Chapter 1

Introductory Chapter: "Feel Good" Chemical Dopamine - Role in Health and Disease

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Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/intechopen.81451

> *"People say, "I wish I had more motivation today, because then I would try something." But our thinking is backward. The way our brain works is that dopamine - the so-called feel-good chemical - is released the second we actually do something. So the motivation doesn't come before, it comes after."*
>
> *—Brendon Burchard*

1. Introduction

Dopamine (DA) (3,4-dihydroxyphenethylamine) is a member of the catecholamine family (a monoamine, an organic compound that has a catechol and a side-chain amine) of neurotransmitters in brain and is an antecedent to epinephrine (adrenaline) and norepinephrine (noradrenaline). DA is produced in the body (primarily by nervous tissue and adrenal glands) initially by the hydration of the amino acid tyrosine to DOPA by tyrosine hydroxylase and further by the decarboxylation of DOPA by aromatic-L-amino-acid decarboxylase. It is a key transmitter in the extrapyramidal system of the brain and crucial in synchronizing movement. A group of receptors (dopamine receptors) facilitates its function.

DA performs critical role in reward and movement control in the brain. Further, it has a function to play in modulation of behavior and cognition; voluntary movement, motivation, inhibition of prolactin production, sleep; dreaming; mood; attention; working memory; and learning. DA has multiple other functions outside the brain. In blood vessels, it impedes norepinephrine delivery and acts as a vasodilator (at endogenous concentrations); in the kidneys, it increases sodium evacuation and urine yield; in the pancreas, it diminishes insulin making; in the digestive system, it lessens gastrointestinal motility and guards intestinal mucosa; and in the immune system, it diminishes activity of lymphocytes. In the circulation, DA is primarily deposited in and transported by blood platelets [1]. Performing multiple unrelated critical biological functions makes this smart chemical, a "VVIP" for sustenance of life both in health and disease.

2. Synthesis, metabolism, and reuptake of dopamine

Tyrosine hydroxylase (TH) is a rate-limiting enzyme in the biosynthesis of DA and other catecholamines (**Figure 1**). Altering expression level of this critical enzyme, which eventually regulates the synthesis of DA, assists in developing promising therapeutic approaches and strategies to promote human health and address disease [2]. In presynaptic neurons,

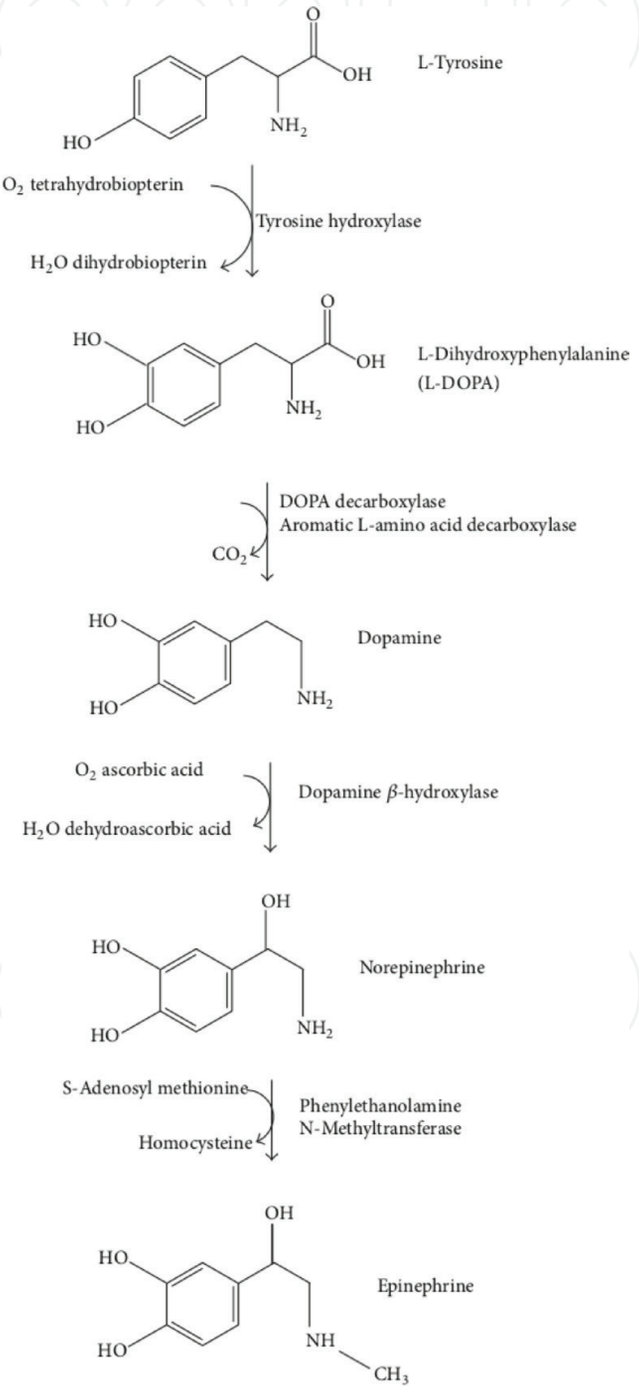

Figure 1. Catecholamine biosynthesis (reproduced with approval from Olguin et al. [8]).

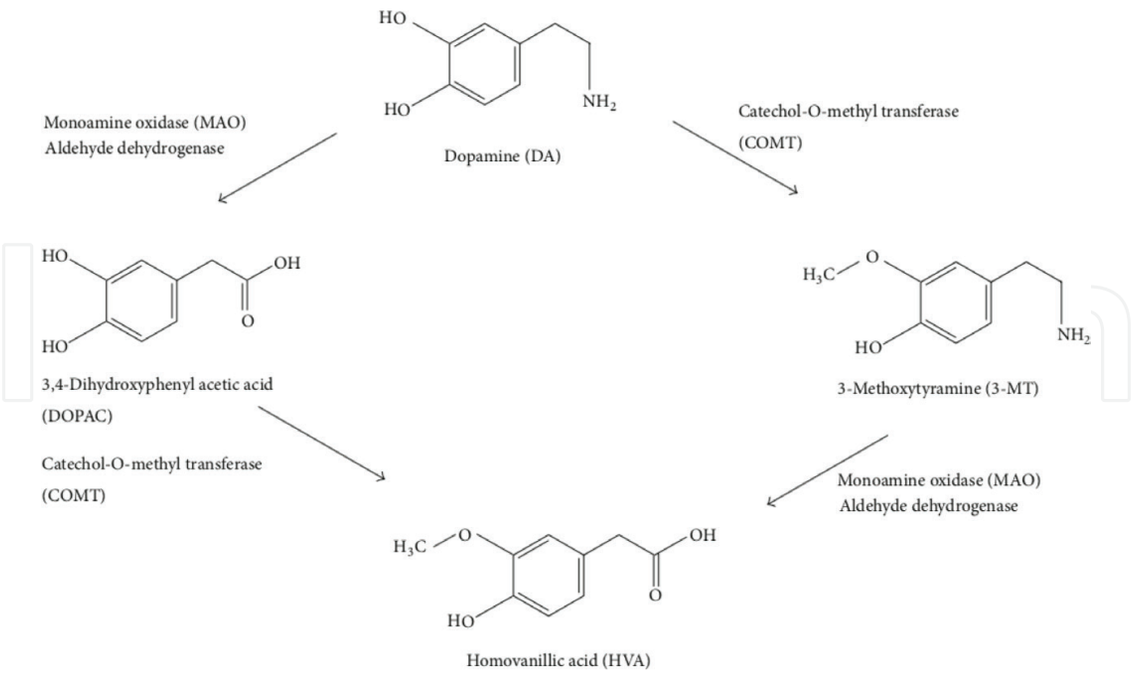

Figure 2. Dopamine metabolism (reproduced with approval from Olguin et al. [8]).

DA is encapsulated into synaptic vesicles and stored (this process is regulated by VMAT2 (vesicular monoamine transporter 2)). Later, synaptic vesicles release the DA into the synapse. Then, it binds either to presynaptic receptors (the signal can either inhibit (leading to inhibit the synthesis and release of neurotransmitters) or excite the cell) or to postsynaptic receptors. Once after the execution of function, DA is taken up into the presynaptic cell either by DAT (DA transporter) or by plasma membrane monoamine transporters (**Figure 2**).

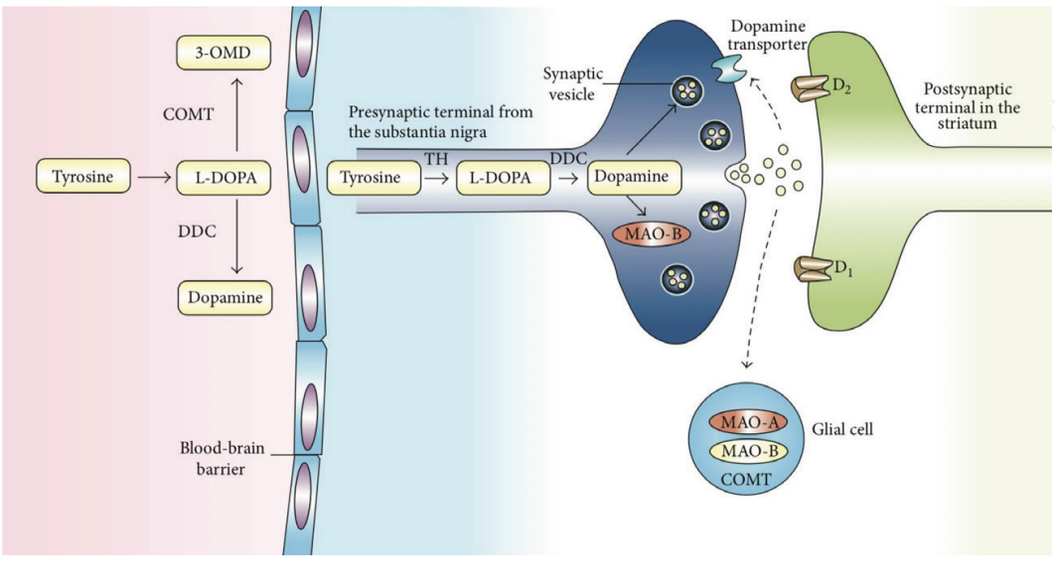

Figure 3. Dopamine release and reuptake process (reproduced with approval from Olguin et al. [8]).

COMT (catechol O-methyl transferase, principally expressed by glial cells) and MAO (has two isoforms A and B: monoamine oxidase A, primarily found in catecholaminergic neurons (e.g., neurons of *substantia nigra*) and monoamine oxidase B, chiefly found in astrocytes) are two critical enzymes responsible for breakdown of dopamine. COMT breaks down DA to 3-MT (3-methoxytyramine), which is subsequently reduced to HVA (homovanillic acid) by MAO. On the other hand, MAO converts DA to DOPAC (3,4-dihydroxyphenyl acetic acid), which is reduced by COMT to HVA and excreted out through urine (**Figure 3**). Therefore, inhibition of MAO can be a potential therapeutic strategy, which would decelerate the breakdown of DA and confer neuroprotection in neurodegenerative diseases like Parkinson's disease [3].

3. Dopamine: health and disease

DA acts upon to elicit feelings of enjoyment and bolstering, which motivates an animal to perform certain tasks repeatedly. In other words, reward system of the brain is strongly associated with "feel good" chemical DA. In certain areas of brain such as nucleus accumbens and prefrontal cortex, release of dopamine primarily due to fulfilling experiences such as food, drugs, physical exercise, sex, learning new tasks, figuring out unknown things, and neural stimuli correlated with these actions [4].

Parkinson's disease (PD) is a degenerative ailment causing tremor and motor impairment and is instigated by a loss of dopamine-secreting neurons in an area of the midbrain called *substantia nigra.* Dopamine agonists (drugs such as Mirapex (pramipexole), etc.) by mimicking dopamine bind and activate dopamine receptors, mirroring the activity of dopamine, leading to tricking the brain as if it has dopamine by conferring the biological functions of dopamine. Hence, these agonists are used as therapeutic agents in treating depression and Parkinson's disease. Replenishing dopamine levels through L-Dopa improves the PD symptoms, which is time-tested therapeutic strategy for PD [5].

There is evidence that schizophrenia comprises distorted levels of dopamine activity [6, 7], and most antipsychotic drugs utilized to cure this are DA antagonists, which reduce dopamine activity [8]. Therefore, antagonists have a significant therapeutic value in treating psychiatric conditions such as schizophrenia, which result due to overexcited dopamine organization. Attention-deficit hyperactivity disorder, bipolar disorder, and addiction are also characterized by defects in dopamine production or metabolism [9–12]. When present in sufficiently high levels, dopamine can be a neurotoxin (chemical that disorders neural tissue) and a metabotoxin (endogenously produced metabolite that causes adversarial health consequences at persistently elevated levels). Chronically high levels of dopamine are linked with neuroblastoma, Costello syndrome, leukemia, pheochromocytoma, aromatic L-amino acid decarboxylase deficiency, and Menkes disease (MNK). High levels of dopamine can lead to hyperactivity, insomnia, agitation and anxiety, depression, delusions, excessive salivation, nausea, and digestive problems [9].

http://dx.doi.org/10.5772/intechopen.81451

4. Natural ways to boost brain dopamine levels for healthy living

Though DA is available in certain food materials, as it does not cross blood-brain barrier, it will not be available in brain. Therefore, other way of enhancing brain dopamine levels in a simple way is consuming foods containing the precursor of dopamine, tyrosine that can cross blood-brain barrier and enter brain where dopamine will be synthesized from tyrosine.

Foods such as bananas, eggs, avocados, almonds, fish, and chicken are rich in tyrosine. Recent studies substantiate the fact that certain bacteria (probiotics) in gut synthesize dopamine and influence mood and behavior. Velvet beans (*Mucuna pruriens*) contain significant levels of L-Dopa, the precursor molecule of dopamine, and assist in enhancing brain dopamine levels [13]. Studies illustrate that regular exercise [14] and listening to music [15] enhances the brain dopamine synthesis and also upregulates the number of dopamine receptors, which eventually helps for good mood and happy living.

5. Conclusion

The book "*Dopamine - Health and Disease*" focuses on multiple biological functions of dopamine relating to health and disease. This basic understanding is fundamental in developing and implementing therapeutic methods and strategies, which eventually contribute for promoting quality living of mortals. The authors' contributions lean toward the aspect that by taking advantage of fundamental understanding and knowledge relating to dopamine *per se* and its biological functions, how efforts can be made to translate the discoveries/innovations to promote human well-being, rather than from the perspective of hard-core scientific paper. Reader would appreciate this perspective as it directly influences the value of our lives.

Therefore, the very nature and purpose of the present endeavor aims at understanding the fundamental knowledge relating to dopamine and applying the same for supporting human life, which is very essence of biomedical research. At the same time, it is essential to realize the basic fact that practice of balanced lifestyle, meaning moderate consumption of food along with good physicomental (Yoga, Dahn, Shinshin-Toitsu-Do, etc.) and recreational activities, as practiced in ancient civilizations, can sustain the optimum levels of neurotransmitters and hormones and promote happy living. Here comes the importance of traditional/indigenous practices and knowledge of multiple age-old civilizations in promoting human health. The contents of this book fulfill the aim with which this project is initiated and moved on and successfully brought to a shape.

Acknowledgements

This work is supported by funding from Department of Biotechnology (DBT), India, grant numbers (BT/405/NE/U-Excel/2013 and BT/PR16868/NER/95/328/2015), and DST-SERB (Department

of Science and Technology-Science and Engineering Research Board), India, grant number (EMR/2016/002375).

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