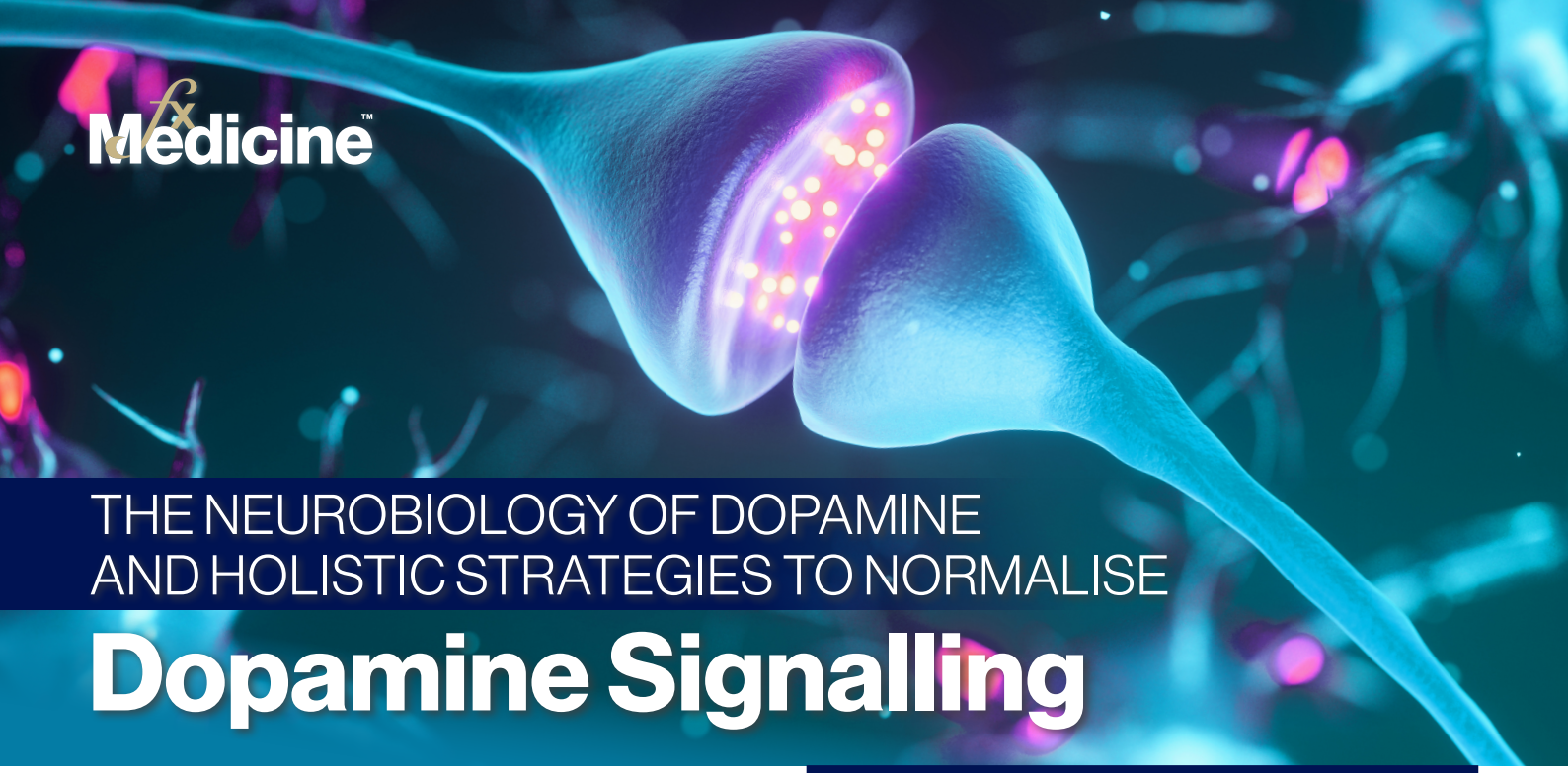

THE NEUROBIOLOGY OF DOPAMINE AND HOLISTIC STRATEGIES TO NORMALISE Dopamine Signalling

ARTICLE BY
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Dopamine is a pleiotropic neurotransmitter with essential roles in motivation, reward, movement, cognition, and the modulation of prolactin. Often incorrectly referred to as 'the pleasure molecule'; dopamine is best associated with the 'want' to do something, rather than the 'liking' or pleasure associated with doing something.[1,2]

Dopamine disturbances

Due to its many essential functions, disturbances in dopamine activity can have profound health effects. For example, adult animals with damage to their dopamine system become akinetic (a loss in the normal ability to move muscles) and, if not artificially fed, will die of starvation.[3]

Dopaminergic disturbances are common, whereby researchers have described the increasing problem associated with a 'hypodopaminergic society'.[4] (See Table 1)

KEY HIGHLIGHTS:

- Dopamine is crucial for motivation, reward, movement, and cognition, but is incorrectly labeled as 'the pleasure molecule'.
- Disruptions in dopamine can lead to severe health issues, including akinesia and death by starvation in animals.
- Dopamine dysfunction is associated with addictions, depression, bipolar disorder, schizophrenia, ADHD, Alzheimer's, Parkinson's, and restless legs syndrome.
- Factors affecting dopamine activity include genetics, ageing, diet, medications, drugs, nutritional deficiencies, stress, inflammation, sleep, hormones, and gut health.
- Effective management includes addressing stress, diet, nutrition, sleep, inflammation, hormones, physical activity, and using supportive supplements and herbs.

Table 1. Characteristics of dopamine disturbance[4]

REDUCED DOPAMINE CHARACTERISTICS	STRONG DOPAMINERGIC CHARACTERISTICS
Cognitive and memory deterioration	High intelligence
Lack of motivation or difficulty in achieving goals	Sense of personal destiny
Attention span limitation	Religious/cosmic preoccupations
Low spirituality	Obsession with achieving goals
Reward seeking through substance abuse or risky behaviour	Emotional detachment
Aggression increase	Risk-taking behaviour[4]
Pain tolerance reduction	
Blunted ability to achieve pleasure states	

As can be seen from these two contrasting states, the 'Goldilocks' rule applies to dopamine. Not too high and not too low. Its activity needs to be just right.

The physiology of dopamine

The synthesis of dopamine is complex, and there are several steps in its production, breakdown, transportation, and communication that can go askew. (See Figure 1.)

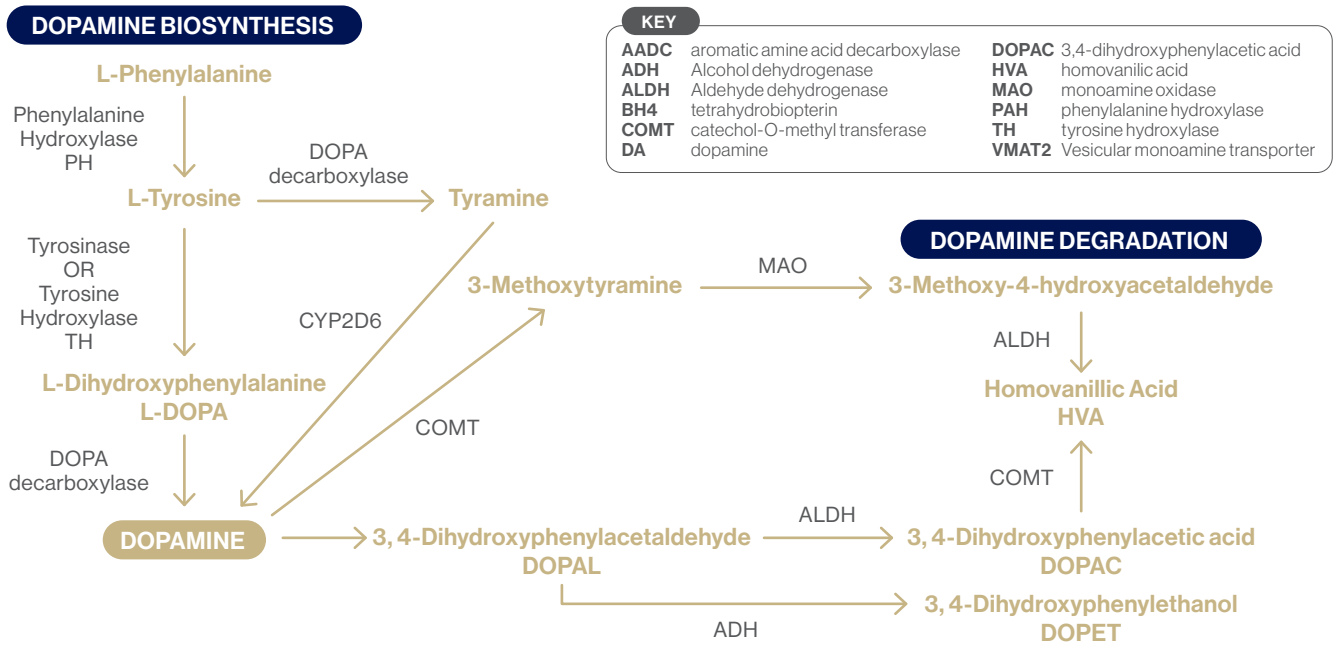

Figure 1. Dopamine synthesis and degradation

The precursors to dopamine are the amino acids phenylalanine and tyrosine. Phenylalanine is converted into tyrosine by the enzyme phenylalanine hydroxylase (PAH), and then tyrosine is converted into L-Dopa by the enzyme tyrosine hydroxylase (TH). Both PAH and TH require another enzyme known as tetrahydrobiopterin (BH4), and methylation is important to produce adequate levels of BH4.[5] In the final step of its synthesis, L-dopa is converted into dopamine, which requires another enzyme called L-dopa decarboxylase. Other important enzymes involved in dopamine metabolism are catechol-O-methyl transferase (COMT) and monoamine oxidase (MAO). These enzymes break down dopamine into its inactive metabolites.

Dopamine transmission

From a transmission standpoint, dopamine binds to postsynaptic and/or presynaptic receptors. Dopamine also has transporters that incorporate it into synaptic vesicles and the cellular cytosol, such as vesicular monoamine transport 2 (VMAT2) and the dopamine transporter.[6] Given these several crucial mechanisms, problems associated with dopamine can be due to disturbances in the concentrations of its precursors, enzymes involved in its synthesis, enzymes involved in its breakdown, receptor sensitivity, and/or transporters. (See Figure 2.)

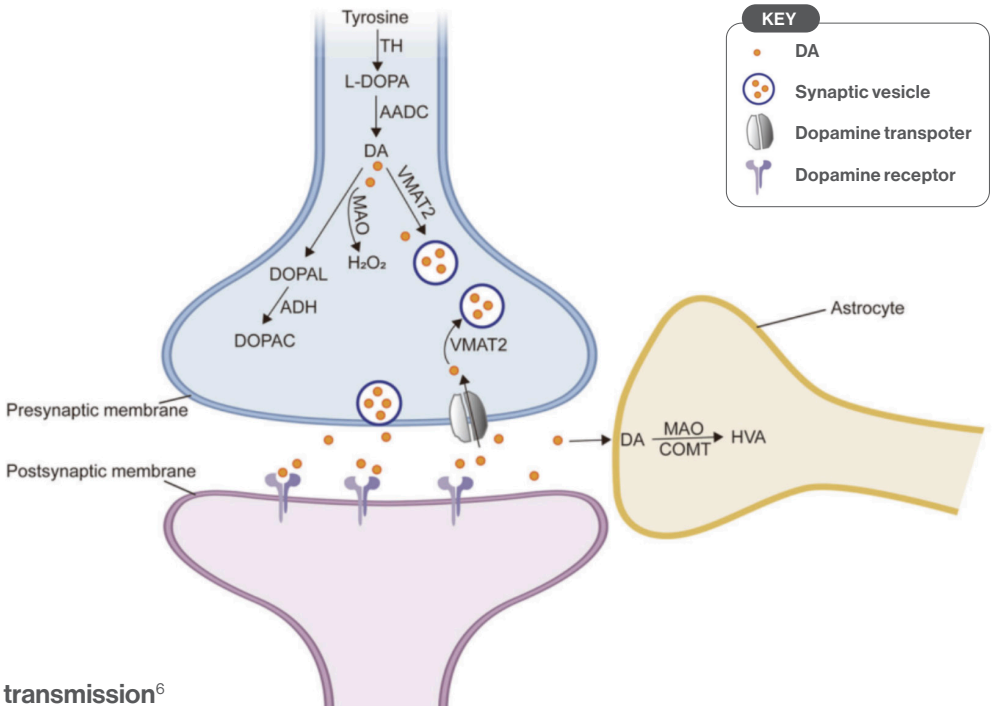

Figure 2. Dopamine transmission[6]

Disorders associated with dopaminergic disturbances

Dopamine disturbances have been implicated in an extensive range of conditions. For example, dopamine seems to play a role in addictions to illicit drugs, nicotine, alcohol, certain foods, gambling, pornography, and even internet addiction.[2,3]

In drug addiction research, imaging studies have found that faster increases in dopamine after drug use are associated with a more reinforcing effect from the drug. Gamblers also have a higher rate of dopamine turnover than non-gamblers.[7] Several mental health disorders are associated with dopamine disturbances. Anhedonia, an inability to feel pleasure, is a core feature of major depressive disorder, and dopamine plays a pivotal role in hedonic deficits and the drive to do things. Disturbances in dopamine have also been identified in bipolar disorder, schizophrenia, attention deficit hyperactivity disorder (ADHD), Alzheimer's disease, Parkinson's disorder, and restless legs syndrome.[8-11]

Table 2. Causes of dopaminergic disturbances

The causes of most physiological disturbances are multifactorial, and the same applies to dopamine. We are still learning more about dopamine, but the research indicates that the following factors can influence dopaminergic activity:

CAUSE	EXPLANATION
Ageing	There is a loss of 5 to 10% of dopaminergic neurons every decade.[13,14]
Biological	COMT and methylation are important processes in dopamine synthesis, with COMT and MTHFR polymorphisms potentially affecting dopamine synthesis.[12]
Diet	Foods high in fat and/or sugar can downregulate dopamine receptor activity in the striatum, and people who overconsume high-energy foods have a decreased expression of dopamine receptor activity.[2,15]
Environmental neurotoxicants	Research has demonstrated that lead exposure can induce dopaminergic dysfunction,[18] and a broad-spectrum insecticide known as Rotenone can affect dopamine activity. Moreover, chronic exposure to Rotenone has been linked to Parkinson's disease.[19]
Gut dysbiosis	Several gut bacteria can produce dopamine. Examples include some *Bacillus strains*, *Escherichia coli*, and *Klebsiella pneumoniae*.[29]
Hormonal imbalances	Hypothyroidism can lead to the loss of dopaminergic neurons,[27] and sex hormones such as testosterone can affect dopamine signalling.[28]
Illicit and licit drugs	Illicit drugs such as cocaine and amphetamines and legal drugs such as nicotine and alcohol can affect the reuptake of dopamine, dopamine receptor sensitivity, and dopamine transporters.[2,3]
Inflammation	Inflammatory cytokines can affect mood, motivation, and motor activity, potentially due to the effect of inflammation on dopamine. Dopamine levels in different brain areas are negatively impacted by excess inflammation. Inflammation also decreases BH4 availability and the activity of dopamine transporters.[25]
Medications	Several pharmaceutical medications can affect dopamine activity. These include: • antipsychotics • ADHD medications • anti-Parkinson's drugs such as Levodopa • antidepressants • anticonvulsants • antibiotics[16,17]
Nutritional deficiencies	Vitamins B, C and D, iron, omega-3 fatty acids, folate, and choline are examples of nutrients important for dopamine production.[20-22] In an animal study, the administration of omega-3 fatty acids restored deficits in dopamine neurotransmission after a traumatic brain injury.[23] As phenylalanine and tyrosine are the building blocks of dopamine, deficiencies in these amino acids can also affect dopamine synthesis.
Sleep disturbances	Research has demonstrated that sleep deprivation can downregulate dopamine receptors in the ventral striatum.[26]
Trauma and chronic stress	Stress affects dopamine levels and dopaminergic activity in different brain areas. Childhood adversity can also affect COMT activity and dopamine receptor activity.[24]

Assessment and treatment of dopaminergic disturbances

The simplistic approach to alter dopaminergic activity is to prescribe pharmaceutical medications such as antipsychotics, antidepressants, anticonvulsants, and L-dopa. Unfortunately, this approach does not necessarily treat the causes of dopaminergic disturbances and is associated with many side effects. See Table 3. for a list of ways to support dopamine regulation.

Table 3. Assessment and treatment of dopaminergic disturbances

INTERVENTION	RATIONALE
Chronic stress and trauma	Assessment and treatment of stress and trauma
Dietary improvement	Minimising the intake of foods and beverages high in processed sugar and unhealthy fats
Nutritional deficiency assessment	Restore levels through diet and supplementation
Sleep disturbances	Teach healthy sleep practices
Potential drivers of inflammation	Reduce inflammation by increasing the intake of antiinflammatory foods and prescribing anti-inflammatory herbs and nutraceuticals such as omega-3 fatty acids, curcumin, ginger, and boswellia
Thyroid and sex hormonal disturbances	Identify and treat thyroid and sex hormonal disturbances
Spend more time in sunlight	In one study, dopamine receptor availability was higher in people with greater sunshine exposure[30]
Physical activity	Assess levels of physical activity
Genetic polymorphism assessment	Such as those associated with methylation and COMT activity, and provide appropriate dietary, lifestyle, and supplementation recommendations
Digestive disturbances and gut dysbiosis assessment	Restore healthy bacterial diversity through the many effective techniques you have at your disposal.
Herbal and nutraceutical supplements	Support dopamine activity including: tyrosine, phenylalanine, B vitamins, omega-3 fatty acids, vitamin C, iron, and plants such as ashwagandha, *Rhodiola rosea*, ginseng, green tea, astragalus root, saffron, and *Bacopa monnieri*.[31-34]

SUMMARY

Dopamine is a neurotransmitter with far-reaching effects on our body. Despite mainstream medicine primarily treating its disturbances with pharmaceutical medications, its activity is influenced by many factors that can be altered to help optimise its activity. Practitioners with a holistic perspective are well-placed to assist clients with dopaminergic disturbances.

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