



# Exercise as treatment for substance abuse

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## Summary

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Addiction has negative consequences on a person's life, physically as well as mentally. Addiction develops in stages, the feeling of reward is important in the reinforcement of addiction. Eventually, a switch in neuronal pathways results in craving. An addicted person constantly thinks about the substance and will take it despite negative effects. In treating addiction, there are several aspects that can be focused on. Pharmacological treatment is used to support behavioural methods because it reduces withdrawal symptoms. It is important to prevent craving by removing cues from the environment and behavioural therapy is used to decrease associations between drug use and habits. A more healthy behaviour that increases hedonic feelings can be a possible substitute for the drug-taking reward. Physical activity is a healthy behaviour with positive effects on body and mind states. If exercise works to reduce substance intake and prevents relapse, it would be a proper treatment method against addiction and exercise is easily accessible and cost-effective. Exercise affects the same dopaminergic pathways as are affected in addiction and it is shown in both animal and human studies that increased physical activity is related with reduced substance use. Exercise causes alternative feelings of reward and reduces withdrawal symptoms. An improved fitness is also associated with reduced risk of relapse. This indicates exercise works as a proper treatment against addiction. However, forced exercise showed increased substance intake. Besides, individuals who are sensitive for reward are more prone to develop new addictive behaviour. Addicted patients starting with exercise as treatment have a higher chance to develop exercise addiction. Even though exercise is healthy behaviour, exercise addiction is accompanied with negative effects such as higher prevalence of injuries and decreased social relationships. Exercise can have positive effects during the recovery period of addicts, provided that it is performed at moderate intensity and will not develop into a new addiction. Correct application of exercise as treatment is important, but more research on this topic is necessary to make definitive conclusions about exercise as prescription.

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# Chapter 1: Introduction

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The term 'addiction' is often heard in the news or daily life. An addiction has a big influence on the personal life of an individual. Substance abuse, also called drug addiction, is seen as a neuropsychiatric disorder. It places a burden on society because of the influence on crime rate and healthcare (Robbins & Everitt, 1999). Data from an epidemiological study from 27 community studies in European countries reveal a 12-month prevalence rate for any substance dependence of 3.4% of the adult population (Wittchen & Jacobi, 2005). Even though addiction is seen as a chronic illness, recovering from an addiction is possible. Exercise has recently risen in popularity as treatment for mental disorders. Exercise is seen as an activity with positive effects on mental as well as physical health. People who exercise at a regular base have reduced risk of health problems (Rijksoverheid). Physical activity seems to be the perfect, healthy solution for any problem, but to what extent does this apply to substance abuse?

In this paper the underlying mechanisms of addiction will be explained to understand which aspects are important for a proper treatment. Subsequently, it will be described how exercise works as a therapy. Eventually, it will be discussed if exercise will work as an appropriate intervention in treatment against addiction but also the downside of exercise as therapy for substance abuse will be discussed.

## Chapter 2: Addiction

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### What is addiction?

Addiction is a term often used in daily life and has consequences on the health and social life of the addicted person. An addiction can be defined as 'when someone is physically and mentally dependent on the use of a substance or performing a certain behaviour, despite adverse consequences on health or social life' (WHO). There are two types of addiction: addiction to substances and addiction to a behaviour. Substances often seen in substance abuse are alcohol, nicotine and several types of drugs. Types of addictive behaviour include gambling, overeating, sex and exercise. The initial drive for drug-taking behaviour is positive reinforcement but during the development of addiction, a person moves to a more compulsive stage of drug-taking in which the drive shifts to negative reinforcement (Koob & Le Moal, 2005).

Not everybody who drinks alcohol or smokes is addicted. International agreements are made about criteria points to determine factors related to addiction. This has resulted in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (American Psychiatric Association, 2013). The DSM-5 is used to classify mental disorders and consists of eleven criteria. The criteria according to DSM-5 are shown in Table 1. The classification degree determines the severity of the addiction, depending on the number of criteria the patients meet. The most important added criteria point in comparison with the previous version, DSM-4 (American Psychiatric Association, 1980), is 'craving'. Craving describes the psychological dependency and is nowadays seen as the central characteristic of addiction (Koob, 2003).

### Risk of addiction

There are several factors that can contribute to a higher risk of developing addictions. People who lack a strong sense of self-identity can use substances as coping mechanisms for low self-esteem or emotional distress (Landolfi, 2013). People with psychological and emotional characteristics such as depression, loneliness, social anxiety, impulsivity, distraction have also a higher risk on developing addiction (Kim, 2013). Additionally, genetic factors, as well as environmental factors, play a role in the development of addiction (Hersenstichting). The influence of these factors varies between individuals.

### Development of addiction

Addiction does not come out of nowhere. It is a gradual process that can be divided into several stages. In this part, the different stages of addiction are explained by using underlying neurological mechanisms. The development of addiction starts typically through social use of an addictive drug (Kalivas & O'Brien, 2008). Different types of drugs and behaviours affect different neurotransmitters and their systems (Hersenstichting). Regular use of drugs causes structural changes in the brain and can therefore eventually lead to addiction.

### Reward

The main neurotransmitter involved in addiction is dopamine. Dopamine is a catecholamine and involved in a number of physiological and behavioural processes, like motivation and reward. There are two dopaminergic pathways important in addiction. The mesolimbic dopaminergic system and the nigrostriatal dopaminergic system.

The mesolimbic dopaminergic system is important in the early reinforcement of specific (substance taking) behaviour and reward (Koob & Volkow, 2009; Hyman & Malenka, 2001).

**Table 1**  
*The eleven DSM-5 criteria of substance dependence*

<i>Category</i>	<i>Criteria</i>
<b>Craving or using more than intended</b>	<p>Taking the substance in larger amounts or for longer than you meant to</p> <p>Wanting to cut down or stop using the substance but not managing to</p> <p>Spending a lot of time getting, using or recovering from use of substance</p> <p>Cravings and urges to use the substance</p>
<b>Negative consequences, also for others</b>	<p>Not managing to do what you should at work, home or school, because of substance use</p> <p>Continuing to use even when it causes problems in relationships</p> <p>Giving up important social, occupational or recreational activities because of substance use</p> <p>Using substances again and again, even when it puts you in danger</p>
<b>Tolerance and dependence</b>	<p>Continuing to use, even when you know you have physical or psychological problem that could have been caused or made worse by the substance</p> <p>Needing more of the substance to get the effect you want (tolerance)</p> <p>Development of withdrawal symptoms, which can be relieved by taking more of the substance</p>

*From American Psychiatric Association, 2013.*

All drugs have in common that they affect the reward system in our brain (Hersenstichting). The mesolimbic pathway originates in the ventral tegmental area (VTA) and innervates the ventral striatum (nucleus accumbens (NAc)). The VTA also projects on other brain areas, like the prefrontal cortex (PFC, personality), hippocampus (important in learning and memory) and amygdala (important in emotions) (Kalivas & O'Brien, 2008).

Dopamine is crucial for memory formation and helps to remember positive and negative experiences (Phillips, Vacca & Ahn, 2008). Therefore, dopamine release gives the motivation to repeat the positive experiences to receive a feeling of reward. Rewarding feelings are pleasurable and motivating (Hyman, 2007) and the feeling of reward is the underlying cause to take a certain drug or perform a certain behaviour. All addictive drugs are rewarding by causing an increase of dopamine in the mesolimbic dopaminergic system, although all by different molecular mechanisms of action (Kalivas & O'Brien, 2008). Mice without the dopamine D1 receptor do not self-administer cocaine (Caine et al., 2007), indicating that this dopamine system is crucial for repeated drug-taking behaviour.

The reward system (mesolimbic dopaminergic pathway) evolved to respond to natural rewards which were evolutionary important for survival, reproduction and fitness, like food intake and sex (Kelley & Berridge, 2002). The reward system is important in natural behaviour and therefore the feeling of only reward is not enough to develop an addiction.



## Sensitization

The feeling of reward is the first stage of addiction, but for developing an addiction the feeling of reward is not enough. In sensitization, a repeated stimulus strengthens the involved neuronal network and therefore also the response will be more intense. In the reward system, these changes are caused by changes in dopamine release. Addictive drugs increase the strength of the excitatory synapses on dopaminergic neurons in the VTA by releasing dopamine with greater amplitude and duration than can be achieved by natural physiological mechanisms (Kalivas & O'Brien, 2008). An increase in dopamine in the NAc is seen in rats after repeated use of several drugs and alcohol use (Nestby et al., 1999). The repeated intake of a drug increases the strength of synapses of dopamine neurons in VTA, which leads to increased activation in the areas that receive input from the VTA.

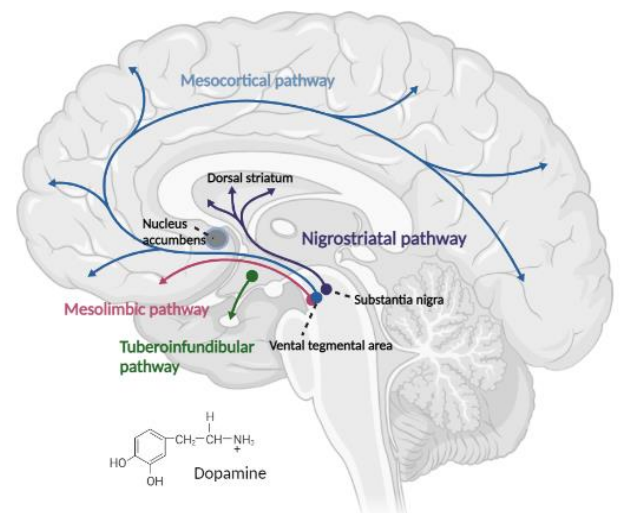
Sensitization contributes to higher motivation for a drug (Vezina, 2007) and is an important process in the development of addiction.

## Habits

The reward-effect and sensitization developed because of repeated substance use, will eventually lead to a shift in the neuronal network. Because of the increased activation in the regions that receive input from the VTA, the dorsal striatum will be activated. The dorsal striatum is part of the nigrostriatal pathway, the other dopaminergic pathway. The substantia nigra (implicated in habit learning) is the starting point from the nigrostriatal pathway. The dorsal striatum has a minor role in the acute reinforcing effects of an addictive drug but has a key role in the transformation of only social use to compulsive use (Everitt et al., 2008).

Prolonged cocaine-seeking increases dopamine release in dorsal striatum but not in the ventral striatum (Ito et al., 2002) and higher dorsal striatal activity in heavy drinkers, compared to ventral striatal activity in social drinkers (Vollstädt-Klein et al., 2010) indicates there is a shift between the mesolimbic (reward) and the nigrostriatal system after prolonged drug use and in the development of addiction. The different dopaminergic pathways and brain structures are indicated in figure 1.

A person experiences pleasurable effects of the substance, which reinforces the behaviours that cause the substance to be delivered to the brain (steps to prepare the substance, getting the substance, intake of the substance). This causes anticipation of the substance and associations accompanied with taking the drug are formed. The environment in which a drug is taken plays an important role in this process. The location of substance use, way of intake and other environmental cues can be linked to the rewarding effect of drug use. These associations will form habits of taking a drug. The underlying mechanism of behaviours that become habitual is the involvement of the dorsal striatum after increased dopamine release in the mesolimbic system by repeated self-administration of the drug. In addicted persons, habits (not the drug itself) cause dopamine release in the dorsal striatum. In non-addicted persons, there are no habits formed and the dopamine release is caused by the NAc as a consequence of the actions of the drug on the mesolimbic system and a rewarding feeling is the result. Habits play an important role in the origin of craving



**Figure 1.** Dopaminergic pathways in the brain. The mesolimbic pathway is important in the feeling of reward. In later stages of addiction, the nigrostriatal pathway is activated. This pathway is important in habits and craving and the switch between the systems is crucial in the change from liking to wanting.

periods. A craving is a period in which a person really 'wants' a drug and it can be described as compulsive drug-taking behaviour (Robinson & Berridge, 1993).

Because of the changed brain structures and strengthened structures in the reward system after repeated substance use, this neuronal network will be activated quickly if a stimulus is present. This stimulus can be an environmental cue associated with the feeling of reward (or a habit). Volkow et al. (2006) showed an increase in dopamine in the dorsal striatum in cocaine-addicted subjects who watched a video that showed cocaine cues. Due to these associations, an addicted person is unconsciously triggered to perform a behaviour that leads to drug intake. Despite the negative consequences, craving makes the person unable to resist the drug.

To conclude, the release of dopamine in the NAc leads to the acquisition of substance abuse (addiction to a substance) by the rewarding feeling after taking the drug which can lead to repeated use of the substance. Changes of dopamine release to the dorsal striatum are responsible for the establishment of the drug-taking habit and the change from liking (reward) to wanting (dependence).

### Tolerance

At the beginning of the development of an addiction, dopamine release by the reward system causes a hedonic feeling. Sensitization strengthens this process and when substances are used repeatedly, habits will originate and cause anticipation for the effect of the drug. Habits cause a compensatory response in the dopaminergic systems and this results in tolerance. Tolerance is the decreased sensitivity to a drug as a consequence of exposure to it. To get the same feeling of reward, you need a higher dose of the substance (Ramsay et al., 1998). Tolerance in addiction is about the anticipation of a drug because of the habits (Siegel, 2005). Maximal tolerance effects are seen in environments with most cues for the drug-taking behaviour.

Habits are not only the main cause for anticipatory mechanisms but are also the reason why withdrawal symptoms occur. These symptoms occur when a person is not taking the drug, but the brain already has anticipated it. Some addictive substances activate mechanisms that suppress pain and distress signals, withdrawal symptoms occur when these mechanisms are not activated anymore. The symptoms represent negative reinforcement effects that can contribute to increase the habit-forming impact of a drug and drug cravings (Wise, 1988). Withdrawal symptoms from all drugs of dependence result in mood disturbances (West & Gossop, 1994). Other symptoms are anxiety, dysphoria, insomnia, and autonomic hyperactivity and vary per type of drug (Kenny & Markou, 2001; Weddington et al., 1990; Bayard et al., 2004). They are caused by a period of stress during exposure to habits. When a person is addicted, the motivation to use a substance is to prevent the unpleasurable withdrawal symptoms (Koob et al., 2014). An individual is then physically dependent on the drug and will crave for it. Patients constantly think about the drug and will take it despite its negative effects.

### Relapse

Anticipation mechanisms are working during exposure to habits that lead to withdrawal and a craving for the substance one is addicted to. In an addicted person, the control centre in the PFC is not working as self-regulation. The environmental cues related to habit are important in the process of relapse (Hyman & Malenka, 2001) and patients will take the substance.



## Chapter 3: Treatment of addiction

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The different factors which are important in the development of addiction are described in the previous chapter. Since addictions are accompanied by negative effects on health and social life, treatments are desirable.

When a person is addicted, taking the drug seems the only possible solution to get rid of withdrawal symptoms. Addiction is seen as a chronic medical disorder (Kalivas & O'Brien, 2008) but different kinds of treatments are possible.

Reward is an important mechanism in the brain by the acquisition of addiction. The feeling of reward is caused by dopamine release in the NAc after drug intake and this can lead to repeated use of a substance. Eventually, dopamine is not released by the NAc as a result of drug intake, but the dorsal striatum releases dopamine. The release of dopamine by the dorsal striatum is caused by habits associated with drug intake. An important characteristic of addiction is craving for a specific substance. This craving is often caused by environmental cues, associated with drug intake. All these factors are important in the development of addiction. Treatment of addiction is mainly focused on a single outcome: the absence of addiction (Miller & Miller, 2009). The ultimate goal in controlling addiction is to prevent relapse, in this section the factors to consider when choosing a treatment are explained.

Habits, craving and tolerance are characteristics in an addicted person. Reward and sensitization are important in the development of addiction. The brain of an addicted person is changed. Habits are hard to suppress and the feeling of craving cannot be ignored.

For treating addiction it is necessary to tackle the habits. In abstinence from the drug, craving is elicited by cues and contexts previously associated with the drug, this contributes to relapse (Lee et al., 2007). Habits are often complex and prevalent in the daily surroundings of an addicted person and are hard to avoid. It can be a solution to move to another environment temporarily, to escape the environmental cues that cause craving mechanisms. Admission to a rehab clinic is one way to get people out of their daily environment (Hersenstichting) and there is no more drug intake in that period.

It is important to take withdrawal symptoms and relapse into account during treatment. Pharmacological treatments are aimed at physical effects like detoxification and counteracting withdrawal symptoms (Hersenstichting) to make abstinence more comfortable. A variety of pharmacological treatments exist nowadays and are specific for drug types (van den Brink & Geerlings, 1999). These pharmacological treatments are a helpful tool in the treatment of addiction, but only the use of medication will not be enough to prevent relapses.

Behavioural therapy can be used to prepare someone for return to society. In society, cues are present that can cause craving and relapse. The goals of behavioural therapies are aimed to prevent relapse. Craving is one of the reasons drug users fail to abstain from drug use.

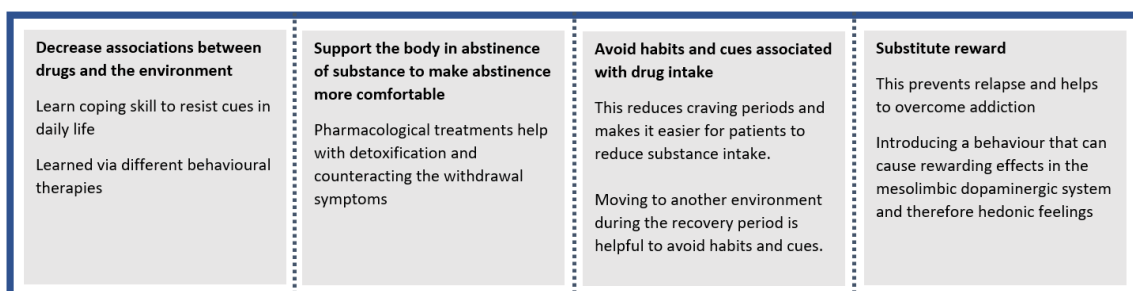
In the first stage of clinical treatments, habits are eliminated as far as possible. Anything that might trigger cravings of the patient is avoided. Besides that, pharmacological treatment can help to reduce any withdrawal symptoms. In the clinic, people get used to not using drugs in environments without habits. It, however, is important to prepare people for an environment with habits and decrease their associations between certain habits and drug intake. There are several treatments that are focused on these associations. Cue-exposure therapy (CET) can be used to extinguish associations between drugs and cues. CET aims to do that, by repeated exposure to the cues related to the addictive substances without consuming the

addictive substance. Patients can practice responses to cues in real-life situations. The results of this treatment are promising (Drummond & Glautier, 1994; Monti et al., 1993; Marissen et al., 2007). Coping-skills training (CST) is also a behavioural therapy used as treatment. CST focuses on factors that can be responsible for relapse, like stressful situations. Therapists can train patients coping skills specific for high-risk situations and general social skills (Monti & Rohsenow, 1999).

Another important factor in addiction is the reward system and the switch between the mesolimbic dopaminergic pathway and the nigrostriatal dopaminergic system. This switch is caused by repeated drug intake that increases the strength of synapses in these brain regions (see Chapter 2). The reward system is changed and there is a decrease in dopamine D2 receptors (Volkow, Fowler & Wang, 2003). This drug-induced neuroplasticity is worsened by increased drug-intake and long-term persistent decrease in function of normal motivational systems are driven by decreased function of the brain reward system and increased anti-reward system (Koob & le Moal, 2005). In the end stages of addiction, the drug does not have pleasurable effects anymore.

Introducing a behaviour that can cause rewarding effects in the mesolimbic dopaminergic system and therefore hedonic feelings can maybe help in preventing relapse and overcoming addiction. People who are sensitive to the rewarding properties of addiction may also have a higher risk of using other kinds of drugs (Gutgesell & Canterbury, 1999; Loxton & Tipman, 2017), since risk factors of addiction are not specific for any type of drug or behaviour. Addicted people might therefore also be sensitive to other activities that increase reward. More healthy behaviours that increase hedonic feeling can maybe substitute for the drug-taking reward. Glasser (1976) described that it is possible to become addicted to a positive behaviour, that develops character and the body might help one to overcome negative addictions. A positive addiction might lead to an integrated and rewarding life, while a negative addiction has mainly negative effects on health and social life. According to McKay (2017), treatment should not just focus on eliminating substance use, but instead it can be used to show patients that other activities can cause rewarding feelings too. The desire to feel comfortable, that is received by craving and taking a drug, can also be received by positive addictions (Zeig, 2008) and therefore negative addictions can be substituted by positive addictions.

To conclude, treatment is possible for addiction. Withdrawal symptoms occur in abstinence of a drug and cause several illness complaints. Pharmacological treatment is used to counteract withdrawal symptoms and decrease physical complaints. To help a person deal with a life without drugs, it is helpful to start in an environment without cues that lead to cravings. These cues are present in the daily environment of a person. It is therefore helpful to move the patient to a different place during the treatment period, in this way the person can learn how to cope with the cues to rehabilitate step-by-step. Several behavioural therapies focus on learning how to resist cues. The hedonic feelings can also be received by behaviours with more positive effects on health. People that are sensitive to addiction might become addicted to positive behaviours and create a positive addiction. These positive addictions can be a substitute for a negative addiction. It is important to change lifestyle to new and more healthy behaviours. In figure 2 the aspects that can be tackled in treatment of addiction are summarized.



**Figure 2.** Aspects important in treatment for addiction

## Chapter 4: Exercise

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### What is exercise?

Physical exercise is all bodily activity or movement that enhances and maintains overall health and physical fitness. There are all kinds of exercise types. Aerobic exercise moves the large muscle groups with alternate contraction and relaxation. It focuses on deep breath and blood flow with adequate tissue oxygenation. Therefore it is also called cardiovascular exercise. Long-distance running, cycling or swimming can be seen as cardio training. Another form of exercise is anaerobic exercise, which is focused on a forceful contraction of muscle with stretching, usually mechanically aided and helps to build up muscle strength and muscle bulk, like weight lifting, pushing and sprinting. Flexibility exercise is one type of stretching exercise to improve the movements of muscles, joints and ligaments, gymnastics for example (Siddiqui, Nessa & Hossain, 2010). Physical exercise evokes alterations in every part of the body (Bortz, 2019).

### Can exercise cause rewarding feelings?

Physical exercise is a behaviour. Motivation to initiate behaviours are dependent on positive reinforcement or reward to establish new behavioural patterns. Physical activity has positive reinforcements like the stimulation of the vestibular apparatus that has rewarding effects because it is a basic source of enjoyment, the feeling of achievement and a decrease in feelings of tension and depression. Also, endorphins are produced during strenuous physical exercise. It is produced during regular, prolonged aerobic exercise and causes feelings of relaxation, euphoria and a decrease in pain (Wessels, 1983). The feeling of reward is an important factor in the take-up and maintenance of exercise behaviour (Huppertz et al., 2014).

According to Csikszentmihalyi (2014) flow is 'a mindset people can enter when they are fully immersed in and enjoying an activity'. It is a brief moment found in times of activity, rather than in passive moments. It occurs when people face tasks that are within their ability to perform, like activities that have clearly established rules for action. A person in flow is in control of his actions and of the environment. Flow is the result of a change in mindset rather than a change in the environment. Entering this feeling is unique to each person and personality differences result in differential responsiveness to flow activities. Flow is the changed perception of an experience, and therefore the activity will be a more positive experience

(Csikszentmihalyi, 2014; Sutton, 2019). The flow is also associated with better physical performance. Stavrou (2007) performed research on 220 athletes from seven sports and found that athletes reported a sense of control, more experiences of flow and better performance when the skills matched the challenge. The reward system is associated with exercise performance. Increased dopamine levels improve endurance exercise performance and blockade of D1 or D2 receptors impair exercise performance (Zheng et al., 2014).

This indicates that several types of exercise exist and they might have different effects on the body and brain. Exercise is associated with reward and joy.

### STATE OF FLOW

Mountain climber R. Schultheis described how entering a state of flow helped him complete one of the hardest physical feats in his life. He climbed a mountain called Neva in the Colorado Rockies in the winter of 1964. The journey to the summit was relatively straightforward, but during the descent something went wrong. He became stuck and was unable to climb up or descend in a safe way. Eventually, he fell but landed on a narrow edge, close to a cliff. He was injured and had a long way to go after this incident and it already became dark. Schultheis claims that entering a state of flow made it possible to return safely (Schultheis & Sutherland, 2021).

## Chapter 5: Exercise as therapy

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Exercise plays an important role in the treatment and prevention of several diseases and improves overall well-being (World Health Organization). Physical activity offers physical and psychological benefits in patients with cardiovascular diseases (Dubbert, Rappaport & Martin, 1987) and can promote health benefits in obese patients (Pacy, Webster & Garrow, 1986). Regular exercise causes improved insulin sensitivity, lipid and lipoprotein profile, glycemic control and blood pressure. It helps to prevent obesity and diabetes mellitus and reduces the risk of death (Bouchard, Depres & Tremblay, 1993; Siddiqui, Nessa & Hossain, 2010).

Exercise also has psychosocial benefits such as relaxation, increased social contact, promotion of self-care and self-esteem (Smith et al., 1996). Participation in sport increases the feeling of control (Karoly et al., 2013). Furthermore, the effects of exercise on mental health are examined and have shown to be positive. The results of the effects of aerobic exercise or anaerobic exercise remain contradicting. Some studies state that aerobic exercise training has better antidepressant and anxiolytic effects and protects against harmful consequences of stress than anaerobic exercise (Salmon, 2001). Nevertheless, several studies indicate positive effects of anaerobic exercise. Aerobic, as well as anaerobic exercise, operate as effective antidepressants (Martinsen, 1990; North et al., 2008; Doyne et al., 1987). Patients suffering from depression indicate exercise as the most important element in comprehensive treatment programmes (Martinsen, 1990). Aerobic exercise is beneficial for anxiety reduction. Even a short training (5 minutes) induced an anxiolytic effect. Physical exercise regimens extending over several months are most effective. Aerobic exercise that elevates heart rate significantly above resting pulse rate for over 21 minutes significantly enhances stress responsibility, in particular stress related to lifestyle or work. Both aerobic and anaerobic exercise can be associated with an elevated mood state (Scully et al., 1998). Participation in any type of physical activity improves self-esteem (Sonstroem, 1984). This indicates that all forms of physical exercise have positive effects on health and mind state.

Exercise can be cost-effective, flexible and accessible for everyone. Several types of exercise can be performed individually, but other types can be performed in teams. It can be indoors or outdoors, whatever one prefers (Brown et al., 2010). Exercise also has minimal side effects compared to pharmacological treatments (Broocks et al., 1998). In conclusion, exercise is beneficial for physiological and psychological problems. Participating in physical activities is a kind of therapy since it works to decrease mental health problems and improves social contact and self-esteem.

## Chapter 6: Brain and exercise

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The effects of exercise on health are described in chapter 5, but what happens actually in the brain during exercise? In this section, the focus will lie on the mechanisms in the brain important for the reward systems since these pathways are important in the development of addiction. Surveys and questionnaires can be used to find out how people are feeling, but understanding the underlying brain mechanisms is important at first.

The application of existing neurosciences techniques to exercise psychology is complex (Brown et al., 2010) but animals are a good model to investigate brain mechanisms.

Physical exercise has several effects on the brain. Exercise improves neuronal connections in areas important for learning and memory (learning a new behaviour) like the hippocampus. Neurogenesis, the growth of new neurons, is stimulated by exercise as well (Bardo & Compton, 2015). An experiment in rats by Maynard & Leisure (2013) showed that exercise itself does not cause neurogenesis, but it is responsible for recovery after damage caused by alcohol. Exercise stimulated growth factors like brain-derived neurotrophic factors support neuronal functions and work as a protecting factor.

Chronic use of alcohol is also the main reason for the decrease of white matter quality. White matter is important in neuronal communication and helps to adapt behaviour in different situations. Exercise induces improvements in the amount of white matter volume in the brain (Karoly et al., 2013). Voluntary exercise reduced the vulnerability of dopamine neurons to neurotoxic effects of a 6-OHDA infusion (Mabandla et al., 2009).

Links between dopamine and exercise are also found. In rats extracellular dopamine release has been observed in the NAc during treadmill running. This indicates a possible mesolimbic dopaminergic function related to motivation and reward during exercise (Wilson & Marsden, 1995; Iwase et al., 2013). In rodents acute rewarding effects of exercise were linked to changes in the dopaminergic functioning (Greenwood et al., 2011), indicating that physical activity affects the dopaminergic system (Huppertz et al., 2014). Hattori, Naoi & Nishino (1994) evaluated the action of striatal dopamine in exercising rats. They found an increase in both the synthesis and metabolism of dopamine in response to physical exercise. Electrical self-stimulation of the VTA motivates treadmill running (Burgess et al., 1991) and weight lifting (Garner et al., 1991) in rats, so in both aerobic and anaerobic activities. The role of the mesolimbic dopamine system in the motivation of voluntary physical activity is not fully understood (Dishman et al., 2006). Treadmill running increases dopamine release (Meeusen, Piacentini & De Meirleir, 2001), turnover (Hattori, Naoi & Nishino, 1994) and up-regulation of dopamine D2 receptors (MacRae et al., 1987) in the striatum of rats.

The effects of aerobic exercise on human striatal dopamine release are also investigated using a PET scan (Wang et al., 2000). No difference in the dopamine D2 receptor or synaptic dopamine concentrations were detected. These contradictory results from animal studies might be due to a failure of the PET scan measurements. However, exercise has been shown to result in acute improvements in mood disturbances and withdrawal symptoms in women, possibly mediated by exercise effects on the endogenous opioid system and potentiation of dopaminergic systems linked to the experience of enhanced mood and pleasure (Brown et al., 2010). This indicates that exercise in humans affects the dopaminergic systems in addiction.



## Chapter 7: Exercise

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Addiction and exercise seem to be related. They both have an influence on reward mechanisms via the same neuronal mechanisms. This suggests that exercise could be a healthy alternative for an addicted person. In addition, exercise can reduce physical health problems that make a person more likely to develop an addiction. Physical activity can work as a therapy to improve brain diseases and it improves social aspects of life. By improving self-image in young people, exercise has a preventive effect on substance abuse (Collingwood et al., 2000). Several studies show that exercise has positive effects in the treatment for substance abuse.

In animal studies, it is shown that mice with access to a treadmill and perform physical activity took significantly less alcohol than mice without access to a treadmill. In males, this effect was not as big as in females, but it shows that mice change their pattern of alcohol intake when they increase physical activity (Ehringen, Hoft & Zunhammer, 2009). Reduced alcohol intake was also seen in a strain of mice with high alcohol preference, but two weeks after an exercise intervention, the alcohol consumption increased again (Pichard et al., 2009). Zlebnik & Carroll (2015) showed that aerobic exercise attenuates cravings for drugs of abuse and reduces escalation and reinstatement of drug-seeking behaviour in animal models. Differential levels of voluntary exercise can explain different results. In this research, the authors also mentioned that eight weeks of supervised aerobic exercise in methamphetamine-dependent individuals helped restore D2/3 receptor availability to control dopamine levels. Gender differences are also seen in another study on cocaine. Access to an exercise wheel reduces cocaine self-administration and suppresses cocaine-primed reinstatement in female rats. During maintenance, female rats respond more to cocaine than males (Zlebnik, Saykao & Carroll, 2014).

Clinical studies in humans reported positive effects of exercise on addiction. Twenty-five participants of an exercise program of 12 weeks had a significantly reduced alcohol consumption compared to controls. Next to the physical activity, people also attended group sessions aimed at cognitive and behavioural components like motivation, setting goals, social support and time management. However, 12 weeks after the program there were no differences between the control and exercise groups in alcohol consumption anymore (Brown et al., 2014). These results correspond to the results found in animals and indicate that regular exercise over a longer period of time is necessary to avoid old behavioural patterns. Roessler (2010) reported that exercise reduces alcohol and drug problems. In addition, changes in body awareness and an increased energy level were seen. Some of the participants of this experiment experience the same feeling during exercise as when taking drugs. Roessler does not use sport as a substitute for alcohol or drugs, but sports can help to distract the addict's thoughts away from craving. Exercise can offer a feeling of being in control. People in recovery from drug addiction were positive about the integration of sports in the treatment period (Read et al., 2003).

As indicated earlier, reward is the underlying mechanism in both exercise and addiction. A possible factor in the treatment of addiction might be the possibility to find another way to experience reward. Due to reductions in dopamine production and dopamine receptors in addiction, drug-dependent patients have an impaired capacity to experience pleasure during early recovery but exercise might cause the experience of positive mood states without the use of drugs (Adinoff, 2004; Bressan & Crippa, 2005). Exercise's ability to facilitate dopaminergic transmission may prevent drug use by serving as an alternative reinforcer (Lynch et al., 2013).



Exercise is also important to prevent relapse. Relapse and withdrawal symptoms are connected to each other. Withdrawal symptoms are reduced when a patient has better physical fitness (Taylor & Ussher, 2005). Aerobic exercise during withdrawal from cocaine self-administration decreased cue-induced cocaine-seeking behaviour (Zlebnik & Carroll, 2015), and also a reduced risk in relapse to smoking in adults who are physically active is seen (McDermott, Dobson & Owen, 2009).

Furthermore, exercise alleviates sleep disturbance and it improves cognitive functioning, processes which are both disrupted in early drug recovery and predictive of relapse. Exercise can be an effective relapse prevention. Improved mood, regulated reward systems, reduced depressive symptoms, improved sleep and cognitive function all may serve to reduce the risk for relapse (Brown et al., 2010).

Another crucial aspect in the treatment of addiction is to get the patients away from cues responsible for cravings. A positive effect of exercise is that it easily can be performed in new environments, where no cues are present.

Exercise as a treatment is effective in the prevention of relapse and therefore valuable in the recovery period of patients. Exercise causes substitutional reward experiences and distracts patients from withdrawal symptoms. Physical exercise is easily accessible for everyone and therefore an appropriate intervention in treatment against addiction.

## Chapter 8: The downside of exercise as therapy for substance abuse

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The results in both animal and human studies show that exercise is an accessible and effective treatment for addiction, as it shows promising results in decreasing substance intake and preventing relapse. However, there are also indications that exercise has negative effects.

Intense physical exercise can have adverse effects during the recovery period in addicts. Pichard et al. (2009) showed that forced intense physical activity in mice caused higher alcohol intake than mice that have voluntary access to a running wheel, in which a decrease in alcohol intake was seen. In humans, performing higher than average amounts of physical exercise is related to the risk of mental illness and alcohol dependence. A possible explanation for this phenomenon is dopamine dysfunction and a higher risk of people with alcohol addiction to perform activities that have rewarding effects (Dakwar et al., 2012). Besides, it is possible that chronic high levels of exercise mimic the effects of chronic drug exposure and enhance vulnerability to relapse (Lynch et al., 2013).

Sensitivity to reward mechanisms makes an individual more prone to other drugs, a phenomenon called cross-sensitivity (Werme et al, 2002). In treatment for addiction, it must be taken into account that substitute behaviour predisposes people to a new addiction (Hatcher, 1989). This can actually be seen in real life. 52% of internet addicts have already had alcohol or drug abuse in the past (Young, 1999) and Murphy and Hoffman (1993) discovered that 25% of the patients that quit alcohol use, developed another addiction (substance or behaviour) within a year after the experiment.

When talking about addiction, the focus mainly lies on the use of alcohol and drugs. But one prone to developing addictions can also develop behavioural addiction, like exercise addiction. Exercise addiction also brings some adverse problems (Lichtenstein et al., 2017). Physical activity can have damaging effects, psychological as well as physical (Landolfi et al., 2013), therefore it is not a positive addiction. In people with exercise addiction, a greater amount of exercise is needed to feel satisfied and craving will happen. The components of exercise addictions are similar to substance addiction and therefore the development of exercise addiction occurs in similar ways.

There are several factors that play a role in the development of exercise addiction. The motivation for exercise addiction is related to personal characteristics. Preference for rewarding activities is one of the risk factors for people to develop an addiction. There are also high-risk personality characteristics, like impulsivity (Savitz et al. 2008) and perfectionism (Gizem, Potenza & Szabo, 2021; Landolfi et al., 2013). Perfectionism causes people to strive for better performance and this can be a drive to exercise more often and with higher intensity to improve. Just as with substance addicts, exercise addicts have a lack of social relationships and poor self-esteem (Landolfi et al., 2013). Using physical activity as a coping mechanism is typical for exercise addicts. People start performing physical activities as healthy methods to cope with stress and as mood modification (Szabo, 1995; Szabo & Griffiths, 2007), but exercise is not an ideal solution for dealing with life stressors (Landolfi et al., 2013). Once engaged in physical activity, both males and females continue for fitness and health benefits. However, being more committed to physical activity is a predictor to exercise addiction in males (Dawson & Peco, 2004). In exercise addiction, physical activity is performed despite negative consequences like injuries and problems with social relationships.

Exercise addiction is more prevalent in competitive runners (Smith et al., 2010) than in non-competitive runners. Amateur athletes are less able to control their behaviour and increase

their amounts of exercise to receive the same rewarding effects as when they start working out (López et al., 2021). Sports activities are a source of joyfulness and happiness in amateur runners, but an increase in the amount and intensity of exercise can become maladaptive (Lukács et al., 2019). People in recovery from an addiction should therefore be supervised by professionals when they start participating in sports. The maladaptive effects are demonstrated mostly in people performing individual sports. Team sports might be more convenient as treatment since sporters are guided by coaches and there are also more social aspects involved.

Summarizing, some studies indicated increased drug or alcohol intake when there is forced physical activity. Besides, people who are recovering from substance abuse may be more prone to exercise addiction. Too high amounts and intensity of exercise performance can lead to injuries and problems in social life. This indicates that exercise can have disadvantages on patients during recovery.

## Conclusion

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In this thesis, the mechanisms of addiction and possible treatments are explained. Exercise shows promising effects when applied to patients that want to recover from addiction. It has positive effects on patients' mental health, by promoting self-esteem and showing antidepressant effects. Exercise and addiction affects similar dopaminergic systems in the brain and training can therefore be used as a substitute for rewarding effects from drugs. Moreover, higher amounts of physical exercise is associated with reduced substance intake, in both human and animal studies. Patients performing physical exercise experience reduced withdrawal symptoms and improved physical fitness reduced the risk of relapse during recovery. An additional benefit of exercise is that it can be performed in environments with less to no triggers that might stimulate cravings. This is highly important in the recovery state. Next to improved physical fitness that can help in the process of recovery, exercise is a new behaviour that can substitute for the unhealthy behaviour accompanied with substance abuse.

However, there are also some adverse effects seen in exercise as treatment for addictive behaviour. In contrast with voluntary exercise, forced exercise results in a higher intake of substances of abuse. Besides, persons that are more sensitive to reward, a characteristic seen in addicts, are more prone to develop other addictions, so they are more likely to become addicted to exercise.

Exercise has positive effects on mental and physical health, but an exercise addict performs physical activity despite negative effects like injuries or problems in social life because of the high commitment to the sports.

Addiction is very unique per person and the triggers for developing an addiction and relapse varies between individuals. These individual differences should be taken into account when it comes to proper treatments. The efficacy of exercise as treatment can be variable when applied to different individuals. More research is necessary to decide what types and durations of exercise are most convenient as treatment method.

However, substitute behaviours predispose people to new addictions and an increase in the amount and intensity of exercise can become maladaptive. Therefore professional supervision is important when exercise is used as a treatment method in addicted patients.

Exercise can have positive effects during the recovery period of addicts, provided that it is performed at moderate intensity and will not develop into a new addiction. Correct application of exercise as treatment is important, but more research on this topic is necessary to make definitive conclusions about exercise as prescription.

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