



MEET ME IN MONTAUK: THE SCIENCE OF TARGETED MEMORY ERASURE

By Rosabel Tan

In *Eternal Sunshine of the Spotless Mind*, two unhappy lovers erase their memories of each other: a desperate attempt to escape the haunting pain of their failed relationship. It's a simple procedure, as Dr Howard Mierzwiak explains, a mild form of brain damage comparable to a night of heavy drinking. And when you wake up, the pain is gone. You remember nothing.

We've all wished we could forget, at one stage or another. We wish we could forget trivial embarrassments: the time we texted a booty call to our mum by mistake, or the time we vomited chunks of mushroom and merlot in the shadows of Myers Park. We wish we could forget the heartbreaks, the failures, the things that make us cry.

For a long time, these wishes were purely that: a flight of fancy. So much so that *Eternal Sunshine* won the Saturn Award for Best Science Fiction Film the year it was released. Targeted memory erasure is, after all, a ludicrous concept, and one destined to exist only in fantasy and film – or so we thought.

THE HUMAN MEMORY SYSTEM

The main reason targeted memory erasure seems so implausible is because our memories are incredibly complex. Rather than being located in one specific area of the brain, the human memory uses a number of different neural structures, reflecting the different types of memories we have.

First of all, we have our short-term memory. This refers to our ability to hold information in our mind over a short space of time, usually only a

matter of seconds. Although individuals differ in their capacity, we can, generally speaking, hold 7 ± 2 chunks of information (partially why telephone numbers are seven digits long). Rehearsing information in our short-term memory results in it being consolidated into our long-term memory, where it can then later be retrieved.

Long-term memory can be categorised according to 'declarative' and 'non-declarative' systems. Declarative memories are those which we are explicitly aware of and are able to articulate, and can be either episodic or semantic. Episodic memories catalogue our past experiences, and are typically associated with a specific time and place. Semantic memories, on the other hand, refer to our knowledge for generic facts. These memories lack the temporal and contextual component that characterise episodic memories, so although we all know that a light year is exactly 9,460,730,472,580.8 kilometres, we are unlikely to remember the precise moment when we learnt this.

Non-declarative memories, on the other hand, are more implicit in nature. They include physical skills, like riding a bike or doing sweet karate moves; spatial knowledge, like how to find your way around your house in the dark; and emotional associations, like how the smell of matches reminds you of birthdays.

The difficulty in erasing a specific memory is twofold. Firstly, sensory information is stored accordingly throughout the brain. Visual details are stored in our visual cortex, auditory details in our auditory cortex, and emotional details in the areas associated with emotional processing.

Memory storage is further fragmented because different types of memories are stored in different types of the brain, and any specific memory we have will typically involve these different types. Let's take, for instance, our memory of the time our big brother handcuffed us to a shopping trolley and then ran away, leaving us there for two hours before our mother found us sobbing in the dog-food aisle, our pants a sodden mess. This memory is likely to involve not only episodic information, but also semantic information like the name of the supermarket (Foodtown Grey Lynn); emotional associations, such as how the smell of dog-food now makes you weep; and spatial information, like the layout of the different aisles and the convoluted path we took as we tearfully searched for help.

Every time we retrieve that sordid ordeal from the recesses of our brain, the neurons associated with this memory are simultaneously activated and, as a result, strengthened. This is best summarised by Hebb's rule that 'cells that fire together, wire together'. Every time a memory is activated, the relationships between the neurons associated with it grow stronger, making it easier to remember. This is why repetition works: the more practice those specific neurons have at communicating with each other, the more efficiently they can be retrieved. This process – by which the associations between neurons are strengthened – is called long-term potentiation, and is integral to remembering.

Every time we retrieve a memory, we reconsolidate (or re-save) it. The neural activity involved in this process mirrors that initial process of consolidating information: after all, we're basically re-running that process of transferring information from our short-term to our long-term memory. During reconsolidation, however, the memory being retrieved is temporarily vulnerable to modification. We tend to give specific details greater emphasis, for example – we're more likely to remember the ugly dress your boyfriend's bitchy ex was wearing than her inane comment about the sociology paper she's doing. Over time, our memories are slowly re-edited. Details are lost while others are retained.

This process of reconsolidation is key to targeted memory erasure. If disrupted, our memories might not get properly re-saved. In some cases, they might not get re-saved at all. Although a number of neurochemicals are involved in the processes of long-term potentiation and reconsolidation, the two enzymes PKM ζ and α CaMKII play a particularly important role in the retention of our long term memories, and hence have been the focus of research thus far.

BYPASSING MEMORY LANE

Despite the staggering complexity of our memory system, targeted memory erasure is well on its way to becoming a reality. Studies have found that blocking either PKM ζ or α CaMKII result in specific memories being erased, presumably because it disturbs the reconsolidation process. Researchers have, for example, developed a drug called ZIP that blocks the activity of PKM ζ in the brain. In one study, rats were trained to press a lever in order to get a treat of cheese. Typically, once rats learn this be-

haviour, they don't forget it. When a single dose of ZIP was administered during the execution of a lever press (and hence the process of reconsolidation), however, the response stopped. The specific memory (knowing that pressing the lever resulted in food) ceased to exist.

It isn't just classically conditioned behaviours either. Studies have also erased rats' memories for spatial information, including their ability to navigate their way through a maze whilst avoiding areas resulting in mild electric shocks. Thus, when ZIP was administered, the rats forgot their previously learnt knowledge of the space, and paid the price for it.

Taste memory has also been manipulated in aversion studies, where rats were given sugar water that elicited the symptoms of food-poisoning. As you'd expect, they quickly learnt to avoid drinking said water. One dose of ZIP later, though, and they were lapping it up again, oblivious to the negative consequences of doing so.

Although ZIP has only been used on rats so far, scientists speculate that it will operate in a similar fashion in the human brain. Theoretically, then, if you administered ZIP while retrieving a specific memory, that memory could be erased forever. All those painful memories - the unnecessary fight you had with your boyfriend last week or the time you (accidentally) called out Anne Tolley's name in the throes of passion - wouldn't just be a thing of the past, they'd be gone forever.

HELLO OBLIVION, GOODBYE SHAME?

The implications of these findings are huge. Drugs like ZIP could potentially serve as a 'cure' for psychological disorders like post-traumatic stress disorder (PTSD) or drug addictions. But although their potential benefits are clear, whether such memories *should* be erased is another question altogether. We remember for a reason. We remember because it helps us learn, adapt, and ultimately, to survive.

Sure, we can forget that the obese homeless guy who sleeps on the K Road over bridge once cornered you and demanded that you hand over your wallet. And sure, maybe then we'll stop shaking in fear every time that odious stench of bourbon, sweat, and pee wafts past us. But if we forget, we fail to learn. If we forget, we live in a state of perpetual ignorance. Erasing traumatic memories means that we'll continue to strut obscenely down that seedy stretch of road screaming "I'm rich, bitch!" and we won't be a better person for it.

Erasing traumatic memories may offer an instant reprieve, but it will also hinder the natural process of recovery. If we erase these memories, we stunt our personal development, and our perception and understanding of the world becomes severely skewed: terrible things become less terrible, shameful acts seem less shameful, and we deny accountability for our actions.

Perhaps most importantly, erasing our memories means erasing a part of who we are, not just as individuals but society as a whole. Our memories shape who we have become, without them we are vacuous vessels. San-

tayana's observation that those who do not remember the past are doomed to repeat it springs to mind: what if, for instance, we erased everybody's memories of the Holocaust?

Likewise, erasing the physical and psychological aspects of addiction sounds great - in theory. On the one hand, it has all the makings of an idyllic, addiction-free society. On the other hand: we become addicted for a reason. Providing the means through which addictions can be easily overcome may simply encourage greater experimentation, and an increased proclivity towards addictive behaviour.

Of course, many argue that the benefits of forgetting outweigh the costs. Walter Glannon at the University of Calgary maintains that "when a condition is intractable to other interventions, when it severely affects one's quality of life, and when it poses a significant risk of harm to oneself and to others, considerations of immediate efficacy can override considerations of long-term safety." The man has a point. PTSD can stem from horrific experiences like the time your dad made you bomb a small village in the South Island. The symptoms - which include flashbacks, nightmares, and depression - impact greatly on your ability to function in daily life. Nevertheless, rather than searching for a quick fix, emphasis should be placed more on addressing the actual experiences causing it. PTSD develops for a reason, and those reasons aren't necessarily unavoidable.

REMEMBERING THE PAST: RO15-4513

The development of Ro15-4513 in 1984 raised similar ethical questions. Initially developed as an antidote to alcohol overdoses, commercialisation of Ro15-4513 was halted due to the legal issues surrounding its effects. Just as ZIP blocks the effect of PKM ζ , Ro15-4513 was found to block the effect of ethanol without removing it from the bloodstream. In other words, you could knock back an entire bottle of whisky, do a little dance, realise you have a test in an hour, administer a dose of Ro15-4513 and sit your test sober (but fail because you didn't actually study). The implications of this drug were concerning to say the least, largely due to its short half-life. Multiple doses were necessary for patients who were significantly intoxicated because the drug would wear off before the alcohol had metabolised in the body. There was, as a result, the possibility of a false sobriety. If alcohol was still being metabolised when the drug wore off, individuals would become incredibly drunk again, possibly resulting in serious accidents (like passing out on the motorway and plummeting to your death).



BOTH RATS ABOVE RECEIVED THE SAME AMOUNT OF ALCOHOL, BUT THE ONE FACING US ALSO RECEIVED AN INJECTION OF RO15-4513. PHOTOGRAPH COURTESY OF STEVEN M. PAUL, NATIONAL INSTITUTE OF MENTAL HEALTH, BETHESDA, MD.

It's not all bad though. One of the implications of ZIP is that it offers a starting point to develop a drug that enhances, rather than blocks, the activity of PKM ζ or α CaMKII. If this is the case, the progression of neurodegenerative disorders that affect memory, like Alzheimer's, could be slowed down. Of course, even the development of a drug like this poses a number of ethical issues: How much is too much?

A POSSIBLE FUTURE WHICH OWES NAUGHT TO MEMORY

Picture this: The year is 2093. A new drug has been released into the market, aptly named ZIP. In townhouses all over the world, parents zealously crush up these pills on their Formica tabletops before sprinkling them carefully onto their kid's cornflakes. They then wait impatiently, fervently hoping that their baby will become the next Stephen Hawking or Charles Xavier, minus the wheelchair.

Universities are swarming with lazy students who pop a couple ZIP at the beginning of their day. Cramming time is cut in half while drinking time triples. Weary lecturers keep jars of ZIP by their journals, their eyes darting suspiciously around as their shaky hands reach for yet another hit.

Meanwhile, in the back-alleys of New York, a sweaty horse of a man clutches a handful of UnZIP as he waddles back to his loft. There, he greets his love. She stares back at him with muted eyes, her mumbling stifled behind the dirty rag tied roughly around her ashen cheeks. She squirms desperately in her chair as he descends upon her, but can do nothing as he crams the UnZIP down her throat. She whimpers as the memories of her captor melt away.

In a prison cell, a man grimly brings a bottle of UnZIP to his lips as he mentally relives the vicious stabbing of his son and his wife. Across the way, a rakish young lad shakes his head. "Has it come to this?" he asks.

The man gulps down a fistful of regret. "Yes." He mutters hoarsely. "Yes, it has."

OR NOT.

This is, of course, a future way beyond our grasp. Despite all the research, we still don't know that much about the human brain, let alone our memory system. Although PKM ζ and α CaMKII play a significant role in the retention of our memories, they're not the only neurochemicals involved in this process, and the reality of targeted memory exposure is still a far way off. Indeed, Larry Squire, one of the leading researchers in the field of memory, warns that "it's likely that any effects are reversible, temporary. You may be able to bring up a memory, weaken it, but eventually the memory comes back. The effect is more like interference than real change."

The possibility of such a process is, however, there nonetheless, lurking in the shadows and sparkling in the sky. Be warned. Be prepared. And remember: