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Review

Dopamine in Allergy and Inflammation: Cellular Mechanisms and Therapeutic Potential

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ABSTRACT

Dopamine (DA), well-known as a crucial neurotransmitter in the central nervous system, also exerts significant regulatory effects on the immune system. The effects of DA on immune cells such as T cells, dendritic cells, and macrophages are context-dependent, and its dual role in promoting both pro-inflammatory and anti-inflammatory responses highlights its complex regulatory function. In particular, DA plays an important role in diseases such as allergic asthma by regulating T-cell differentiation, particularly through receptor interactions such as dopamine receptor D4. The effect of DA on the nuclear factor kappa B and NOD-like receptor family pyrin domain-containing protein 3 inflammation pathways highlights its potential in the treatment of inflammation-related diseases. This review examines the different roles of DA in modulating the activity of immune cells and its implications for the treatment of allergic and inflammatory diseases, with a particular focus on the signaling pathways involved and the receptor-specific effects of DA.

Keywords: Allergy, dopamine, immune modulation, inflammation.

Dopamine (DA) has significant regulatory effects on the immune system in addition to being one of the central nervous system's key neurotransmitters.[1]

D1-like and D2-like receptors are the two primary kinds of dopamine receptors (DRs). Numerous signaling pathways that affect the immune system can be started by these receptors.[2] It has been demonstrated that DA acts via autocrine and paracrine pathways via receptors in cells of the immune system, hence affecting immunological responses like inflammation and allergy reactions. Depending on the cell type and circumstance, these DA actions can vary. Both pro- and anti-inflammatory reactions can be triggered by this neurotransmitter.[3]

In particular, it has been shown to regulate inflammatory processes by influencing the differentiation of T cells and various functions of immune cells. Dopamine can promote the differentiation of T helper 2 (Th2) cells, potentiating allergic reactions. These effects play an important role in the development of diseases such as allergic asthma in children, especially at a young age. Dopamine regulates T cell responses through a specific dopamine receptor D4, and this mechanism may vary depending on age.[4,5]

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The inflammation-related effects of DRs are particularly concentrated on the NOD-like receptor family pyrin domain-containing protein 3 inflammasome and the nuclear factor kappa B pathway. These signaling pathways are important targets in the treatment of inflammation-related diseases, such as Parkinson's disease, rheumatoid arthritis, and systemic lupus erythematosus. The interaction of immune cells, especially group 2 innate lymphocytes (ILC2), with DA, is another example of its regulatory effects on allergic inflammation.[6] In this review, the role of DA in allergic responses and inflammation processes will be explained, and the mechanisms behind these effects will be discussed.

DOPAMINE

Dopamine is a neurotransmitter that acts on both the nervous system and the immune system. It is synthesized primarily in the substantia nigra,

ventral tegmental area and hypothalamus in the brain.[7] While it modulates functions such as motor control, reward mechanism, and mood regulation in the brain, it also affects immune response and inflammation in peripheral tissues. The synthesis of DA starts from the amino acid tyrosine and acts on two main receptor families (D1 and D2). It regulates behavior and learning processes with both slow and fast signaling.[8]

Dopamine and the Immune System

Dopamine has been shown to affect immune responses in direct and indirect ways by interacting with dopaminergic receptors on immune cells. This demonstrates the potential of DA as an immunomodulating agent. Immune cells express dopaminergic proteins such as DRs (D1-D5 subtypes), dopamine transporters, and enzymes involved in DA synthesis. Interestingly, immune cells can produce, store, and release DA under certain conditions, especially during inflammation. As a pro-inflammatory effect, activation of D1-like receptors (D1, D5) can increase the production of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin (IL)-1β, and IL-6. In terms of anti-inflammatory effects, D2-like receptors (D2, D3, D4) generally exert a suppressive effect on cytokine production and reduce inflammatory responses by promoting the release of IL-10.[9]

IMMUNE CELLS

T Cells

T cells are central players in the adaptive immune response and express DRs. T cells can react to DA impulses thanks to these receptors. T cell function in inflammatory and regulatory situations is impacted by DA's ability to control T cell differentiation and activation.[10]

Dopamine at low levels can stimulate dormant T cells, causing them to proliferate and produce more cytokines. Dopamine, however, can have harmful effects and cause cellular malfunction in larger quantities. Through the D3 receptor, DA has been shown to enhance CD4+ T cell production of interferon-gamma (IFN-γ), which in turn promotes Th1 differentiation. On the other hand, interleukins like IL-4 and IL-10, which have been linked to Th2 and regulatory T cells (Tregs) responses, were suppressed by DA.[10,11] This suggests that DA inhibits Th2 activity and promotes Th1 immunological responses. Human T cells have a comparable dopaminergic modulation, confirming the importance of DA in influencing T cell responses to diverse stimuli. These results are not exclusive to mouse models.[12,13]

Regulatory T Cells

Tregs are critical for preventing autoimmune reactions by maintaining immune tolerance. The effect of DA on Tregs is complex and context-dependent. Activation of D1-type receptors on Tregs can reduce the production of immunosuppressive cytokines such as IL-10 and transforming growth factor-beta, which can weaken the suppressive functions of Tregs. However, this effect is mostly observed in activated Tregs, indicating that the activated state of Tregs may affect their sensitivity to DA signalling. This is further complicated by the fact that DA may exert different effects on Tregs depending on the presence of specific inflammatory signals.[14]

Dendritic Cells

Dendritic cells (DCs) are important antigen-presenting cells that link the innate immune and adaptive immune systems. These cells not only express DRs, but they can also synthesize and store DA and release DA in their interactions with T cells.[15,16]

The effect of DA on DCs is associated with the receptor subtype. Activation of D1-type receptors promotes the differentiation of Th2 cells by increasing DA synthesis; these cells are associated with allergic responses. On the other hand, activation of D2-type receptors suppresses Th1 responses by inhibiting the release of pro-inflammatory cytokines, potentially promoting a Th2-dominant immune environment. This bidirectional regulation highlights DA's complex role in balancing immune responses.[17,18]

Monocytes and Macrophages

Macrophages are versatile immune cells that perform many functions, such as phagocytosis and cytokine production, and they also respond to DA. Like T cells and DCs, macrophages express a variety of DRs. D2-type receptors on macrophages regulate phagocytic activity, and activation of these receptors suppresses the production of pro-inflammatory cytokines such as IL-2, IL-4, and IFN-γ.[19,20]

On the other hand, activation of D1 receptors inhibits the production of inflammatory cytokines and helps resolve inflammation by increasing the release of anti-inflammatory cytokines such as IL-10. Interestingly, the D5 receptor in macrophages can reduce the production of IL-12 and IL-23, which are critical for Th1 and Th17 differentiation. This suggests that DA signaling through D5 receptors may produce a

more anti-inflammatory macrophage phenotype.[21,22] In some disease states, such as multiple sclerosis and HIV infection, disruption of dopaminergic signaling can lead to dysregulation of macrophage activity and chronic inflammation and tissue damage.[23,24]

DOPAMINE AND ALLERGY

Dopamine is a neurotransmitter often associated with mood, motivation, and pleasure, but in recent years, its effects on the immune system and inflammation have also been investigated.[25] The role of DA in allergic reactions and immune modulation is becoming increasingly understood with new studies in this field. The potential role of DA in the treatment of conditions such as allergic rhinitis, asthma, and other immune-related diseases makes research in this area even more important.[26,27]

The effects of DA on the immune system are largely mediated through DA receptors. These receptors have several subtypes, D1, D2, D3, D4, and D5, and are widely present in immune cells. This indicates that DA can directly modulate immune responses. In particular, the D2 receptor has been identified to play an important role in immune regulation. Activation of the D2 receptor can affect both innate immune responses and adaptive immune responses. The interactions of DA with immune cells play a critical role in understanding the process of allergic inflammation. Dopamine modulates the function of immune cells such as T lymphocytes, DCs, and macrophages. For example, in allergic asthma, DA has been reported to inhibit the activation of type 2 cytokines such as IL-5 and IL-13. These cytokines play an important role in the development of allergic inflammation. The fact that DA suppresses these cytokines suggests that it may attenuate the inflammatory chain characteristic of allergic responses.[28]

Another important aspect of the effects of DA in allergic inflammation is its effects on ILC. In particular, ILC2 cells are known to play a central role in allergic inflammation. Studies in animal models have shown that DA suppresses the response of ILC2 cells to IL-33 and reduces the secretion and proliferation of type 2 cytokines by these cells. This effect suggests that DA plays a regulatory role in allergic responses, but does so without adversely affecting cell viability. Dopamine also plays an important role in diseases such as allergic rhinitis and asthma. Allergic rhinitis is a common allergic disease characterized by inflammation of the nose, and the role of DA in this disease is receiving increasing attention. It has been shown that DA regulates immune responses via D2 receptors and that this mechanism is particularly effective in areas of the brain, such as the olfactory nerves. By activating these receptors, DA has been found to reduce the production of pro-inflammatory cytokines such as TNF-α and IL-6, which are common in allergic inflammation. This suggests that DA may alleviate the symptoms of allergic rhinitis and reduce neurological effects such as olfactory impairment.[29]

The effects of DA on asthma are also better understood with recent studies. Asthma is characterized by chronic inflammation of the airways and is often triggered by exposure to allergens in early life.[30,31] Dopamine has been found to modulate the activation of allergen-specific T cells and thus may prevent the development of allergic asthma. Furthermore, the effects of DA on airway epithelium, immune cell infiltration, and pro-inflammatory cytokine production suggest that it may control asthma exacerbations and prevent long-term airway remodeling. The potential of DA in the treatment of allergic diseases is supported by the positive effects of DA D2 receptor agonists in neurological diseases such as Parkinson's disease and ischaemic stroke. These agonists can improve disease symptoms by reducing neuroinflammation. A similar treatment strategy could be considered for allergic diseases. Dopamine D2 receptor activation may control allergic inflammation by suppressing the activation of immune cells and pro-inflammatory cytokines.[31,32]

DOPAMINE AND INFLAMMATION

How immune cells are affected by DA has been the subject of research, especially in the context of inflammation. Dopamine regulates immune functions such as cell proliferation, cytokine release, chemotaxis, antigen presentation, and phagocytosis. The degree of this effect varies depending on the type of immune cell, the level of activation, and the type of DRs interacting. For example, in allergic asthma, the effect of DA on ILC2s has been investigated. The ILC2s produce the type 2 cytokines IL-4, IL-5, and IL-13, and these cytokines promote inflammation in the airways. Inhibition of the activation of ILC2 cells by DA may reduce allergic inflammation in the lungs. Dopamine may also affect the activity of T-lymphocytes, especially Th1 and Th2 cells. The balance between Th1 and Th2 responses determines the outcome of allergic and autoimmune diseases. Th1 cells are associated with pro-inflammatory responses, while Th2 cells are associated with allergy and asthma. The effect of DA on these cells can alter the immune response, which can increase or

decrease inflammation. These interactions reveal the complex nature of the immune system's response to inflammation.[33,34]

The interaction of DA with immune cells is highly complex. The context and the specific receptors that interact determine how DA influences immune cell activity. This bidirectional role reveals the effects of DA in conditions such as neurodegenerative diseases and its potential to modulate both inflammation and immune responses in line with the pathological state of tissues. Some immune cells, such as microglia and macrophages, are powered by DA signaling. This interaction may play a central role in chronic inflammation by modulating the production of pro-inflammatory cytokines. In diseases characterized by dopaminergic deficiency, such as Parkinson's disease, dysregulation of DA signaling may increase neuronal damage, contributing to chronic neuroinflammation.[28,29]

It is also important to note that DA is not limited to the brain. In peripheral tissues, it has also been found that DA can modulate immune responses.[6] For example, in asthma, DA has been shown to modulate the activity of immune cells in the lungs, limiting airway hyperresponsiveness and reducing the severity of allergic inflammation. Clinical studies reveal that DA agonists reduce inflammation and improve pulmonary function in asthma patients. The effect of DA on immune cells is not limited to simple activation or inhibition. Instead, it involves complex signaling pathways, such as the regulation of the oxidative phosphorylation pathway, which plays a critical role in cellular energy production and activation of immune cells.[35] Dopamine has been shown to modulate inflammation by regulating these metabolic processes in immune cells. These findings suggest a role for DA in controlling inflammation through the regulation of metabolic processes that support immune functions.[36]

DOPAMINE ON ALLERGIES AND INFLAMMATORY PROCESSES

Understanding the effects of DA on allergies and inflammation is an important step in regulating immune responses and developing potential treatment strategies. Allergic reactions occur as a result of hypersensitivity of the immune system to environmental allergens. These reactions are characterized by degranulation of mast cells, usually triggered by IgE antibodies, and are one of the major causes of inflammation. Research on how DA affects this process suggests that DA can modulate immune responses. Various receptors of DA can directly affect the functions of immune cells. In particular, it has been demonstrated that DA D1 and D2 receptors can modulate the degranulation of mast cells and the release of inflammatory cytokines.[37,38] This means that DA can increase or decrease the severity of allergic inflammation. The effects of DA on inflammation, on the other hand, have a more complex structure.

In conclusion, dopamine, traditionally known as a neurotransmitter, plays a pivotal immunomodulatory role by influencing various immune cells through its distinct receptor subtypes. It can exert both pro-inflammatory and anti-inflammatory effects depending on the receptor subtype, cell type, and microenvironment. Dopamine's interaction with T cells, dendritic cells, macrophages, and innate lymphoid cells demonstrates its broad regulatory capacity in allergic and inflammatory responses. Notably, DA appears to attenuate allergic inflammation by modulating Th2 and ILC2 activity, offering promising insights into diseases like asthma and allergic rhinitis. Furthermore, its impact on immune cell metabolism highlights a deeper level of immune regulation. The ability of DA to suppress cytokine release and limit immune cell activation supports its therapeutic potential. Targeting dopaminergic signaling may thus provide novel treatment strategies for allergic and chronic inflammatory diseases.

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REFERENCES

1. Cao Y, Li Y, Wang X, Liu S, Zhang Y, Liu G, et al. Dopamine inhibits group 2 innate lymphoid cell-driven allergic lung inflammation by dampening mitochondrial activity. Immunity. 2023 Feb 14;56(2):320-335.e9. doi: 10.1016/j.immuni.2022.12.017. Epub 2023 Jan 23. Erratum in: Immunity. 2023 May 9;56:1148-51.
2. Feng Y, Lu Y. Immunomodulatory Effects of Dopamine in Inflammatory Diseases. Front Immunol. 2021 Apr 9;12:663102.
3. Thomas Broome S, Louangaphay K, Keay KA, Leggio GM, Musumeci G, Castorina A. Dopamine: an immune transmitter. Neural Regen Res. 2020 Dec;15:2173-85.
4. Wang W, Cohen JA, Wallrapp A, Trieu KG, Barrios J, Shao F, et al. Age-Related Dopaminergic Innervation Augments T Helper 2-Type Allergic Inflammation in the

Postnatal Lung. Immunity. 2019 Dec 17;51:1102-18.e7.
5. Juárez Olguín H, Calderón Guzmán D, Hernández García E, Barragán Mejía G. The Role of Dopamine and Its Dysfunction as a Consequence of Oxidative Stress. Oxid Med Cell Longev. 2016;2016:9730467.
6. Nolan RA, Reeb KL, Rong Y, Matt SM, Johnson HS, Runner K, et al. Dopamine activates NF-κB and primes the NLRP3 inflammasome in primary human macrophages. Brain Behav Immun Health. 2020 Feb;2:100030.
7. Berke JD. What does dopamine mean? Nat Neurosci. 2018 Jun;21:787-93. 2023 Jan 23. Erratum in: Immunity. 2023 May 9;56:1148-51.
8. Sorgun O, Çakır A, Bora ES, Erdoğan MA, Uyanıkgil Y, Erbaş O. Anti-inflammatory and antioxidant properties of betaine protect against sepsis-induced acute lung injury: CT and histological evidence. Braz J Med Biol Res. 2023 Nov 13;56:e12906.
9. Channer B, Matt SM, Nickoloff-Bybel EA, Pappa V, Agarwal Y, Wickman J, et al. Dopamine, Immunity, and Disease. Pharmacol Rev. 2023 Jan;75:62-158.
10. Contreras F, Prado C, González H, Franz D, Osorio-Barrios F, Osorio F, et al. Dopamine Receptor D3 Signaling on CD4+ T Cells Favors Th1- and Th17-Mediated Immunity. J Immunol. 2016 May 15;196:4143-9.
11. Durankuş F, Budak K, Albayrak Y, Sever İH, Özkul B, Uyanıkgil Y, et al. Atorvastatin Improves the Propionic Acid-Induced Autism in Rats: The Roles of Sphingosine-1-Phosphate and Anti-inflammatory Action. Cureus. 2023 Mar 29;15:e36870.
12. Levite M. Dopamine and T cells: dopamine receptors and potent effects on T cells, dopamine production in T cells, and abnormalities in the dopaminergic system in T cells in autoimmune, neurological and psychiatric diseases. Acta Physiol (Oxf). 2016 Jan;216:42-89.
13. Wang XQ, Cai HH, Deng QW, Chang YZ, Peng YP, Qiu YH. Dopamine D2 receptor on CD4+ T cells is protective against inflammatory responses and signs in a mouse model of rheumatoid arthritis. Arthritis Res Ther. 2023 May 26;25:87.
14. Contreras F, Prado C, González H, Franz D, Osorio-Barrios F, Osorio F, et al. Dopamine Receptor D3 Signaling on CD4+ T Cells Favors Th1- and Th17-Mediated Immunity. J Immunol. 2016 May 15;196:4143-9.
15. Solmaz V, Kaya M, Uslu FB, Atasoy O, Erbaş O. Papaverine Has Therapeutic Potential for Sepsis-Induced Neuropathy in Rats, Possibly via the Modulation of HMGB1-RAGE Axis and Its Antioxidant Prosperities. J Invest Surg. 2020 Aug 25;35:7-13.
16. Yin X, Chen S, Eisenbarth SC. Dendritic Cell Regulation of T Helper Cells. Annu Rev Immunol. 2021 Apr 26;39:759-90.
17. Nakagome K, Imamura M, Okada H, Kawahata K, Inoue T, Hashimoto K, et al. Dopamine D1-like receptor antagonist attenuates Th17-mediated immune response and ovalbumin antigen-induced neutrophilic airway inflammation. J Immunol. 2011 May 15;186:5975-82.
18. Nakano K, Higashi T, Takagi R, Hashimoto K, Tanaka Y, Matsushita S. Dopamine released by dendritic cells polarizes Th2 differentiation. Int Immunol. 2009 Jun;21:645-54.
19. Erbaş O, Ergenoglu AM, Akdemir A, Yeniel AÖ, Taskiran D. Comparison of melatonin and oxytocin in the prevention of critical illness polyneuropathy in rats with experimentally induced sepsis. J Surg Res. 2013 Jul;183:313-20.
20. Li N, Guo Y, Gong Y, Zhang Y, Fan W, Yao K, et al. The Anti-Inflammatory Actions and Mechanisms of Acupuncture from Acupoint to Target Organs via Neuro-Immune Regulation. J Inflamm Res. 2021 Dec 21;14:7191-224.
21. Matt SM, Gaskill PJ. Where Is Dopamine and how do Immune Cells See it?: Dopamine-Mediated Immune Cell Function in Health and Disease. J Neuroimmune Pharmacol. 2020 Mar;15:114-64.
22. Neumann J, Hofmann B, Dhein S, Gergs U. Role of Dopamine in the Heart in Health and Disease. Int J Mol Sci. 2023 Mar 6;24:5042.
23. Erbaş O, Akseki HS, Eliküçük B, Taşkıran D. Antipsychotic-like effect of trimetazidine in a rodent model. ScientificWorldJournal. 2013 Oct 22;2013:686304.
24. Liu L, Wu Y, Wang B, Jiang Y, Lin L, Li X, et al. DA-DRD5 signaling controls colitis by regulating colonic M1/M2 macrophage polarization. Cell Death Dis. 2021 May 17;12:500.
25. Liu C, Kaeser PS. Mechanisms and regulation of dopamine release. Curr Opin Neurobiol. 2019 Aug;57:46-53.
26. López-Enríquez S, Múnera-Rodríguez AM, Leiva-Castro C, Sobrino F, Palomares F. Modulation of the Immune Response to Allergies Using Alternative Functional Foods. Int J Mol Sci. 2023 Dec 29;25:467.
27. Wang W, Garcia C, Shao F, Cohen JA, Bai Y, Fine A, et al. Lung dopaminergic nerves facilitate the establishment of TH2 resident memory cells in early life. J Allergy Clin Immunol. 2023 Aug;152:386-99.
28. Bangs DJ, Pepper M. Dopamine primes TH2 cells in the lungs. J Allergy Clin Immunol. 2023 Aug;152:359-61.
29. Liu P, Qin D, Lv H, Fan W, Zhou F, Gao Z, et al. Activation of Dopamine D2 Receptor Alleviates Neuroinflammation in a Mouse Model of Allergic Rhinitis With Olfactory Dysfunction. Allergy Asthma Immunol Res. 2021 Nov;13:882-95.
30. Yildirim N, Simsek D, Kose S, Yildirim AGS, Guven C, Yigitturk G, et al. The protective effect of Gingko biloba in a rat model of ovarian ischemia/reperfusion injury: Improvement in histological and biochemical parameters. Adv Clin Exp Med. 2018 May;27:591-7.
31. Cabezas GA, Israili ZH, Velasco M. The actions of dopamine on the airways. Am J Ther. 2003 Nov-Dec;10:477-86.
32. Sakaguchi S, Yamaguchi T, Nomura T, Ono M. Regulatory T cells and immune tolerance. Cell. 2008 May 30;133:775-87.
33. Pacheco R, Contreras F, Zouali M. The dopaminergic system in autoimmune diseases. Front Immunol. 2014 Mar 21;5:117.
34. Levite M. Dopamine and T cells: dopamine receptors and potent effects on T cells, dopamine production in T cells, and abnormalities in the dopaminergic system in T cells

in autoimmune, neurological and psychiatric diseases. Acta Physiol (Oxf). 2016 Jan;216:42-89.

35. Furgiuele A, Pereira FC, Martini S, Marino F, Cosentino M. Dopaminergic regulation of inflammation and immunity in Parkinson's disease: friend or foe? Clin Transl Immunology. 2023 Sep 29;12:e1469.
36. Moore SC, Vaz de Castro PAS, Yaqub D, Jose PA, Armando I. Anti-Inflammatory Effects of Peripheral Dopamine. Int J Mol Sci. 2023 Sep 7;24:13816.
37. Xu H, Shi X, Li X, Zou J, Zhou C, Liu W, et al. Neurotransmitter and neuropeptide regulation of mast cell function: a systematic review. J Neuroinflammation. 2020 Nov 25;17:356.
38. Bora ES, Erdoğan MA, Özkul B, Sever İH, Söğüt İ, Hürdağ C, et al. Short term protective effect of digitoxin in sepsis-induced acute lung injury. 2021 Oct 46;433-39.