F1. Advances in Neuroscience & Neuroethics

Chapter Objectives

As our knowledge of the brain increases we are able to alter its function; therefore, it becomes important to integrate neuroscience and neuroethics into the foundations of learning. This chapter aims to:

1. Introduce the nervous system.
2. Point to a diversity of neuroethics.
3. Draw attention to the revolutionary nature of current research.
4. Discuss Parkinson’s disease to highlight major issues of ethics in neuroscience.

F1.1. The Human Nervous System

Neuroscience is the study of the nervous system. The nervous system is made up of the central nervous system (CNS) and the peripheral nervous system (PNS). The central nervous system consists of the brain and spinal column; the peripheral nervous system includes the cranial and spinal nerves and an extensive network of motor and sensory nerve cells – or neurons – interconnecting all parts of the body (see Figure). The brain functions as the main coordinating centre for nervous activity and so controls, directs and integrates all nerve impulses of the human body. It controls physical functions like movement, balance and breathing, and mental functions like our behaviors, emotions and intelligence. The CNS, therefore, is the physical substance that provides us with genetically determined ways of behaving and also ways of changing this behaviour.

The brain is really the enlarged anterior part of the vertebrate CNS, which is enclosed within the cranium of the skull. It is composed of billions of interconnected neurons that transmit information to one another and to peripheral neurons throughout the body by means of chemical and electrical signals (see Chapter F2). In short, the nervous system receives, interprets and integrates information from the outside world, or from within the body, and then formulates appropriate responses for target organs such as muscles and glands. Appropriate, graduated responses in the target organs are produced as follows: the more neurons that are involved in signaling a muscle to contract in your arm for example, the larger the contraction will be. If the arm is involved in lifting a weight, the heavier the weight the more nerve fibres are activated to enable the muscle to lift the greater load. While many neurons are excitatory in nature, that is, they enhance responsiveness of their target, others are inhibitory. The inhibitory neurons reduce the responsiveness at their target in order to prevent a buildup of stimulating signals. For instance, to smoothly pull your hand towards your shoulder both inhibitory and excitatory responses are needed so that some muscles are inhibited while others are excited.

The brain is always active therefore it requires a large percentage of the body’s oxygen
supply and oxygen-delivering blood circulates through at an average flow of 650-700 ml per minute. A disruption of the oxygenated blood supply (ischemia) to specific areas of the brain may bring on a stroke and consequent dysfunction of the damaged brain tissue.

With new technologies, it has become possible to understand healthy brain function and its dysfunction in disease. Neuroscience is an area of scientific investigation that includes many specializations concerned with growth, development, and function of the nervous system. Consequently, neuroscientists have to be knowledgeable in a range of subjects including anatomy, physiology, biochemistry, molecular biology, pharmacology, computer science and neuroethics.

The nervous system viewed from behind.

The nervous system is composed of the central nervous system or brain and spinal cord, and the peripheral nervous system. The peripheral nervous system is a series of pathways that transmit impulses between the central nervous system and the other body tissues (figure adapted from Woodburne, R. ‘Essentials of Human Anatomy’. Oxford University Press, N.Y. 1965).

F1.2. Body or Mind – Where is the Difference?

Our environments (internal and external) are being monitored continuously by the sense organs. The sense organs (e.g., eye, ear, nose, taste bud) collect information and convert it into nerve impulses. Only when impulses reach the central nervous system are they interpreted and ‘sensed’ as light, sound, smell, taste and so on. Different parts of the brain are responsible for interpreting different impulses. For example, you may ‘see stars’ from a blow
to the head simply indicating that the light interpreting region of the brain has been stimulated.

**Meditation Exercise:** Close your eyes and concentrate on the space inside your head for a while. Visualize a lemon, visualize cutting it into segments, visualize slowly sucking on the segments – one by one …… What sensations are you experiencing? Concentrate on taste, saliva flow, colors and shapes – please write them down after the exercise. Did your mind create physical changes in your body? Do you feel that your mind is separate from your body? Can you imagine measuring love or anger in the same way as you can tastes, heart beat or breathing? The more doctors and scientists learn about the inner workings of the mind, the more they realize that there is no mind-body dualism – mind and body are inseparable. Thoughts and emotions are the result of complex electrochemical interactions within and between nerve cells which, in turn, communicate with the rest of the body. For example, the disembodied voices of schizophrenia and the low-self esteem of depression are generated by distortions in brain chemistry. Mental states and physical wellbeing are intimately connected. An unhealthy body can lead to an unhealthy mind, and an illness of the mind can trigger or worsen diseases in the body. Researchers are learning how these distortions arise, how to lessen their severity and, in some cases, how to correct them.

**Q1:** Scientists believe that the human ability to be ethical has evolved over hundreds of thousand of years. Do you agree or disagree?

**F1.3. Neuroethics**

Neuroethics is a new field that deals with the pros and cons of research conducted on the brain as well as the social, legal and ethical implications of treating or manipulating the mind. Neuroethicists propose that we consider the ethics now rather than wait until new technologies have been developed and are being used. Access to information is an important consideration but there are also wide implications for the rights of the individual.

Brain scans can identify early signs of brain disease and risk factors for mental health. New advances in brain scans use blood flow, and tend to focus on basic brain processes. Interestingly, scientists are expanding on traditional research into general brain functions, organization and evolution to explore the more subtle functions which make us individuals. For example, advances in neuroimaging technology may improve our ability to make predictions about an individual’s future. Scientists will learn how different patterns of brain images, taken under varying circumstances, strongly correlate with different future behaviors or conditions. Advances in neuroimaging will provide access to the mental processes involved in recalling a memory, whether true or fabricated, and assist neurologists to differentiate between the two (see Chapter F2). Future neuroimaging will provide insights into individual traits such as intelligence, cognitive abilities, personality characteristics such as violence and addiction, and mental illness. Specific neuroimages may also predict the onset of particular neurodegenerative diseases such as Alzheimer’s and Parkinson’s.

Prediction of the onset of a particular disease potentially could lead to prevention of onset or early treatment. However, there are many ethical concerns that must be considered before the potential is exploited.

**Q2.** Accurate predictions could lead to useful preventative interventions but what if those predictions are wrong or misleading?  
**Q3.** Should you feel guilty for a crime you might commit?

**Q4.** What happens if the information about your potential to commit a crime...
or become ill gets into the wrong hands such as private businesses and insurance companies?

We now know that the prefrontal cortex of the cerebral cortex is responsible for cognition, emotional regulation, control of impulsive behavior and moral reasoning. Should the prefrontal cortex be damaged or its function impaired by risk factors such as alcohol or stress, an individual may be unable to appropriately regulate his/her behavior despite knowing right from wrong.

**Q5. Are criminals whose prefrontal cortex is damaged responsible for their criminal behavior?**

**Q6. Should they be punished or rehabilitated?**

**Q7. If scientists can read your thoughts, do you think that they can also change them?**

*Note of Interest:* Gifted children use their brains in completely different ways to most of us. Their brains are far more active and they generate many more connections compared with the average ability brain.

**F1.4. Finger-Printing - Can Machines Read Your Mind?**

As technology continues to develop, there is the potential that machines could be created that are capable of reading an individual’s thoughts and memories. Presently, the polygraph is used to detect lying. Detection is done by recording involuntary responses such as heart rate, blood pressure and sweating. But can a machine that measures brain activity accurately detect lying? More sophisticated brain fingerprinting techniques are being developed that can reveal a person’s knowledge of an event or incident (see section F2.1).

If a device could accurately measure hidden knowledge, how should it be used? Do the benefits of this technology – as in detecting criminals or terrorists or company employees who cannot be trusted – outweigh the possible harms? If this technology is forced on an individual, or done without consent, what happens to their right of privacy against mental intrusion? Modern neuroscience poses many dilemmas because the brain is who we are – it’s our personality, consciousness, behavior, ideas and spirituality. How and what we think, feel and act is very personal and often we choose not to reveal every aspect of ourselves. Is modern neuroscience opening up a Pandora’s Box?

**Q8. If brain machines manage to interpret the very secrets of the brain, what uses will it be put to and who will have the controls?**

**Q9. Who should have the right to the information in your brain? Lawyers, doctors, family members, employers, insurance companies, marketing agencies, government intelligence organizations?**

**F1.5. Case Study: Parkinson’s Disease**

Parkinson’s disease is a neurodegenerative disorder caused by damaged or dead dopamine cells in the region of the brain that controls balance and coordinates muscle movement. Dopamine is an inhibitory neurotransmitter that is responsible for ensuring that signals between the brain and muscles are coordinated to allow for smooth and fluid movements. As dopamine neurons begin to die, the line of communication between the brain
and the muscles cannot be regulated effectively, and the brain is no longer able to control muscle movement. Symptoms include tremors in the hands, face and legs; stiffness of the limbs and trunk; slowed movement and speech; and impaired balance and coordination.

It is well established that the loss of dopamine cells resulting in Parkinson’s has genetic as well as environmental causes. With current technology, it is possible to screen for one specific Parkinson’s gene but the process is complicated and costly. At the moment, the test is only useful for those who are likely to exhibit early onset of the disease; that is, showing symptoms at about 30 years of age. Research may soon lead to similar tests that can effectively screen for those people susceptible to the disease, regardless of time of onset and it may even be possible to screen for the disease prenatally. This could reduce the incidence of the disease by selectively screening fetuses and carrying to term only those who do not carry the gene.

Embryologists continue in their efforts to develop safer and more reliable screening methods for severe genetic disorders, but for many conditions having a certain gene, or gene combination, merely means that the carrier has a heightened risk of developing that genetic illness. This especially holds true for the lifestyle diseases such as heart disease and cancer, where risk of expression will have to be evaluated in an environmental context. Chapter F3 section F3.4 details how health and wellbeing interact among genes, living conditions and behavioural habits.

F1.6. Intracerebral Grafting of Fetal Stem Cells for Parkinson’s

Another important challenge to neuroscience is the application of stem cells to repair neurological damage - particularly important in Parkinson’s disease. Stem cells are cells that have the potential to grow and develop into specialized cell types, such as neurons. There are two main sources of stem cells – embryonic stem cells and adult stem cells. Recently scientists were able to take a special type of stem cell from rat embryos and successfully treat a Parkinson’s-like disease in rats. Neural stem cells that can develop into nervous tissue were injected into rats which showed about a 75% improvement in motor function 80 days after treatment. Can we as a society ignore the potential benefits of this kind of research?

A prominent ethical topic is the use of aborted fetal brain tissue containing the required stem cells. Several nations have provided ethical guidelines for the use of embryos and fetuses in clinical and experimental research. These guidelines advocate that the decision to abort a fetus should be wholly independent from the decision to use that fetus in research. This guideline is designed to reduce the chance of a fetus being aborted solely for the purpose of providing organs. Under these guidelines organ donation from an aborted fetus is considered no different from donation from a deceased child or adult.

Q10. A number of the potential therapies for the treatment of Parkinson’s disease are quite controversial. For example, stem cell treatment would require large numbers of aborted embryos. Is it ethical to pursue such research when the condition may be managed with drugs?

Q11. If neuroscience could provide a safe and accurate prenatal screening test for Parkinson’s disease, is it ethical to use this information to decide whether to keep or abort a pregnancy?
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

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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.

![Diagram of neuron synapse](image)

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 minds 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?
F3. The Neuroscience of Pleasure, Reward and Addiction

Chapter Objectives

Certain areas of our brain regulate and reinforce behaviours that are pleasurable or rewarding. On the whole, this mechanism encourages us to repeat behaviours that are beneficial to our wellbeing (i.e. eating). Non-life enhancing substances, including certain drugs, can however, alter these mechanisms, which may over time ultimately lead to drug abuse and addiction. This chapter aims to:

1. Introduce the delicate biological balance between reward and addiction.
2. Describe how drugs of abuse affect the dopamine reward pathway.
3. Discuss lifestyle factors that influence addiction and the ethical issues associated with drug abuse.

F3.1. What is Addiction?

Addiction is often described as an ‘excessive appetite’ for something and is characterised by an uncontrollable motivational drive to seek out the object of the addiction. Individuals are described as addicted when they can no longer control their behaviour and find it difficult, if not impossible, to refrain from consuming something (e.g. drugs), or partaking in an activity (e.g. gambling). When we think about addictions we typically think of an inability to control behaviours that are detrimental to our health or wellbeing. However, life in itself can be viewed as a series of addictions; such as addiction to air, food and water, that are needed to ensure the survival of an individual and the species. This chapter will focus on drug addiction and takes the medical perspective as defined in Mosby’s Medical Dictionary ‘Addiction: a compulsive, uncontrollable dependence on a substance, habit, or practice to such a degree that cessation causes severe emotional, mental, or physiological reactions’.

Drug addiction, or substance dependence, is characterised by three basic features:

- A compulsion to seek and consume the drug of choice.
- A loss of control in limiting its consumption.
- The experience of negative emotional states, such as sadness, anxiety or irritability, when access to the drug is prevented.

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Addiction does not simply relate to the positive reinforcement derived from a drug and the desire for the euphoria, or ‘high’, that it produces. Two other features also characterize addiction: tolerance and dependence. Tolerance refers to the individual's need to progressively consume increasing amounts of the drug to get the same euphoric feeling as before. Dependence refers to the negative physiological consequences of withdrawal, such as nausea and irritability. In this way, drug abuse is not only driven by the pleasurable and rewarding effects of the drug, but also by the desire to avoid the negative effects that withdrawal can incur. Both tolerance and dependence are believed to result from the adaptations that occur within the underlying dopamine neuronal system on which most drugs of abuse act (section F2.2).

People consume drugs for a variety of reasons, some may do so purely for the pleasure, while for others it may be an attempt to cope with emotional pain arising from, for example, conflict, stress and/or anxiety. Regardless of the reasons why an individual starts to consume a potentially addictive drug, they will likely become addicted if they continue to take it for a period of time - although the amount required to induce addiction varies substantially between individuals. This variation can be due to lifestyle factors, genetic traits or both. For example, the amount of stress that an individual experiences in early life, or while taking drugs, affects their tendency to become addicted, with those exposed to higher levels of stress becoming addicted more easily (section F.3.4). While genetic traits can enable the neuronal circuits within the brain that mediate addictive states to 'hard-wire' faster and more effectively in response to drugs of abuse so that some are more prone to addiction than others. The mechanism involved in ‘hard-wiring’ the neuronal circuits regulating addiction are similar to that involved in the formation of memories, whereby the connectivity between neurons in the circuitry is strengthened (Chapter F2).

The goal of current neuroscience research is to understand the basic biological changes that occur within the brain that lead to the loss of behavioural control over drug seeking and drug consumption that are involved in addiction. Many recent insights in behavioural neuroscience have been gained through research conducted on animals which have enabled researchers to pinpoint the changes that occur within neuronal cells and between them (at their synapses) in the 'reward pathway' after repeated activation (as occurs with drug consumption). For example, researchers have implanted electrodes directly into the brain’s ‘reward pathway’ of a rat and have allowed them to self-stimulate these neurons by pressing a lever which sends an electrical current through the electrode. Rats quickly find this sensation pleasurable and rewarding and will press the lever continuously until they are exhausted, going without food and water, until experimenters intervene.

In other behavioural neuroscience experiments researchers have inserted electrodes into the ‘reward pathway’ of the rat’s brain and provided electrical stimulation when the rat responds correctly to, for example, directional cues. These rats learn very quickly to turn in the correct direction to receive their mental reward. Experiments such as these have allowed scientists to gain a better understanding of the problems associated with drug addiction by providing insight into the function of neuronal reward systems and the repetitive behavioural responses associated with them. However, a crucial ethical issue for debate is whether the experimental animal has lost its freedoms, in particular, the freedom to survive of its own accord and whether this loss of freedom is justified in terms of the information gained; that is, whether it will ultimately lead to the alleviation of suffering.

Can we draw a parallel between the loss of self-directed choice that occurs during human addiction and the loss of the rat’s autonomy in these experiments where the responsibility for its wellbeing is left in the hands of the experimenter controlling it?
Q1. Write a diary entry of one day in the life of a controlled rat. Pay attention to all feelings and emotions such as confusion, happiness, discomfort and so on. Do you think that experiments such as these are ethical?

F3.2. Dopamine: The Courier of Addiction

Pleasure, which scientists call reward, is a very powerful biological force that helps to direct our survival. If you do something pleasurable, the brain is wired in such a way that you tend to do it again. Life-sustaining activities, such as eating, activate a circuit of specialised nerve cells devoted to producing and regulating pleasure. One important set of neurons involved in this circuit (situated at the very top of the brainstem in the ventral tegmental area) uses a chemical neurotransmitter called dopamine (see figure). These dopaminergic neurons release dopamine onto nerve cells situated in a limbic structure called the nucleus accumbens. Release of dopamine in the nucleus accumbens is involved in reinforcing behaviours, which makes an animal more likely to repeat them in the future. Other dopamine fibres make contact in relevant parts of the frontal region of the cerebral cortex to form the dopamine reward pathway. In addition to reinforcing behaviours, the activity of dopamine cells provides the sensation of pleasure through connections to other regions of the limbic system involved in regulating emotion.

All drugs that are addictive activate the dopamine cells of the ventral tegmental area to enhance the amount of dopamine that is released in the nucleus accumbens. Natural rewarding activities and artificial chemical rewarding stimuli act on the same dopamine cells, but natural activities are regulated by appropriate feedback mechanisms that protectively control the magnitude of the response. No such regulating restrictions bind the brain’s responses to artificial stimuli. When an animal is hungry, this strongly motivates the animal to seek food because in the hungry state eating is pleasurable. But when the animal has consumed sufficient food, a satiety centre suppresses the reward system connected with feeding. Thus the seeking of pleasure by the healthy animal or human is adaptive and has survival value.

Chemical addiction, along with other addictive behaviours such as gambling or eating disorders (i.e. anorexia and bulimia), can be considered as diseases of the dopamine reward system because they either directly or indirectly result from changes in its normally well-regulated activity. This deregulation of dopamine activity that occurs with addiction can have important consequences for other bodily functions as well. For instance, in addition to forming part of the brain’s reward system, dopamine also functions as a main neurohormone mediating neural interactions with the pituitary gland which controls metabolism, growth and reproduction. Significantly, drug-mediated deregulation of dopamine activity can have adverse effects on fertility and development through well-documented physiological mechanisms (See Chapter E1 on Lifestyle and Fertility).

Over a prolonged period, drug use changes the brain in fundamental and long-lasting ways. These long-lasting changes then regulate the manifestation of addictive behaviours. It is as though there is a figurative “switch” in the brain that “flips” at some point during an individual’s drug use turning what was once a choice, into a compulsion. The point at which this “flip” occurs varies from individual to individual, but the effect of this change is the transformation of a drug abuser to a drug addict.

Q2. The idea that diseases such as alcoholism have a purely biological causation is attractive and forms the basis of some effective therapies. Morally, however, may not the biological model also be used to excuse a voluntary
behaviour without assuming responsibility for the activity or its consequences? In your opinion what are the important distinctions between medical and moral models of addiction?

Q3. Neuroscientists study drugs for many reasons. What are some of the reasons that neuroscientists may have for studying and developing new drugs?

Q4. Is there any difference between 'good drugs' and 'bad drugs', and if so, what are they?

F3.3. The Biology of Drug Addiction

The word ‘drug’, when used in ordinary speech often denotes a substance whose use is forbidden by law. However, nicotine and alcohol are as much drugs as are opiates, amphetamines and cannabis. In general terms a drug is any chemical agent that affects living processes and pharmacology is the branch of science that studies these effects. As indicated above, scientists are beginning to appreciate the common neurobiological mechanisms of addiction, and how it drives compulsive behaviour. However, it should be noted that the stimulation of dopamine is not necessarily the only mechanism behind addictive behaviours. The subjective ‘high’ that these drugs promote corresponds to the sudden increase of brain dopamine activity, either alone, or in combination with other neurochemicals. In cocaine use, for example, both dopamine and another neurotransmitter noradrenaline are artificially enhanced creating heightened alertness and levels of energy. The nicotine found in tobacco smoke, on the other hand, activates specific cholinergic receptors called nicotinic receptors, which are normally activated by the neurotransmitter acetylcholine. Nicotine therefore stimulates acetylcholine-mediated activities including respiration, maintenance of heart rate, memory, alertness and muscle movement. But it is through stimulation of the nicotinic
receptors on the dopamine cells in the ventral tegmental area that triggers the rewarding sensation, or feeling of satisfaction, experienced by smokers.

That nicotine is a highly addictive drug can clearly be seen when one considers the vast number of people who continue to use tobacco products despite their well-known harmful and even lethal effects. In fact, at least 90% of smokers would like to quit, but each year fewer than 10% who try are actually successful. Although, nicotine may produce addiction to tobacco products, it is the thousands of other chemicals in tobacco that are responsible for its many adverse health effects. Smoking either cigarettes or cigars can cause respiratory problems, lung cancer, emphysema, heart problems, and peripheral vascular disease, while chewing tobacco causes cancers of the oral cavity, pharynx, larynx, and oesophagus and damages the gums. In fact, smoking is the largest preventable cause of premature death and disability. Yet its addictive properties; that is, its ability to override the brain's dopamine feedback system, make it difficult for people to exert the self-control required to abstain because their brain has adapted to this artificial stimulation. That is, the natural transmitter acetylcholine is no longer sufficient to maintain dopamine levels because the system has fallen out of balance. Their attention and motivation are therefore directed towards keeping this system active through their consumption of nicotine. So, as levels of nicotine within the body, present from the last cigarette, begin to deteriorate, they will typically crave another cigarette to replenish them. Importantly, lifestyle factors such as stress can enhance this motivation by altering the activity of dopamine cells in the reward pathway (see F3.4).

In summary, drug abuse is a complex phenomenon and a person’s vulnerability to it can be influenced by a multiplicity of environmental and genetic factors. Whatever the cause, the drug of choice often serves to ‘fix’ an acquired or deeply embedded need for an emotional transformation. Owing to dopamine’s potency and biological significance, the body protectively reacts to fake (i.e., drug-induced) stimulation by fading its response to repeated fake stimuli. Thus repeated drug-intake, while initially providing the desired rush, provokes the brain to accommodate to the continued artificial stimulation by decreasing its baseline levels of dopamine which, in turn, forces the addict to increase their drug intake in an effort to bring back previously normal working dopamine levels within the brain.

Q5: Why would part of our brain be devoted to motivating us to repeat certain behaviours? How would this enhance the survival of a species?

F3.4. Lifestyle, Stress and Addiction

In chapter F1 we learned how the mind and body works as an indivisible whole where mental states and physical wellbeing are interconnected. Health, as defined in the Constitution of the World Health Organization (WHO), is a state of ‘complete physical, mental and social wellbeing not merely the absence of disease or infirmity’. In biological terms, health and ill-health are not alternative states; rather they are part of the same continuum. Without doubt our wellbeing depends on our genes, the conditions under which we live and the ways in which we behave. Drug addiction is one such lifestyle factor that has significant detrimental effects on every aspect of our wellbeing, disturbing physical, mental and social functioning.

Since the brain and body communicates in both directions through the immune and the neuroendocrine systems, brain/bodily health is strongly influenced by how an individual can adaptively balance the stress of life. If we respond to change appropriately, stress is good and can be seen as the spice of life. For example, when we react to challenges and survive, we learn from the experience and mature emotionally. In evolutionary terms, if an animal were
injured in a classic fight and flight response, immune function is enhanced through the actions of stress hormones, which helps the animal to fight infection and repair the wound. At the same time, stress hormones help the animal to remember the place of action and stay out of trouble in the future by enhancing memory processes within the brain (Chapter F2). Thus, an appropriate stress response is adaptive as it helps maintain physical resistance and enhances memory processes. However, when an individual is stressed for prolonged periods of time, or if the stress response is not properly turned off once the challenge has been met, it creates wear and tear on the body and mind. This wear and tear is called allostatic load.

Lifestyle diseases such as heart disease, cancer, gastrointestinal disturbances, diabetes, depression or addiction are all influenced by family and community life, socioeconomic structure as well as incidents in childhood and prenatal development – all of which contribute to allostatic load. It is the sense of being in command over our lives that promotes wellbeing more powerfully than an appropriate control of behaviours such as smoking, diet and exercise. Being at the bottom of the social scale, for example, whether provoked by poverty (lower income, lower education, poorer medical care, poorer housing), or advanced by harmful lifestyle (drug dependence, social disengagement, poor diet, lack of exercise), adds to a person’s allostatic load, which in turn affects their health. In short, stress, which results in a high allostatic load is a good predictor of declining physical health, declining cognitive function and declining memory. Conversely, the allostatic load score is typically lower in people with higher education and income and, importantly, in people who have more social ties and networks. We are a social animal so social interaction and support is as important as good dietary control and regular exercise in reducing allostatic load.

High stress/allostatic load has significant consequences for addiction. The neuroactive hormone cortisol, for example, is elevated in individuals with high allostatic load and influences the functioning of a number of neuronal systems, including the dopamine reward system. Within this dopamine system, cortisol acts to enhance the responsiveness of dopamine cells to drugs of abuse and enhances the synaptic changes that are thought to underlie the behavioural expression of addiction. Exposure to stressful events in early life is believed to have a particularly important influence on the manifestation of addiction, as well as other health problems, in later life. Indeed, the nervous system is particularly vulnerable to the effects of stress in early life, during critical phases of growth and development. Evidence for this comes from both animal and human studies, for example, an association has been made between chemically dependent women seeking counselling for problems related to substance abuse, and their experience of childhood sexual abuse. Similarly, men are more likely to seek help for the consequences of sexual abuse (depression, alcoholism) than for the abuse itself. Current neuroscience research is exploring the mechanisms by which stress, particularly that which is experienced during early life, functions to “flip” the figurative switch in the brain that effectively transforms a drug abuser into a drug addict.

**Q6:** In order to develop a mature conscience capable of responsible ethical judgment, the child has to be sufficiently loved. Does that statement seem sound to you and if so, can current biological knowledge be used to enhance the value of human love?

**Q7:** Do you see anything wrong with using drugs if they enhance our ability to focus or improve our mood? What do you think society would be like if drug enhancement became the norm?