

# Pleasure and Achievement: Dopamine and Endorphins

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**Abstract.** Dopamine is a well-known chemical that brings happiness to people and is responsible for signaling excitement and happiness. Dopamine is not only a key regulator of learning and motivation, but also a core substance that regulates the human body. Depression and Parkinson's disease are often associated with a lack of dopamine. Moreover, smoking is addictive, and its main mechanism is also closely related to dopamine: nicotine can cause a burst of dopamine neurons. Another substance with similar effects to dopamine is endorphins. Endorphins attach to morphine receptors and cause the same pain alleviation and pleasure that morphine and other opiates do, similar to a sense of accomplishment. Endorphins bring pleasure, but also lead to drug abuse. Opiate addiction is a severe public health issue that affects a huge proportion of population. People who take drugs produce dopamine and endorphins, and their mental dependence on drugs far exceeds the benefits of dopamine and endorphins.

**Keywords:** Dopamine, endorphins, happiness.

## 1. Introduction

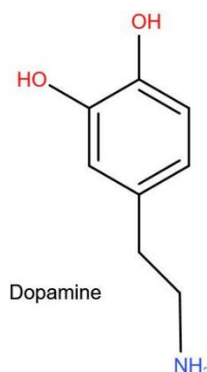
Disorders such as schizophrenia, Attention Deficit Hyperactivity Disorder (ADHD), Parkinson's disease, Tourette's syndrome, and pituitary tumorigenesis are associated with dysregulation of the dopamine system [1]. As a neurotransmitter, Dopamine, the most abundant catecholamine neurotransmitter in the brain, affects a variety of central nervous system physiological activities. This brain hormone is linked to human desires and sentiments, and it sends a message of excitement and delight. Additionally, dopamine has been implicated in various addictive behaviors [2]; unlike dopamine production, endorphins require more experience.

Exercise has profound benefits for the body and mind, while exercise can be addictive [3]. However, the underlying processes of these addictions remain unknown. Endorphins have been shown to bind to receptors and cause analgesic and euphoric effects similar to morphine and opioids. The same as a natural analgesic. It has numerous additional physiological roles than analgesia, including controlling body temperature, as well as cardiovascular and respiratory systems. The usage of Morphine-like medications can boost endorphin release in the brain.

This review focuses on the mechanisms and action of dopamine and endorphins.

## 2. Dopamine

### 2.1. Chemical structure of dopamine



**Figure 1.** Structure of dopamine

As an important neurotransmitter, Dopamine is a substance that assists cells in transmitting impulses. Also known as catechol ethylamine or hydroxylamine (Fig. 1), is a catecholamine, the molecular formula is  $C_8H_{11}NO_2$ . It carries two hydroxyl groups, meaning it has good water solubility. Dopamine can be synthesized by nerve cells themselves or by cells in the synaptic area. In addition to being a precursor to norepinephrine, dopamine is also an important neuromodulator for maintaining extrapyramidal nerve function [4].

## **2.2. Dopamine is a key regulator of motivation and learning.**

Slow (tonic) dopamine swings are assumed to be involved in motivation, whereas quick (phasic) dopamine swings carry acquired reward expectancies [1]. Is dopamine a signal for motivation, learning, or both? A core distinction is the effect of dopamine on future behavior (learning) and the effect of dopamine on current behavior (performance or motivation). When selective, absolute disruption of dopamine pathways was possible (in the 1970s), the apparent behavioral outcome was a severe reduction in exercise volume, in stark contrast to encephalitis, symptoms of intoxication, or loss of movement in humans with advanced Parkinson's disease [3]. This could mean that Parkinson's is associated with dopamine. Coincidentally, if there is a fire in the living area the key signal being a fire alarm going off, people with dyskinesia may get up and run called "paradoxical dyskinesia". The reward process was also not fundamentally flawed. Mice with low dopamine production tasted what they placed in their mouths and appeared to enjoy it. However, a major shift took place in the 1990s, with the reintroduction of periodic dopamine pulses. Encoding reward prediction error, according to this interpretation. Dopamine cells respond to unforeseen stimuli associated with potential rewards but stop responding when these stimuli become expected [2].

Learning is to learn to "look back" on past states and behaviors and update their values. Instead, motivation is "forward-looking" [1]: it uses future reward (value) predictions to appropriately motivate current behavior. Dopamine is closely related to the value of the instantaneous state, which is defined as the anticipated future benefit minus the anticipated time it takes to obtain it. Given that dopamine cell firing is similar to the RPE, the relationship between swift dopamine oscillations and motivational value appears strange [4]. However, the value signal also conveys the RPE, because the time difference in RPE is just a rapid change in value.

## **2.3. Addiction**

Addiction refers to compulsive non-drug self-management. The term is often used in a derogatory sense to refer to someone else taking drugs or taking drugs despite negative side effects. One problem with these definitions is that they do not apply equally to the spectrum of addictive drugs, nor do they apply equally to other powerful rewards. As a result, there has been debate over whether gambling, marijuana, or high-calorie foods are addictive [2].

### **2.3.1. Addiction is linked to four aspects of dopamine function.**

[2]: (A) tonic control of dopamine neurons may contribute to motivation, (B) phasic (reinforcement) learning of dopamine neurons (C) dopamine-deficient animals have only unconditioned reflexes (D) Dependent habits reduce interest in other motivations. Animals depleted of dopamine only have a fixed connection between an external cause and an organism's response to it [5]. Adult animals with selective damage to the dopamine system are non-motor. If not artificially fed, they will starve to death. In short, these animals had unconditioned reflexes and habits before the injury, but they were unable to learn new skills. Furthermore, after an injury, animals lose the incentive to respond to predicted inputs, which is essential for survival. Predictive cues direct animals from one reward to the next. Reward-seeking reduces the expression of dopamine receptors. Chronic use of addictive substances such as opiates reduces the surface expression of D2 dopamine receptors. This effect is also caused by compulsive overeating.

### **2.3.2. Nicotine.**

Nicotine and tar, as the primary harmful substances in cigarettes, have attracted widespread attention about the reasons for the addiction to cigarettes. Nicotine accelerates and enhances the activity of the central nervous system, exposing people to a strong excitement of addictive psychotropic drugs that induce dopamine neurons to fire in a burst. Extracellular dopamine levels are increased and habits can be formed. Non-nicotinic drugs raise dopamine levels by blocking the catabolic enzyme monoamine oxidase. While nicotine is useful, the strong subjective influence it has on novice users is unfavourable. Cues become heightened throughout the delay if nicotine is administered after a 20-minute wait. Nicotine addicts, like cocaine, methamphetamine, opiate, and alcohol abusers, have persistently decreased levels of D2 dopamine receptor expression, which may make them less responsive to non-habitual rewards [2].

## **2.4. Dopamine in diseases**

D2 dopamine receptors are mainly distributed in the olfactory tubercle, the black compact, pituitary, striatum, and ventral overlying areas. D2 dopamine receptors are both presynaptic and postsynaptic. The most abundant subtypes of dopamine receptors in the central nervous system are D1 and D2, while the former dopamine receptors are the most common [6]. The high affinity allows dopamine to readily bind to D2 receptors, primarily activated by burst (high concentrations) dopaminergic neurons. In short, it is not surprising that habitual activation leads to dramatic changes in D2 receptors. However, there is also conflicting evidence that habitual addiction to drug use also reduces D1 receptors.

### **2.4.1. Obesity.**

Experiments found a clear association between obesity and reduced D2 receptor expression in the brains of obese individuals (BMI 40 kg/m<sup>2</sup>). Since DA (the midbrain DA reward system mainly consists of VTA/DAergic neurons and their downstream targets) modulates the brain's reward circuit, producing feelings of pleasure as a response to certain stimuli, the lack of DA effects in these patients may make pathological changes. Ingestion is permanent [7].

### **2.4.2. Depression.**

Depression is a prevalent illness in schizophrenia and Parkinson's disease, and it is known to appear as a dopamine central system failure [1]. Experiments and animal models of human depression reveal that the dopamine system plays a role in depression [8].

In schizophrenia, some depressive symptoms, such as anhedonia (inability to enjoy pleasure) and reduced motor activity, are also found. Parkinson's disease symptoms, such as psychomotor delays and diminished motivation, are frequent in patients who are depressed. Biochemical evidence in depressed individuals comes from studies of a dopamine metabolite homovanillic acid (HVA). Homovanillic acid (Homovanillic acid, also known as 4-hydroxy-3-methoxyphenylacetic acid, is a venous arterial plasma drug concentration gradient found in patients with depression whose metabolites are catecholamines (epinephrine, norepinephrine).

Human and animal research is accumulating evidence that there is a link between dopamine transmission in the central nervous system and depression. When compared to healthy persons, depressive patients had a compensatory elevation of D2 receptor density in the basal ganglia/cerebellum. Consider the theory that there is a link between depression and a lack of dopamine delivery. Surprisingly, dopamine transporter activity was increased. This led to the discovery that depressed patients' reuptake dopamine more efficiently into presynaptic neurons. The expected result is a downward revision. In depressed individuals, the dopamine transporter can compensate for a shortage of dopamine supply. This dopamine transporter is the primary compensatory mechanism and results in low extra synaptic dopamine concentrations.

## 2.5. Treatment.

Not only a dopaminergic receptor agonist, but olanzapine is a new atypical neuroleptic that binds to dopamine receptors, 5-HT receptors, and cholinergic receptors and has antagonists and other antagonists) in resistant individuals, they provide antidepressant efficacy comparable to conventional antidepressants. Desipramine was utilized in the rat forced swim test. Desipramine increased extracellular dopamine concentration in the frontal brain adds to desipramine's antidepressant effect but is insufficient to explain fluoxetine's antidepressant impact on OCD [9].

## 3. Endorphins

Endorphins, often famous as androgens or endorphins, are morphine-like biochemically generated hormones that are endogenous (secreted by the pituitary gland). It is an amino molecule (peptide) released by vertebrates' pituitary glands and hypothalamus. The use of medications can boost endorphin release in the brain. Endorphins are a catch-all word for neuropeptides that have morphine-like action.

### 3.1. Production of endorphins

Objectively speaking, the production of stress is often accompanied by the production of endorphins. Because running is a physical stressor, it is natural to wonder what elements specifically counterbalance the inhibitory impact of negative stresses on adult neurogenesis: endogenous endorphins are an intriguing candidate. Endorphins are known to be released during aerobic activity, and this has long been assumed to be the cause of the "runner's high". During times of acute stress, hypothalamic corticotropin-releasing hormone (CRH) stimulates the production of corticotropin (POMC), a precursor of gonadotropin (ACTH), and  $\beta$ -endorphin, both of which are neurotransmitters. Simultaneously, it is produced by the anterior pituitary gland, allowing the organism to flee rapidly or continue fighting [10].

### 3.2. Carrier and transmission of endorphins

Endogenous Arabidopsis ligands in FQ are classified into four families:  $\beta$ -endorphins, nociceptins, enkephalins, and dynorphins. Receptors for these peptides and their homologs are ubiquitously expressed in neural axons, particularly in pain pathways. There are extensive reviews on Arabidopsis receptor signaling available [11]. Arabidopsis receptors are all linked to inhibitory G proteins ( $G_i$  and  $G_o$ ). When activated by endogenous or exogenous agonists, the G and G subunits separate and engage in a variety of actions and intracellular signaling cascades that ordinarily impede brain activity. It should be noted that MOPR, DOPR, and KOPR have been demonstrated to communicate via an agonist-independent mechanism known as constitutive activity, especially under chronic pain and stress [10].

### 3.3. Forms of endorphins

Endorphins exist in many forms (Table 1), but  $\beta$ -endorphins are the only form with potent pain-relieving properties.  $\beta$ -endorphins are more powerful analgesics than morphine because they operate largely on the mu family of cannabinoid receptors, which are also G protein-coupled receptors like the other two agonist receptors,  $\delta$ , and  $\kappa$ .  $\delta$ -endorphins and other opioids appear to diminish cyclic adenosine monophosphate levels and calcium absorption in the body. This peptide, which suppresses somatosensory fibers and focuses on nociceptors, is generally produced peripherally after painful or stressful situations. Although  $\beta$ -endorphin has the greatest affinity for the mu receptor, it also works on other Arabidopsis receptors, most notably the  $\delta$  Arabidopsis receptor [11].

It has long been assumed that  $\beta$ -endorphin is transiently raised in plasma as a result of anterior pituitary release during exercise and stress. These increases, however, are peripheral-specific since it does not easily pass the brain-brain barrier. The mechanism of  $\beta$ -endorphin signaling in the brain is unclear at this time, however, there are at least three probable pathways [12]. (1)  $\beta$ -endorphins can be

secreted into CSF and delivered to the brain; (2)  $\beta$ -endorphins can be released from the axonal centers of POMC-expressing hypothalamic neurons; or (3)  $\beta$ -endorphins can be carried across the brain-brain barrier after being released from the periphery. The first pathway for  $\beta$ -endorphins in chronic running conditions is to skip the periphery into the cerebrospinal fluid [10].

### **3.4. Addiction**

Drug addiction is a huge public health issue affecting a sizable proportion of the global population, and the research into the neurochemical circuits altered by persistent drug misuse exposure increases our comprehension of this addiction [10]. The neural circuits and substrates engaged in the early stages of drug misuse are not always those involved in the later phases of drug addiction, such as maintenance, regression, or relapse. The transition from the onset of drug dependence to the maintenance phase is unclear. However, it is widely believed that compulsive habits of drug-seeking, acquisition, and use throughout the maintenance period are a distinguishing hallmark of drug addiction. Using addictive medications regularly during the maintenance phase can develop into psychological and bodily dependency, which is characterized by increased drug cravings [12]. Cravings lead to compulsive conduct and the use of medications indefinitely to alleviate unpleasant withdrawal symptoms. Physical withdrawal symptoms subside after the first abstinence, but human cravings for the substance persist. Repeated injection of endorphins can result in analgesic intolerance and morphine-like withdrawal symptoms.  $\beta$ -endorphins have rewarding and enhancing properties when injected directly into the brain or muscle tissue. As a result, they may operate as a neuromodulator of the effects of substance misuse [13].

#### **3.4.1. Opioids.**

Opioids are commonly used recreationally as euphoric agents and in medicine as analgesics. Specifically, the advancement of novel powerful, and very selective opioids for example heroin and fentanyl, as well as the discovery of endogenous opioid peptides and receptors, have both positive and negative consequences on medicine and society. Currently, Opioids continue to be the primary analgesics in cases of severe acute, surgical, as well as persistent discomfort. The use of naloxone can counteract the analgesic benefits of  $\beta$ -endorphins. Exogenous opioids for pain management are associated with a reduction in  $\beta$ -endorphin concentrations in cancer patients, and morphine has been reported to alter the normal  $\beta$ -endorphin-pain response. Many methods and techniques for pain relief are at least partly attributable to fluctuations in  $\beta$ -endorphins. For example, the “warmth” and pain alleviation afforded by connective tissue massage were associated with increased plasma  $\beta$ -endorphin levels [14].

#### **3.4.2. Behavior control.**

Much of the control of behavior by  $\beta$ -endorphins is associated with pathways in the brain's reward system and other changes in sexual behavior, food consumption, and more. Though dopamine is primarily concerned with the reward system and how it links to many of the same changes in behavior as  $\beta$ -endorphins,  $\beta$ -endorphins are also involved in many reward system pathways.  $\beta$ -endorphins appear to have a regulatory influence on hyaluronan, limiting its release and controlling its turnover in a region-dependent way, which opioid antagonists can reverse.

### **3.5. Exercise can cause changes in endorphin levels.**

Research found that blood endorphin levels are elevated during various types of exercise, leading to the activation of the endogenous opioid system by exercise [5]. However, endorphin levels in the brain barely changed. Both acute and chronic exercise cause changes in brain function. Exercise improves blood flow to the brain, lowers risk in middle age, prevents age-related brain volume loss, and slows the advancement of many neurodegenerative disorders such as Alzheimer's, Parkinson's, and other dementias, and Chronic Multiple Sclerosis. Furthermore, exercise has several good benefits on mental ability and mental wellness throughout the body.

### 3.5.1. The hypothalamic-pituitary-adrenal (HPA) axis is related to $\beta$ -endorphins.

The HPA axis regulates several activities, including immunological responses and metabolism. When a stressful event causes the creation of the Genotropin-releasing hormone, the HPA is the first to be activated (CRH). This causes the release of gonadotropin (ACTH) and  $\beta$ -endorphin, both of which are created by cleavage of POMC and stored and released simultaneously in secretory vesicles. HPA has been linked to a number of activities, including exercise, drug usage, sexual activity, and others.

### 3.5.2. Research methods.

Rat swimming experiment is often used to study people who are more likely to raise blood levels in opioid neuropeptides during exercise. Divide the rats into three groups of 6 each (1) with control immobility (2) with a 4-hour swim (3) with a short training period of 7 days, with daily swimming increasing daily. All animals in a group swim in one pool. 65cm<sup>2</sup> sleep at 32.1°C water temperature. Rats were beheaded rapidly following the conclusion of the last round of swimming competitions. Hypothalamus, pituitary, and adrenal glands were rapidly resected and homogenized. Levels of pituitary and hypothalamic-,  $\beta$ -, and  $\gamma$ -endorphins, levels of  $\alpha$ -,  $\beta$ -, and  $\gamma$ -endorphins in adrenal glands, and levels of  $\alpha$ -,  $\beta$ -, and  $\gamma$ -endorphins in plasma were measured.  $\gamma$ -endorphin is the first product of metabolic shortening of the  $\beta$ -endorphin peptide chain. The pituitary  $\beta$ -endorphin content decreased similarly., while the  $\alpha$ -endorphin content showed an upward trend. It is speculated that  $\gamma$ -endorphin is promoted to form  $\alpha$ -endorphin during exercise. Numerous data suggest that athletes are more likely to boost opioid neuropeptide levels in the blood during exercise [5]. These processes are predicated on an increase in the endorphins, possibly because of an increase in pro-cortisol synthesis. The increase in  $\beta$ -endorphin was confirmed by elevated  $\beta$ -endorphin levels in the pituitary, adrenal gland, cerebral cortex, and striatum of rats after training [12].

**Table 1.** Forms of endorphins

Forms of endorphins	Function	References
$\beta$ -endorphins	Most studied, pain-relieving	[10, 12]
$\alpha$ -neoendorphin enkephalins dynorphins	inactive forms	[11]

## 4. Conclusions

It has been proposed to get rid of the addictive “dopamine” and embrace the long-term pleasure of “endorphins”. Dopamine is a neurotransmitter used to help cells transmit impulses. It conveys messages such as excitement and happiness. However, “profit-seeking” is the mechanism of action of dopamine, which is our desire to do something, that is, the driving force. However, the pleasure brought by dopamine is short-lived, and the driving force brought by dopamine has the following three characteristics. 1. The principle of diminishing marginal utility: the pursuit of stimulation. 2. Feedback mechanism: Rewards can only be obtained after rewards 3. Prefer immediate rewards: endorphins are an endogenous (secreted by the pituitary gland) morphine-like biochemical synthetic hormones, which are the compensation mechanism of the brain. Endorphins will bring us benefits in 3 aspects: 1. Relieve physical stress and analgesia. Once endorphins are released, a sense of well-being, trance, and a weakening of the perception of pain would be generated. 2. Relieves mental stress and brings a sense of calm, happiness, and stability. 3. Deepen memory. Understanding characteristics of dopamine and endorphins would help to understand the difference between just-in-time gratification and late gratification faster, as well as to provide further clues of potential effective treatment on dopamine and endorphins associated disorders.

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