F2. Learning to Remember: The Biological Basis of Memory

Chapter Objectives

Our ability to learn, retain and recall information requires that it become 'hard-wired' in the neuronal circuitry of our brain. As our understanding of the biological mechanisms of memory evolves, we face new opportunities in the treatment of memory disorders, as well as in the enhancement of normal memory function.

This chapter aims to:
1. Describe short-term and long-term memory.
2. Outline the biological mechanisms of memory consolidation.
3. Discuss the degenerative memory disorder Alzheimer's disease and associated ethical issues.
4. Discuss the neuroethical concerns associated with artificial memory enhancement.

F2.1. Learning to Remember

When we learn new information it does not necessarily mean that we will retain it and be able to remember it at a later date. Learning simply involves the acquisition of new knowledge, while memory enables us to store that information within the nervous system so that we can recall it sometime in the future. A part of our brain called the hippocampus plays a particularly important role in converting learned information into a memory. We can store our memories for varying lengths of time, ranging from periods of only a few seconds, to a few years, or an entire lifetime. Memories are therefore often classified according to whether they are stored for a short period of time (short-term memories), or a long period of time (long-term memories).

Short-term memory is sometimes referred to as working memory because it is used during the course of intellectual reasoning, with the information being deleted from the memory banks as each stage of the problem is resolved. For example, working memory is often used when dialling a new telephone number. To do this, you would typically look the number up in a telephone directory, store that information in your short-term or working memory, dial the number (without referring back to the directory), and then conveniently forget the telephone number as you begin your conversation. Yet, if you repeat this process a number of times, you will begin to store the information more permanently in your long-term memories.

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memory. Unlike short-term memory, when events or facts are stored in a person's long-term memory they are reasonably permanent, and not easily forgotten. Even if the information is seemingly lost, a long-term memory can usually be recalled with a few hints.

Interestingly, memories can be modified by our perceptions, beliefs, or through suggestions made by others about a specific situation after the event has occurred. Memories are, therefore, not always accurate recollections of an event since they can be altered to become what are known as ‘false memories’. Scientific research has shown that when people who witness a particular incident are later exposed to new and misleading information about this event, their recollections can become distorted. In particular, misinformation has the potential to invade our memories when we socialize with others, when we are suggestively interrogated, when we imagine a scenario, or when we read or view media coverage about some event that we may have experienced ourselves. Over the last two decades researchers have learned a great deal about the conditions that make people susceptible to memory modification. In particular, research has shown that memories can be modified through suggestion and imagination, and that they are altered more easily when the passage of time has allowed the original memory to fade.

Q1. Memories are fragile and can change over time, that is, memories that people believe to be true may in fact be a modified version of the actual event (a false memory). Different areas of our brain are involved in processing true and false memories and their activity can be identified using neuroimaging techniques. Should neuroimaging be used to support the testimonies of eyewitnesses to a crime when there is good evidence that their recollections may be distorted to a degree?

Q2. Some mental health professionals encourage patients to imagine childhood events as a way of recovering supposedly buried or repressed memories. Since imagination is a mechanism by which false memories are instilled, what are the ethical concerns of this form of ‘therapeutic’ intervention?

F2.2. Making Memories

The transfer of information from short-term memory to long-term memory is known as consolidation. During the process of consolidation, pathways in the brain are strengthened or ‘hard-wired’ as brain cells (neurons) become more efficient in their ability to transmit information to one another. This strengthening process occurs as the spaces between neurons (synaptic junctions) develop more effective means of transmitting a chemical message (neurotransmitter) from one neuron to another (see figure). These neuronal pathways are called memory traces or memory circuits because the strengthening of the synaptic junctions is believed to hold the key to the storage of memories within the brain. Once memory traces are established they can be activated by the thinking mind (the frontal cortex) to reproduce, and sometimes modify, memories.

Another form of memory, known as negative memory, actively reduces the strength of connectivity between neurons so that the brain can ignore information that is of no survival significance to the individual. This occurs because our brain is continually inundated with fresh sensory information from the outside world and if our minds attempted to remember all of this information the memory capacity of our brains would be exceeded within minutes.
Thus, the brain not only strengthens certain pathways, but it also inhibits others which are processing ‘useless information’ so that insignificant memory traces are not established.

Information is transmitted from one neuron to another across a space called a synapse. Chemical signals, known as neurotransmitters, are released from vesicles in the presynaptic neuron. The neurotransmitters diffuse across the synapse to bind to receptors on the postsynaptic cell’s membrane. Changes at the synapse can either enhance or reduce the efficiency with which this neurotransmitter signal is transmitted from one neuron to another by altering the amount of neurotransmitter that is released from the presynaptic cell, or the amount of receptors present on the postsynaptic membrane.

As a way of enhancing the consolidation of long-term memories, the brain has a natural tendency to rehearse information that catches the mind’s attention. The type of information that tends to be circled repeatedly through the mind is typically that which has an emotional component to it. Information that does not have significant value to the individual typically requires conscious effort to consolidate. In other words, we have to actively cycle the information through our mind. You may be familiar with this phenomenon, for example, most people find it is relatively easy to remember an emotional event such as a time when they were embarrassed in front of their friends, yet find it difficult to recall a mathematics formula that they have actively tried to store in their memory. This occurs because in circumstances where we are excited or scared, hormones such as cortisol are released within the body as part of the stress response. Cortisol is a neuroactive hormone that acts to fast track the consolidation process by enhancing synaptic changes between neurons.
The body’s natural tendency to enhance the storage of emotionally laden memories has important survival value for many animals, including humans. For example, in dangerous circumstances we will typically experience emotions such as fear or anger that help us to respond appropriately to the threat (either fleeing the scene or putting up a fight). These emotions, along with the body's 'stress response' which elevates levels of cortisol, help us to remember this important event so that we are better able to respond if faced with a similar situation in the future. Thus, the brain’s tendency to store emotional memories is an adaptive mechanism that enhances our ability to negotiate the environment in which we live. This adaptive process has important consequences for the neuronal processes involved in addiction, which are similar to those involved in the storage of memories (see chapter F3 for a discussion of the stress response and its role in addiction).

Q3. In 1999 researchers genetically engineered a mouse that outperformed regular mice on learning and memory tasks. Should this technology be used in humans to produce people with superior mental abilities?

F2.3. Fading Memory: Alzheimer's Disease

As we age our ability to store and recall memories often deteriorates and many older people experience minor forgetfulness due to degenerative changes that occur in areas of their brain involved in memory processes - the cortex and hippocampus. Yet, the memory loss and neuronal changes that occur in Alzheimer's disease are far more severe. Alzheimer's disease is memory disorder that starts with minor forgetfulness, but progresses to serious memory loss, often leaving the individual suffering from confusion, delusions, depression, restlessness, sleeplessness and loss of appetite. Alzheimer's disease typically occurs in older aged people, but can occasionally strike those in their 30's. The occurrence of Alzheimer's disease becomes more common with age, affecting almost 5% of people between 65-70 years, and almost 50% of people over 85 years of age in the US.

Environmental and genetic factors influence our susceptibility for developing Alzheimer's disease. For example, environmental toxins can increase the occurrence of this disease. The first clue to the genetics of Alzheimer's came from observations that people with Down syndrome, a disorder caused by having an extra copy of chromosome 21, almost invariably suffered from Alzheimer's if they survived until middle age. A gene on chromosome 21 is now known to be involved in early onset Alzheimer's and more recent research has demonstrated that certain variations of genes found on chromosomes 1, 14, and 19 are also involved in the development of this disease. Each of these genes is involved in the production of a normal protein in the brain - the amyloid protein. In most people the amyloid protein does not have a negative effect on brain function, however the version found in Alzheimer's brains (a slightly larger protein) cannot be broken down as easily and so it deposits in the brain to impair, and ultimately, destroy neuronal cells.

Modern understanding of the genetics of Alzheimer's, particularly those genes involved in the early onset of this disease, commands serious ethical consideration. Inevitably, parents with a history of Alzheimer's disease in their family will have the opportunity to screen for this disorder in the early stages of a pregnancy. But if the results return positive, should they then consider terminating the pregnancy in an attempt to prevent any suffering that their children may experience later in life? Research into the treatment of this disease is constantly expanding and so the opportunities available to those suffering from Alzheimer’s disease in the future are certainly not going to be as limited as they are at present.
As discussed in chapter F1, stem cell research offers exciting possibilities for the treatment of neurodegenerative disorders such as Parkinson's disease, and this research also holds much potential for the treatment of Alzheimer's, yet it remains limited by the ethical debate which surrounds it. Other treatments, such as the development of new pharmaceutical drugs also hold much promise for future Alzheimer's treatments. For instance, memory enhancing drugs may be beneficial in revitalizing the activity of healthy neurons in the Alzheimer's brain, to improve memory and other mental functions in patients. Alternatively, other drugs could be developed which can prevent the accumulation of amyloid proteins in the brain tissue which are at least partly responsible for the neuronal damage that occurs in Alzheimer's.

In addition to these drug treatments, researchers are currently investigating ways in which they can help a person's own body fight Alzheimer's disease. In this case, genetic screening for the genes involved in Alzheimer's disease may become particularly important if effective preventative treatments are developed. Recent research in mice with a genetic tendency to overproduce the damaging amyloid protein has pointed towards an intriguing new avenue for investigation and eventual treatment. If young mice genetically prone to develop the symptoms of Alzheimer's are given a small injection of the amyloid protein, their immune system will destroy it and they, in turn, develop immunity to it. Once immunized, these mice are able to destroy the protein over the course of their lives, preventing its aggregation in the older brain, along with the associated symptoms of Alzheimer's disease.

Q4. Recent improvements in the medical field have enhanced people's life expectancy across the globe, particularly in developed countries. Yet, while we have extended the life of our bodies, we have not yet managed to prevent, or even adequately treat, the degenerative disorders of the brain such as Alzheimer’s disease. What ethical implications can you see in this trend?

Q5. Should parents use genetic pregnancy tests to screen for genes involved in the early onset of Alzheimer's? What ethical issues may arise from a positive finding?

Q6. If an individual partakes in genetic screening and receives a positive result for Alzheimer's genes, what right do they have to privacy of information? Do health insurance companies have a right to know that this individual is at high risk of developing Alzheimer's disease?

F2.4. Memory Enhancement Therapies

If medications can improve memory in people with memory impairment, what will they be able do for normal healthy people? As described above, a major research effort is being directed towards the development of memory-enhancing drugs. These drugs target the molecular mechanisms involved in strengthening the synaptic junctions between neurons that are involved in the process of memory consolidation. Although this research is aimed at finding treatments for dementia, such as that which occurs in Alzheimer's disease, there is reason to believe that some of the products under development would enhance normal memory as well, particularly in middle and older age when a degree of increased forgetfulness is normal.
There are three primary areas of ethical concern surrounding memory enhancement therapies. The first and foremost concern is safety. Side effects and unintended consequences are a concern with all medications and procedures, but neuroscience-based memory enhancement requires that we intervene in a highly complex system, the functioning of which is not fully understood. This complexity, combined with our lack of understanding of the risks associated with memory enhancement warrants that we proceed with extreme caution. In addition to this, the drug safety testing that must be conducted prior to a drug's release onto the market does not routinely address health issues associated with long-term use, trans-generational effects if consumed while pregnant, or the consequences of consumption during periods of nervous system development, such as childhood or adolescence.

Another ethical issue of concern relates to the social implications of introducing a memory enhancing drug onto the market. How will the lives of all individuals, including those who choose not to consume the drugs, be influenced by living in a society with widespread memory enhancement? In competitive situations such as examinations that determine a person’s acceptance into higher education or the workforce, we may require the equivalent of the regulations used for performance-enhancing drugs at sports events. What’s more, the freedom not to enhance one’s memory may be difficult to maintain in a society where at least some of the competition are using memory-enhancing drugs. While for those who do wish to consume the drug, social barriers such as cost will inevitably prevent some from doing so. This inequality could, in turn, further exacerbate the disadvantages already faced by people of low socioeconomic status in education and employment.

The third category of ethical concern relates to our values and our sense of self. We generally view self-improvement as an admirable goal, but does this include enhancing our capabilities with drugs? Improving our natural endowments for traits such as memory, not only incurs medical and social hazards, but also runs the risk of altering our perceptions of what we consider normal. That is, what we may have previously considered and accepted as a normal memory may in time be considered a pathology deserving of treatment. In addition to this, if it becomes commonplace to improve our productivity by taking a pill, we may also undermine the value and dignity of hard work, tinkering with the human brain as if it were merely a machine worthy of constant upgrades. This line of thinking flies in the face of many religious and philosophical ideals.

There is emerging neurological evidence from work with Buddhist monks who regularly practice a variety of meditation techniques demonstrating that mental training can modify and improve the functioning of the human brain. If this is the case, should people with normal memory function be allowed to boost their memory with a ‘quick fix’ drug treatment, when the brain can be modified through conscious effort?

**Q7. A number of pharmaceutical companies are developing new chemicals to improve memory. Would it be a good idea to take a pill to improve your memory and attention? Would a desire to perform well at school outweigh any potential side effects that you may experience, particularly if those side effects would not arise until later in life? What ethical issues can you see arising from the development of such a drug?**