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.

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 F3.4). 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 addition 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?

The dopamine reward pathway
Dopamine cells in the ventral tegmental area project to the nucleus accumbens and prefrontal cortex of the forebrain to form the dopamine reward pathway. The release of dopamine in these brain regions regulates and reinforces reward-mediated behaviours, be they adaptive (i.e. eating) or maladaptive (i.e. drug consumption).

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 reactively 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 communicate 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?