation and reconsolidation. Many have helped to identify specific brain regions, interactions, and molecules crucial to numerous and diverse memory functions. These and further studies continue to add to the understanding of the human memory, but they also raise questions about the potential future uses for methods of memory modification. Memory interventions such as these could have many beneficial

roles in realms such as medicine, therapy, and criminal justice, among many other fields. Unfortunately, any artificial modification of the human memory, whether through behavioral, pharmacological, or technological intervention, also carries significant concerns. While the interventions currently in use for research purposes may not necessarily make it into human practice in any real capacity, they all provide existence proof for targeted memory modifications. In light of the recent advancements and developments in the fields of psychology and neuroscience, our knowledge of the human brain will propagate more precise and less risky methods of memory modifications, and thus, the intentional modification of human memories merits an ethical framework for how and when it should be employed.

Some of the potential therapeutic effects of memory modifications have already been discussed through research on patients with PTSD, depression, and addiction problems. While these effects have been realized in limited research studies and clinical trials, in the case of propranolol as a potential treatment for PTSD patients, physicians may soon employ the drug as an off-label treatment due to the promising results. Whether it has of yet been proven effective or not, memory modifications could have therapeutic effects for numerous conditions and disorders ranging from general memory disorders, such as dementia and Alzheimer's, to anxiety disorders and depression. They could further be used as treatment options for obesity and addiction, or even as therapeutic methods of promoting a generally healthy behavior or mindset.

The main ethical concern for therapeutic memory treatments is safety. Most available treatments for medical or psychiatric problems come with risks and side effects. Ideally, the benefit of the treatment outweighs the potential risks involved. A current issue

with memory modifications, and many interventional treatments of the brain, is that the risks and side effects are not largely known. Because of the interconnectivity of the brain, treatments targeted at specific regions or even for specific memories could have unforeseen downstream effects. Similarly, memories are not housed in a single cell, but across networks of interconnected cells all throughout the brain. It is not certain how altering one cell or group of cells will affect other memory functions. Here exists the potential for unintentional reinforcement of pathological memories, whereby an enhancement in one area may result in an unintended effect such as an increased sensitivity to pain (Hui & Fisher, 2014). This could be due to enhanced activity of memory-engram neurons that have other nervous system roles besides the connection to that particular memory.

Even if we could somehow subvert the safety problems that arise from the brain's intricate interconnectivity, there are still substantial side effects that can arise from altering memories. The main argument for molecularly targeted memory interventions, especially those that work with or against the consolidation or reconsolidation process, is that they are highly specific, do not affect short-term memory or learning, and do so without changing the brain circuitry. Molecular memory modification with PKMζ or propranolol, which has been shown to interfere with highly emotional memories, then should theoretically alter very specific memories with little side effects. Other molecular enhancements to memory currently in use, such as stimulants that affect attention, do not affect long-term memory reconsolidation and have a wide range of health concerns. However, in using PKMζ to strengthen taste-aversion memories in rats, non-targeted taste-related behaviors were changed (Shema et al., 2011). This example shows how changing a

memory might have effects that are not immediately apparent. Because our memory of the past shapes our present experiences, memories have the capacity to shape our future behavior. This connection between memory and future behavior was also explored through false memory experiments (Bernstein et al., 2005; Clifasefi et al., 2013). It is extremely hard to predict the behavioral consequences of enhancing or suppressing memories, especially for emotional memories.

Behavioral changes and other changes that occur as a result of memory modification in humans may be hard to research or observe. If changing a memory also changed an individual's behavior and/or emotions, it would be hard to determine because the altered memory would feel genuine to the individual (Hui & Fisher, 2014). This is because there is no way for individuals to discern between real and modified memories. Because reconsolidation is a natural process following reactivation of a memory, reconsolidated memories should appear no more different than memories recently consolidated from short-term memory, except that they may be strengthened as a result of the process. Thus, the only way of a person knowing that a memory intervention had occurred would be the episodic memory of the intervention technique, assuming they were conscious and that memory was not dampened alongside other reactivated memories.

Another concern is that even though molecular memory modifications may not change the brain circuitry as far as changing patterns of synapses, they can still have effects at individual synapses throughout the brain. More straightforwardly, Hui and Fisher claim "flooding the brain with PKMζ or a related molecule might give rise to too many receptors, eliminating meaningful differences between neurons… [and] could cause wider, network-level imbalances by disproportionately overemphasizing certain memories, possibly

leading to intrusive thoughts or triggering amnesia by interfering with the recall of unenhanced memories" (Hui & Fisher, 2014). While molecular memory modifications should theoretically be specific and have minimal side effects, it is hard to know the extent to how the neurons in the brain will adapt to artificially heightened or lowered levels of a particular molecule.

Along the same note, there has not been enough research on the long-term neurological effects of many of these molecules. Without long-term experimentation, possible late-onset side effects such as a connection to a degenerative brain disease cannot be known. Metabolic and other non-neurological side effects of such molecules should also be taken into account.

Propranolol has been used for years as an oral medication for cardiovascular conditions. Consequently, the effects of oral propranolol treatment are well known. The side effects are generally minor in comparison to the effects of high blood pressure and irregular heart beats. As such, the potential benefits as a treatment for PTSD should also outweigh the metabolic side effects. Propranolol has been shown effective in dampening the emotional content of memories for PTSD patients in multiple clinical trials (Pitman et al., 2001; Vaiva et al., 2003) and laboratory research experiments (Brunet et al., 2008; Brunet et al., 2011). A large issue with the use of propranolol is the possibility of it interfering with episodic memories rather than just the emotional content of those memories in the amygdala. This is a legitimate concern, however "no severe memory problems have surfaced among the tens of millions of individuals who have taken propranolol for heart conditions and high blood pressure" (Henry et al., 2007). But even if propranolol does only affect the emotional content of memories, there are still reasons to

proceed with caution in using it for targeted memory dampening. Overuse of propranolol could result in an individual's reduced ability to respond to emotional stimuli. Walter Glannon writes that this type of "chronic manipulation of neural mechanisms mediating emotional responses to the natural and social environment might weaken or even destroy inhibitory mechanisms controlling harmful behavior and thus also the capacity to conform to social norms" (Glannon, 2011). Not only could this diminish an individual's social functioning, but also, it could lead to a lessened ability to associate fear in given settings, which is a basic survival mechanism to avoid harmful or otherwise painful scenarios. Further, even though propranolol only acts on the emotional content of memories, there is not enough evidence to support the types of emotional memories that it will target when administered. Propranolol treatment could therefore inadvertently act to dampen some of the positive emotional aspects of untargeted episodic memories, resulting in a loss of the positive emotions associated with past life experiences (Glannon, 2011). Assuming that the negative emotional memories that will be targeted through propranolol treatment are sufficiently detrimental to an individual's further well being, the benefits of treatment may even still outweigh these possible unintended effects; however, much of the current clinical use of propranolol as a treatment option for traumatic experiences is immediately following the trauma. In these situations, it can often be hard to tell how the experience will eventually affect the person with or without treatment. A more ideal treatment would involve dampening of the reconsolidation of these types of emotional memories after a patient has already been diagnosed with PTSD, but clinical trials for this type of intervention using propranolol are not as common. Nonetheless, propranolol is a drug that is readily available and much cheaper than psychotherapy and other antidepressant drugs,

so its efficacy as a treatment or prevention therapy for PTSD should continue to be explored.

There are other proposed methods for therapeutic memory modification without many of the safety concerns involved with molecular interventions. Transcranial direct current stimulation (tDCS) and deep transcranial magnetic stimulation (dTMS) are two examples of non-invasive neuromodulation technologies that have shown promising results as interventions during the consolidation and reconsolidation of memory. They can be targeted to specific brain regions in order to affect different types of memories, and they have the power to enhance memory, by aiding consolidation or reconsolidation, or suppress memory, by disturbing the normal consolidation and reconsolidation processes. I would also propose that they could be used in tandem with suggestive misinformation to alter the content of memories. Their effects on memory, however, are understudied, limited to laboratory research settings, and often hard to reproduce. Because of the minimal risk involved in tDCS and dTMS due to their non-invasive nature, their clinical use for depression and schizophrenic patients, and their ability to affect memory in research settings, these and other non-invasive neuromodulation technologies should be examined for therapeutic efficacy in clinical trials. Other neuromodulation techniques used in animals, such as optogenetic interventions, might be avoided for future human use due to their reliance on viral vectors and alterations of cell genomes.

False memory implantation similarly does not rely on flooding the brain with molecules, and therefore, should not have many of the same neurological risks involved with molecular memory modifications. Rather, it is a purely behavioral intervention, dependent on the incorporation of misleading or otherwise false information into past

episodic memory engrams. A theoretical false memory therapy intervention could then be employed, wherein a psychologist, therapist, or even parent might make use of false memory implantation techniques to implant false memories that promote healthy future behaviors.

Herein lies a different ethical dilemma, namely: can the ends ever justify an inherently deceptive set of means? While no ethical framework has been developed to specifically address false memories, Robert Nash and colleagues surveyed a large pool of participants in their article, "Public Attitudes on the Ethics of Deceptively Planting False Memories to Motivate Healthy Behavior." They note the possibility that planting false memories could be of benefit to both individuals and society. They drew off of studies involving false memories that affected future behavior and found that the largest research program so far on the topic involved food studies. While Bernstein and colleagues had shown that a negative false memory could lead to food avoidance with their experiment involving memories of falling ill from either a dill pickle or hard-boiled egg, other studies showed food preferences also changed as a result of positive false childhood memories for foods such as asparagus (Nash et al., 2016). The authors looked at the speculation about such data, such as the media's coining of the term 'False-Memory Diet,' and notions that false memories could be used to "make people less scared of visiting the dentist or make lazy people love to exercise" (Nash et al., 2016). Regardless of the actual legitimacy of such techniques, the authors believe "these moral and ethical questions… are important to tackle as neuroethical and neurophilosophical perspectives assume increasingly crucial roles in the science of memory modification"(Nash et al., 2016).

Nash and his colleagues had the participants in their study read and respond to a

hypothetical scenario where deceptive false memory therapy was used to alter unhealthy behavior. Participants in the first study were then asked to respond with written statements about the acceptability of therapists using the technique to improve eating habits in their patients and the plausibility of its success. Participants of a second study were asked to respond about whether the treatment was acceptable, moral, and ethical and what factors they might consider in their judgment. Results of the first study showed that people tended to believe more strongly that deceptive false memory therapy would be acceptable for use on themselves than on other obese people. Participants were less sure that the therapy could be considered moral and ethical. Also, participants overall were fairly convinced of the possibility of planting false childhood memories, but they were less convinced that those types of memories could affect future eating behavior (Nash et al., 2016).

The results of study two are more interesting in that they provided specific reasons why participants found deceptive false memory therapy acceptable or unacceptable. 37% of the arguments against false memory therapy were based on the potential consequences or dangers of its use. The arguments were further divided into arguments about psychological consequences and the patients' well being, authenticity consequences and the patients' personal identity, and social consequences affecting the patients' relationships after altering a memory. 32% of the arguments against false memory therapy claimed that the ends do not justify the means. These study participants were mostly concerned with the integrity of healthcare professionals, and they expressed a perceived immorality in lying and distaste with modifying peoples' minds. Another 14% claimed that false memory therapy was unacceptable for its potential for abuse. Individual responses in this group

voiced concerns that the therapy could potentially be used for alternative motives other than healthy behavior, such as persuading gay people that they should be heterosexual, or pushing someone to convert to terrorism or commit violent acts. Interestingly, 36% of the arguments made for the acceptability of false memory therapy indicated that the ends do in fact justify the means. These individuals felt that the possible individual or societal benefit outweighed integrity in terms of ethical practice. Other arguments for the acceptability included increasing treatment options and that some people need help and do not know how to get it (Nash et al., 2016). It is important to realize that these arguments are public opinion about a hypothetical scenario, but public opinion can be a good measure of things to consider when making an ethical framework for a new treatment.

One last concern about the idea of false memory therapy not mentioned by the survey respondents is the fact that once false memories are implanted in a subject, they often evolve with details that were not suggested during the implantation. In almost every false memory study, subjects tend to recall details such as what other people were wearing or doing. Thus, it will never be certain what an individual might do with suggested information or how exactly the false memory will result. While false memory therapy can come with these side effects, another interesting ethical consideration about false memory arises when the false memory is itself a side effect of a different type of therapy.

Due to our still limited understanding of normal memory processes, we must proceed with extreme caution with any and all methods of disrupting memory's natural reconsolidation process. The issue with false memory implantation, however, is that it does not solely occur under specific and targeted research trials. Rather, false memories arise in everyday life when individuals are recalling past events. This means that professionals in

fields such as criminal justice and psychotherapy, where individuals are placed under pressure to remember events from their past, must be extremely cautious to avoid providing false or leading information that can be incorporated into their subjects' memory and believed to be true.

Dr. John Cannell and colleagues explored this type of incidental false memory implantation through malpractice suits filed against therapists involved in recovered memory therapy. Cannell, Hudson, and Pope define recovered memory therapy as including the following: "(1) An assumption that patients may harbor 'repressed' memories of traumatic experiences; (2) an assumption that these repressed memories may be recovered after a prolonged period of amnesia; and (3) an assumption that patients may gain relief from psychological disorders by attempting to recover, explore, and understand these memories with the assistance of a therapist" (Cannell, Hudson, & Pope, 2001). While psychotherapists may not have been intentionally implanting false memories into their patients, this technique is very similar to the techniques used in false memory research. Therapists believed that by having their patients dig deeper and deeper into their memories, they would be able to discover memories for past traumatic experiences that had been repressed by some sort of natural defense mechanism. This idea was a popular belief due to a study on women who had a medical history of a prior sexual assault (Williams, 1994). The study found that 38% of the women did not recall or did not report the prior abuse in interviews. While certain professionals viewed this as evidence of repressed memories, there were issues with the manner in which the study was performed. According to Loftus and Polage, "the women were never asked directly about the abuse. In other studies in which individuals have been asked directly, they admit that their failure to

report was not due to lack of memory" (Loftus & Polage, 1999). Despite the popularity of the Williams study, Daniel Schacter writes in his book two years later that there is "as yet little or no scientifically credible evidence that people who have suffered years of violent or horrific abuse after the years of infancy and early childhood can immediately and indefinitely forget about the abuse" and that "the idea that forgetting in abuse survivors is caused by a special repression mechanism – something more powerful than conscious suppression – is still without a scientific basis" (Schacter, 1996). In other words, rather than resurfacing memories of repressed traumatic experiences, these therapists were guiding patients into the creation of false memories.

Many of these false "recovered" memories painted horrifying pictures of abuse. Some even led to criminal convictions for the falsely accused "perpetrators" (Loftus & Polage, 1999). In one instance, "the therapist implanted memories of incest in [a family's] eldest daughter, including memories of giving birth to her father's baby. The daughter's gynecological examination showed her to be a virgin" (Cannel et al., 2001). Another woman "formed false memories of satanic ritual abuse in the course of therapy with a Wisconsin psychiatrist" (Cannel et al., 2001). With these increasingly unlikely memories being formed, psychotherapists began to be sued on the charge that they did not provide informed consent prior to therapy by stating that false memories could be formed. While Loftus and Pickrell's paper on false memories was published about the same time as the Williams study on repressed sexual abuse, many did not consider the possibilities of false memories arising through therapy.

Settlements in the early cases awarded patients up to 10.6 million dollars on the basis of the failure of therapists to obtain informed consent prior to recovered memory

therapy. The settlements mainly concluded that the patients, many of whom were led to believe outrageous false memories of sexual abuse, were not properly informed of the risks of false memory implantation. Many therapists were found to have had a legal obligation to inform patients of the risk of false memories. The American Psychological Association eventually reached four conclusions on the issue: "most people who were sexually abused as children remember all, or part, of what happened to them; it is possible to remember abuse that has been forgotten for a long time; it is also possible to construct convincing pseudo-memories for an event that never occurred; and there are gaps in our knowledge" (Merskey, 1996). While the APA states that it is possible to remember abuse that has been forgotten for a long time, they are likely referring to isolated instances of abuse that were forgotten by natural memory processes rather than some sort of repression mechanism. These cases point out the importance of this type of memory research, and the implications that it has on everyday life.

A very similar effect can occur in the process of eyewitness testimonies. Criminal trials rely very heavily on the accounts of eyewitness testimonies, but it is important to understand that their memories may be heavily influenced and skewed by the time they take the stand. Eyewitnesses may face many rounds of interrogation and interviews following the criminal event. In each instance they are asked to recall their experience, reactivating the memory engram in the process. As such, through multiple reactivations followed subsequently by leading questions and probes, misinformation and suggested evidence could be reconsolidated into the original memory. Worryingly, this reconsolidated memory will not appear to be altered in any way to the eyewitnesses themselves.

Wrongful convictions are a serious issue in the United States. According to the National Registry of Exonerations, there were 139 exonerations in 2017 (National Registry of Exonerations, 2017). The individuals who were exonerated in 2017 spent an average of 10.6 years incarcerated for a crime they did not commit, for a total of 1,478 years lost in the system. Of those 139 exonerations, mistaken eyewitness testimony was a leading factor in 37 of the cases. This report includes only those who were exonerated that year, but it is extremely difficult to estimate the amount of people convicted of serious crimes who are currently incarcerated due to wrongful convictions and especially those due to false memories of eyewitnesses.

The possibility of misinformation being incorporated into eyewitness testimonies needs to be acknowledged in every courtroom. But what if it were indeed possible to enhance an eyewitness' memory of an event, through molecular or other means, instead of possibly altering the memory? Hui and Fisher wonder, "if this were possible, would there be a moral obligation to preserve certain memories?" (Hui & Fisher, 2014). Eyewitnesses could theoretically take doses of PKMζ following the event to enhance consolidation or undergo cue-driven reactivation of the memory with the aid of tDCS or dTMS in order to strengthen the reconsolidation of their memory for the event. Even though false memories may arise in the days in between witnessing a crime and the eyewitness' day in court, intentionally modifying an individual's memory through enhancement methods seems to be too much of an overstep, and "advocates for autonomy would likely argue that pressuring individuals to alter something as deeply personal as their memory would be too much of an infringement" (Hui & Fisher, 2014). Further, given the nature of many violent crimes that people witness, others would argue that enhancing such memories could be

cruel or torturous to witnesses.

While it may not be acceptable to force people to alter their memories for the purpose of eyewitness testimony, many neuroethicists have considered whether or not individuals even have the right to alter their own memories. Many claim that while memories may seem inherently personal, we have a "duty to remember" to society. The main idea here is that personal memories are of value not only to the individual who possesses them, but also to society as a whole. Adam Kolber considers a hypothetical scenario wherein an individual unexpectedly regains consciousness during an invasive surgery (Kolber, 2014). Should the patient have the right to erase their memory of the experience in order to avoid future trauma? It seems as if that right should be up to the patient, but if the patient had become consciously aware of a crime during the process, can his or her own desire to avoid later trauma outweigh the moral duty to remember and report said crime? Walter Glannon disagrees with the idea of a "duty to remember." His viewpoint is that memories are inherently inaccurate and fallible, and thus, even if a patient does hold onto their memory out of duty, it is not likely to be accurate in the first place (Glannon, 2014). It seems a stretch to say that the fallibility of memories makes them completely invaluable as a source in eyewitness testimonies. To make such a claim would be to undermine every eyewitness account ever given, and when we can only rely on those involved or present to corroborate a story, there would be no means of reaching any conclusions beyond a reasonable doubt. The main point here is that we must be weary of the effects of misinformation and suggestible discourse on memory when considering any account based off of an individual's memory. We should also be cautious in allowing people to tamper with their own memories. Even after traumatic experiences where an individual

may elect to take propranolol to dampen the emotional content of his or her memory and avoid the potential of developing PTSD in the future, treatment providers should consider the potential obstruction of justice that such memory modifications can have on future prosecutions.

Memory modification techniques have also been proposed as a future intervention for defendants and criminals. While none of the methods of memory modification that have been discussed are currently at a level of specificity to achieve reliable results in this field, they still raise questions about what the future could bring and what types of interventions should be allowed. Substances such as alcohol and thiopental have been used in the past to gain testimony from criminal defendants (Cabrera & Elger, 2016), but any use of memory modification techniques in criminal interrogations could be deemed as both coercive and illegal. Cabrera and Elger propose two uses for memory modification techniques in the criminal justice system that could serve as an aid to make incarceration and therapy of criminals more economically viable and efficient. The first use would be in dampening the emotional content of an offenders' criminal memory. Many criminals, for example rapists or pedophiles, might relish in the memories of their crimes. By dampening those associated memories, retribution could be achieved "via the loss of enjoyment the offender would suffer," and crime deterrence could be achieved "if such offenders were motivated by the anticipation of savouring these memories and came to know that if they were caught they would lose them" (Cabrera & Elger, 2016). An intervention for other types of criminals would involve enhancing the emotional content of criminal memories. This would lead to heightened feelings of remorse and shame and could hold criminals more accountable for their actions (Cabrera & Elger, 2016). Of course, the ethical issues involved here are no

different than those already discussed. Enhancing memories for a terrible action that someone committed could be cruel or even torturous. Also, criminals still maintain treatment rights, meaning that they would have to agree to any type of memory treatment in the same way as those who would undergo treatment for therapeutic reasons.

The use of memory modifications in the criminal justice system also raises the question of whether or not these types of interventions should be in the hands of the state. If memory interventions are in the hands of the state, they would then have the ability to shape peoples' minds to an extent to which we do not currently know. This could in effect take away our ability to keep checks and balances on the system if they began to shape criminals' civil and moral constitutions towards placid obedience.

Guidelines for ethical practices will help therapists and other professionals to assess and inform their patients or subjects of the risks involved in memory modification techniques as well as the risks of false memories developing through everyday practice, especially with the continuing research devoted to the topic; however, there could be scenarios where memory modifications are used as a tool, such as in CIA and military contracting of psychiatrists and psychologists. The CIA and U.S. military have been known to use forms of psychological experimentation and warfare in the past. Examples include interrogations in an Iraqi prison and Guantanamo Bay, experiments with LSD and brain electrodes, and creating artificial multiple personality disorder using hypnosis (Ross, 2007). Knowing that modified memories can have an effect on future behavior and emotions, it is imperative that these techniques are not used for evil ends.

A final ethical consideration for memory modifications is involved in every type of memory modification and intervention scenario imaginable, namely, the connection

between memory and personal identity. In general, who we are as a person is seated in the brain. Memory is one of the most important parts of who we are, because it allows us to connect with our past selves. However, personal identity is hard to define. Philosophical arguments for what constitutes personal identity are varied, but most rely on some type of numerical identity or narrative or psychological continuity. It is not clear that memory modifications could affect an individual's numerical identity to his or her past self, but modifications to memory certainly have the potential to disrupt an individual's psychological continuity. Still, according to Hui and Fisher, this psychological continuity includes mainly our beliefs, intentions, preferences, and capacity for rational thought (Hui & Fisher, 2014), for which erasure of even critically important memories may not alter.

Our episodic memories are crucial to our personal identity, for without the memory of a past experience, there is no sense of having existed at that time. Thus, our memory implies our past and continual existence as a person. But our beliefs about ourselves, or our dispositional characteristics, are not rooted in our episodic memories. Rather, our "dispositional sense of the self turns out to be resilient across dramatic damage to memory systems. There now exists an extensive database showing that even patients suffering total anterograde and retrograde episodic amnesia can describe their own personal characteristics both reliably and accurately" (Klein & Nichols, 2012). If psychological continuity were all that was required for maintenance of personal identity, then we should have no worries about messing with any and all memories, because episodic memories are not required for this self-trait memory. However, I argue that self-trait memories are not sufficient for personal identity, because without episodic memories, there is no ability for an individual to place him or herself in the past. For example, H.M., who underwent a

bilateral hippocampal lesion surgery and lost the ability to form new memories, was still able to identify with his childhood self. Although he could not remember how old he was currently or what year it was, he was able to provide detailed accounts of memories from his childhood and identify the child in his memories as a young version of himself. There is something remarkable about having such a connection to the distant past while not knowing what occurred 15 minutes prior.

Another way to frame memory's connection to an individual's personal identity is as follows: "a person *P* at time *t* is identical to a person P_1 at a later time t_1 if P_1 at t_1 remembers *P*'s experiences at *t*. Since identity is transitive, it can also arise from overlapping strands of such memory links: if P_2 at t_2 does not remember *P*'s experiences at *t*, P_2 at t_2 and *P* at *t* are nevertheless identical if P_2 at t_2 remembers P_1's experiences at t_1, and if P_1 at t_1 remembers *P*'s experiences at *t*" (Roache, 2015). This interpretation poses identity in terms of a person at a given time. To erase a memory of a particular time is to dissociate from that person, such that that person at that time is no longer identical with the current individual.

Those who argue against memory modification from the view of personal identity believe that our memories are so crucial to our sense of self that they are the basis of who we are as individuals. Regarding memory erasure, Leon Kass argues "… to deprive oneself of one's memory – in its truthfulness also of feeling – is to deprive oneself of one's own life and identity" (Kass, 2003). Those who object to the personal identity argument claim that because memories are naturally and inherently reconsolidated and altered, changes in memory cannot be a threat to identity. While there is a difference between actively and intentionally altering memories and the passive, natural process that occurs in the brain,

the risks to personal identity can be looked at in the same way as risks of safety in treatment. In other words, for those who are in serious need of some sort of memory modification, the issue is likely affecting their true personal identity much more than any memory enhancement or suppression would. While memory modifications can surely be the cause of some personal identity issues, they can also act to combat the same problems in the right scenarios.

Conclusion

Much about the human memory is yet to be discovered. Fortunately, the scientific community has made great strides in the past 50 years or so in understanding the mind. Over time, our perception of memory has evolved from a blank slate written upon through experience to a processing system, involving countless functions, mechanisms, and brain regions. We have a better understanding for why we remember some things and forget others, how memories are physically stored, and why memories of the past are painted over with a new and updated palette each time they are retrieved.

Research into reconsolidation has provided us with a neural mechanism for how we make new connections within and between past memories. It has led to better understandings about the evolutionary adaptations involved in our memory system, namely that we have biological processes in place to strengthen our memories while making new associations between them over time, allowing us to make the most of ever-changing environments. It has also provided critical information for a process that can be manipulated in order to enhance, alter, or suppress memories of many different types and contents.

False memory research has opened people's eyes to the fallibility of our memories. In providing existence proof for a psychological phenomenon wherein people adopt and believe completely fabricated stories to be products of their own memory, it has shed light on important concerns about common practices such as psychotherapy and eyewitness testimony. It has also provided insight into our own memories of the past, notably the knowledge that past memories are not an exact account of past experiences but rather are compounded with new and possibly misleading information with each retrieval.

Molecular memory modification research has helped to identify specific molecules involved in various memory processes. By manipulating the amounts of these molecules or the effects of the processes they are involved in, we continue to add to our knowledge of the physical mechanisms behind memory formation, storage, and retrieval. With this knowledge comes novel ways of enhancing, suppressing, or altering memories through pharmacological interventions, which can be used to treat countless issues stemming from memory disorders or the effects of deleterious memories.

Neuromodulation technologies have given researchers the capability of making causal connections between specific brain regions and their functions. They have also served as methods for non-invasive interventions for not only memory functions, but also a whole range of other problems from depression to schizophrenia. Technologies such as those discussed here will continue to rely on as well as guide future neuroscience research.

The past and current uses of the research on memory modifications pales in comparison to what they mean for the future. Of course, it is important to understand the current state of psychology and neuroscience research in order to begin to look forward, but the real issues to address are the ways in which this research will be put into practice. The most crucial components of the research could be as elementary as simply understanding that a certain phenomenon exists, as was the case with false memories and recovered memory therapy or eyewitness testimony. In other cases, such as molecular modification of memories, there are wide ranges of ethical issues to consider from safety to autonomy and personal identity. In any case, it is important to stay ahead of the research and technologies, because our understanding of and ability to manipulate brain functions is evolving at an exponential rate.

In regards to any type of memory modification used in humans, there is no simple answer for its ethical progression into practice. Rather, each should be considered on a case-by-case basis, because the variables involve not only the particular type of intervention at hand, but also the state of the individual. Some types of memory modifications show promise as potentially effective and low-cost treatments for individuals with debilitating conditions rooted in traumatic or otherwise injurious memories. When considering these treatment options, providers must always consider their efficacy over other treatments, the possible neurological and metabolic side effects, the effects on other memories and quality of life, effects on an individual's personal identity, and most of all, the individual's informed consent to treatment. Because of the potential viability of such interventions, I believe they should be subject to cautious but steady further research in clinical settings.

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Biography

Michael Reul is a graduating senior at the University of Texas at Austin pursuing dual degrees in the Plan II Honors Program and Biology Honors through the Polymathic Scholars Honors Program. Michael will attend Baylor College of Medicine beginning in August of 2018.