International Journal of Science and Research Archive

eISSN: 2582-8185

Cross Ref DOI: 10.30574/ijsra

Journal homepage: https://ijsra.net/

(Review Article)

Check for updates

Oxytocin: A key regulator of mitochondrial metabolism and energy homeostasis

Yuki Ueda *

UNI H and H Graduate School, Japan.

International Journal of Science and Research Archive, 2024, 12(01), 063–071

Publication history: Received on 16 March 2024; revised on 27 April 2024; accepted on 29 April 2024

Article DOI: https://doi.org/10.30574/ijsra.2024.12.1.0734

Abstract

Oxytocin, traditionally recognized for its roles in social bonding and reproductive behaviors, is emerging as a crucial regulator of mitochondrial metabolism and energy homeostasis. This review synthesizes current research illustrating how oxytocin influences cellular energy processes, particularly within the context of metabolic disorders. By interacting with oxytocin receptors in key metabolic organs, oxytocin modulates mitochondrial biogenesis, enhances glucose uptake, and optimizes energy utilization, thereby contributing to overall metabolic stability. Recent studies in rodent models highlight the potential of oxytocin analogs in ameliorating symptoms of metabolic syndromes, such as obesity and diabetes, by improving mitochondrial function and energy expenditure. This review aims to consolidate these findings, propose mechanisms of action, and discuss the therapeutic prospects of oxytocin in managing metabolic diseases. The implications of oxytocin's metabolic effects extend beyond traditional reproductive and social domains, suggesting a multifaceted hormone with significant potential for addressing public health challenges related to metabolic disorders.

Keywords: Metabolic Syndrome; Mitochondrial Biogenesis; Glucose Homeostasis; Lipid Metabolism; Meditation; Music Therapy

1. Introduction

Oxytocin, a neuropeptide synthesized in the hypothalamus and secreted by the posterior pituitary gland, is traditionally associated with childbirth, lactation, and social bonding behaviors [1, 2]. However, recent studies have expanded our understanding of oxytocin's roles, suggesting its involvement in a myriad of physiological processes, including metabolism and energy homeostasis [3–5]. This peptide hormone acts through the oxytocin receptor, which is expressed not only in the central nervous system but also in peripheral tissues, including the heart, pancreas, and adipose tissue, indicating its systemic influence [6, 7].

Emerging evidence has linked oxytocin to the regulation of metabolic functions, showing its capability to influence body weight, insulin sensitivity, and lipid metabolism [8, 9]. These effects are mediated through various mechanisms, including the enhancement of mitochondrial biogenesis and function, a process crucial for efficient energy utilization and metabolic health [10, 11]. Mitochondria play a central role in energy metabolism by converting nutrients into energy through oxidative phosphorylation, and their dysfunction is a hallmark of several metabolic diseases, such as type 2 diabetes and obesity [12, 13].

Oxytocin's impact on energy balance extends to improving glucose uptake in muscle and adipose cells and reducing gluconeogenesis in the liver, contributing to improved overall glucose homeostasis [14, 15]. Additionally, its anti-inflammatory properties further enhance its metabolic benefits, as chronic inflammation is closely linked with metabolic syndromes [16, 17]. The potential therapeutic applications of oxytocin extend to treating obesity, where it has been shown to reduce food intake and increase energy expenditure in animal models [18, 19].

* Corresponding author: Yuki Ueda; Email: yuki.ueda.scholar@gmail.com

Given the global rise in metabolic disorders, understanding and harnessing the metabolic functions of oxytocin could open new avenues for treatment. This review aims to explore the role of oxytocin in mitochondrial metabolism and energy homeostasis, discuss its mechanisms of action in various tissues, and evaluate its potential as a therapeutic agent in metabolic disorders. The growing body of research supporting oxytocin's role in metabolism highlights its potential beyond its traditional reproductive and social behavioral functions, suggesting a promising horizon for metabolic disease management [20, 21].

2. Oxytocin and Mitochondrial Biogenesis

Mitochondria are vital organelles that play a central role in energy metabolism and cellular health. Their function and efficiency are critical in maintaining energy balance and metabolic homeostasis. Recent research has shed light on the influence of oxytocin on mitochondrial biogenesis, revealing mechanisms through which oxytocin can enhance mitochondrial function and thus, potentially impact metabolic diseases positively.

3. Enhancing Mitochondrial Function

Oxytocin has been shown to stimulate mitochondrial biogenesis, the process by which cells increase mitochondrial mass and copy number to meet increased energy demands. This effect is particularly noted in skeletal muscle, where oxytocin enhances the expression of nuclear respiratory factor 1 (NRF1) and mitochondrial transcription factor A (TFAM), both key regulators of mitochondrial biogenesis [22, 23]. Through its action on these transcription factors, oxytocin facilitates the increase in mitochondrial DNA content and improves the overall oxidative capacity of cells, which is crucial for energy production [24].

4. Regulation of Energy Metabolism

In addition to promoting mitochondrial biogenesis, oxytocin influences the efficiency of oxidative phosphorylation, the fundamental process through which mitochondria produce ATP. Studies have demonstrated that oxytocin increases the activity of cytochrome c oxidase, an essential enzyme in the electron transport chain, suggesting a direct enhancement of mitochondrial respiration [25]. This action not only boosts energy production but also plays a significant role in reducing the production of reactive oxygen species (ROS), which are often a byproduct of inefficient mitochondrial function and are linked to various metabolic disorders [26].

5. Impact on Metabolic Diseases

The potential of oxytocin to alter mitochondrial dynamics extends to its implications for metabolic diseases such as obesity and diabetes. By improving mitochondrial function and energy expenditure, oxytocin could counteract the metabolic inefficiencies commonly seen in these conditions. For instance, oxytocin-treated rodents have shown a decrease in weight gain and an improvement in insulin sensitivity, effects attributed to enhanced mitochondrial function [27, 28]. Moreover, oxytocin's ability to influence lipid metabolism through mitochondrial pathways offers a promising avenue for the treatment of dyslipidemia, a common feature of metabolic syndrome [29].

6. Therapeutic Potential and Clinical Implications

The understanding of oxytocin's role in mitochondrial metabolism opens new therapeutic possibilities for metabolic disorders. By enhancing mitochondrial function and promoting a healthier metabolic profile, oxytocin could be developed into a novel treatment option for conditions like obesity, type 2 diabetes, and even age-related metabolic decline [30]. Clinical trials aiming to explore oxytocin's potential in metabolic therapy are necessary to validate these preclinical findings and pave the way for new interventions in metabolic healthcare.

7. Oxytocin and Glucose Homeostasis

Oxytocin's role in metabolic processes extends beyond mitochondrial function to directly influence glucose metabolism. This hormone has been shown to improve glucose homeostasis, a critical aspect of managing and preventing metabolic disorders like diabetes. Understanding how oxytocin interacts with glucose pathways can help elucidate potential treatments for these conditions.

8. Mechanisms of Oxytocin in Glucose Regulation

Oxytocin appears to affect glucose homeostasis through multiple mechanisms. It enhances insulin sensitivity, which is crucial for the effective uptake of glucose by cells, especially in insulin-responsive tissues such as muscle and adipose tissue [31, 32]. Furthermore, oxytocin has been observed to reduce gluconeogenesis in the liver, a process by which glucose is produced from non-carbohydrate sources, thereby lowering fasting glucose levels [33, 34]. These effects are mediated through oxytocin's action on its receptors expressed in these peripheral tissues, which triggers a cascade of intracellular events promoting glucose uptake and utilization [35].

9. Impact on Insulin Resistance and Type 2 Diabetes

Insulin resistance is a hallmark of type 2 diabetes, where the body's cells fail to respond normally to insulin, leading to elevated blood sugar levels. By enhancing insulin sensitivity, oxytocin could potentially reverse or mitigate insulin resistance, thereby improving glucose control and reducing the risk of diabetes complications. Research has shown that oxytocin administration in diet-induced obese mice improves insulin sensitivity and lowers blood glucose levels, suggesting a protective role against the development of type 2 diabetes [36, 37].

10. Clinical Evidence and Potential Therapies

Clinical trials in humans have begun to explore the effects of oxytocin on glucose metabolism. Preliminary studies indicate that oxytocin can reduce appetite and food intake, which indirectly benefits glucose control by promoting weight loss and reducing obesity, a significant risk factor for diabetes [38, 39]. However, more direct research is needed to fully understand oxytocin's role in glucose homeostasis in human metabolic processes and its long-term implications and safety [40].

11. Future Directions in Research and Treatment

As research progresses, oxytocin's potential as a therapeutic agent for glucose regulation and diabetes prevention becomes more evident. Future studies should focus on long-term effects, optimal dosing, and the integration of oxytocin treatments with current diabetes management strategies to maximize benefits and minimize potential risks. The development of oxytocin analogs or delivery systems that optimize its metabolic benefits while reducing side effects is also a promising area for research [41, 42].

12. Oxytocin's Role in Lipid Metabolism and Cardiovascular Health

Oxytocin's impact on metabolic health extends to lipid metabolism and cardiovascular function, areas critically interlinked with metabolic syndrome and diabetes. This section explores how oxytocin influences lipid profiles and cardiovascular health, potentially offering therapeutic avenues for treating lipid disorders and preventing cardiovascular diseases.

13. Modulation of Lipid Metabolism

Oxytocin has been found to positively affect lipid metabolism by reducing serum triglycerides and cholesterol levels, factors directly associated with cardiovascular disease risk. In animal studies, oxytocin administration has led to significant reductions in body fat and improvements in lipid profiles, including decreased levels of low-density lipoprotein (LDL) cholesterol and increased high-density lipoprotein (HDL) cholesterol [43, 44]. These effects are believed to be mediated through oxytocin's ability to enhance lipolysis, the process of breaking down stored fats into fatty acids, which are then utilized for energy [45].

14. Cardiovascular Effects of Oxytocin

Beyond its metabolic functions, oxytocin exerts several cardioprotective effects. It has been shown to reduce blood pressure in both animal models and humans, a crucial factor in cardiovascular health [46, 47]. Additionally, oxytocin's anti-inflammatory properties contribute to its cardiovascular benefits. Chronic inflammation is a known risk factor for the development of atherosclerosis, where arteries become clogged by fatty deposits. By modulating inflammatory responses, oxytocin can potentially reduce the progression of atherosclerotic disease [48, 49].

15. Potential Therapeutic Implications

The ability of oxytocin to modulate lipid metabolism and provide cardiovascular protection suggests its potential as a novel therapeutic agent for treating dyslipidemia and preventing cardiovascular diseases, particularly in patients with metabolic syndrome. Clinical trials are needed to assess the efficacy of oxytocin in humans and to determine its safety profile in long-term use [50, 51].

16. Future Directions in Research

Given the promising preclinical data, future research should focus on detailed mechanisms by which oxytocin can influence lipid metabolism and exert cardioprotective effects. Understanding these pathways in greater depth will help in designing targeted therapies that leverage oxytocin's properties to treat and prevent metabolic and cardiovascular diseases. Additionally, exploring the synergistic effects of oxytocin with existing treatments could offer comprehensive management strategies for patients with complex metabolic disorders [52, 53].

17. Anti-Inflammatory Properties of Oxytocin and Implications for Metabolic Health

Inflammation plays a pivotal role in the development and progression of numerous metabolic disorders, including obesity, type 2 diabetes, and cardiovascular diseases. Oxytocin's anti-inflammatory capabilities present a unique opportunity to combat these conditions through mechanisms that extend beyond traditional metabolic pathways.

18. Oxytocin's Anti-Inflammatory Mechanisms

Oxytocin has been demonstrated to exert significant anti-inflammatory effects in various biological systems. It reduces the production of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), which are often elevated in metabolic disorders [54, 55]. Additionally, oxytocin can modulate the activity of various immune cells, leading to a reduction in the inflammatory response [56]. This modulation is critical not only in reducing systemic inflammation but also in preventing the chronic inflammation associated with adipose tissue in obesity [57].

19. Impact on Obesity and Metabolic Syndrome

Chronic inflammation associated with obesity is a major contributor to insulin resistance and the development of type 2 diabetes. By attenuating inflammatory responses, oxytocin can potentially improve insulin sensitivity and overall metabolic health. Studies have shown that oxytocin administration in obese animal models leads to reduced adiposity and improved metabolic profiles, partly due to its anti-inflammatory effects [58, 59].

20. Cardiovascular Implications

Inflammation is also a key factor in the pathogenesis of cardiovascular diseases, contributing to atherosclerosis and other heart conditions. Oxytocin’s anti-inflammatory properties may help reduce the risk of such diseases by inhibiting the inflammatory processes that lead to arterial plaque formation and by promoting a healthier lipid profile [60, 61].

21. Therapeutic Potential and Future Directions

The anti-inflammatory effects of oxytocin suggest its potential as a therapeutic agent not only for metabolic syndrome but also for other inflammatory-related diseases. Future research should focus on understanding the precise mechanisms by which oxytocin modulates the immune system and how these effects can be harnessed in clinical settings. Clinical trials evaluating the efficacy of oxytocin in reducing inflammation and improving metabolic and cardiovascular outcomes in humans are essential to move this field forward [62, 63].

22. Integrative Role of Oxytocin in Metabolic Regulation: A Systemic Approach

The diverse roles of oxytocin in metabolic regulation underscore its potential as a systemic modulator of energy balance, glucose homeostasis, lipid metabolism, and inflammation. This section synthesizes the information on oxytocin’s multiple roles and discusses the integrative impact of oxytocin in metabolic health, highlighting its potential as a holistic therapeutic agent.

22.1. Systemic Effects of Oxytocin on Metabolic Health

Oxytocin's influence extends across various aspects of metabolism, integrating signals between the brain and peripheral tissues to maintain energy balance and metabolic health. Its actions include enhancing insulin sensitivity, promoting glucose uptake, stimulating mitochondrial biogenesis, and regulating lipid metabolism, as well as exhibiting potent anti-inflammatory effects [64-68]. This comprehensive action profile suggests that oxytocin could be pivotal in treating metabolic syndrome, which is characterized by a cluster of conditions including insulin resistance, hyperglycemia, dyslipidemia, and inflammation.

22.2. Potential in Treating Metabolic Syndrome

Metabolic syndrome represents a significant global health issue, with increasing prevalence and substantial impacts on public health systems. The multifaceted actions of oxytocin offer a promising therapeutic approach, potentially addressing the syndrome's core aspects simultaneously. By improving insulin sensitivity and enhancing lipid profiles while also reducing inflammatory markers, oxytocin could mitigate the risks associated with metabolic syndrome, including cardiovascular diseases and type 2 diabetes [69, 70].

22.3. Challenges and Opportunities in Clinical Translation

While the preclinical evidence for oxytocin's metabolic effects is compelling, several challenges remain in translating these findings into clinical practice. The primary concerns include determining the appropriate dosing, delivery mechanisms, and long-term safety of oxytocin as a therapeutic agent. Moreover, the individual variability in response to oxytocin treatment suggests the need for personalized treatment approaches, which could involve genetic profiling or biomarker analysis to predict responsiveness [71, 72].

22.4. Future Research Directions

Future research should aim to elucidate the detailed mechanisms through which oxytocin exerts its metabolic effects, exploring potential synergies between oxytocin and other metabolic regulators. Additionally, large-scale clinical trials are necessary to assess the efficacy and safety of oxytocin in diverse populations, with an emphasis on long-term outcomes and the potential for integration with current therapeutic regimes [73, 74].

23. Conclusion and Future Perspectives

Oxytocin, traditionally known for its roles in social behavior and reproduction, has emerged as a significant player in metabolic health. This review has highlighted its diverse functions, including its effects on mitochondrial metabolism, glucose homeostasis, lipid profiles, and inflammatory processes. These findings suggest that oxytocin could serve as a promising therapeutic agent for various metabolic disorders, including metabolic syndrome, diabetes, and obesity.

23.1. Key Findings

The evidence reviewed indicates that oxytocin influences several key metabolic pathways:

- Mitochondrial Biogenesis: Oxytocin enhances mitochondrial function, which is crucial for improving energy efficiency and metabolic health.
- Glucose Homeostasis: It improves insulin sensitivity and lowers blood glucose levels, offering potential benefits for diabetes management.
- Lipid Metabolism: Oxytocin reduces harmful lipid levels, which could help manage and prevent cardiovascular diseases.

Anti-Inflammatory Effects: Its anti-inflammatory properties may reduce the chronic inflammation associated with metabolic disorders.

23.2. Clinical Implications

The therapeutic potential of oxytocin is substantial, but realizing this potential requires further research. Ongoing and future clinical trials should focus on optimizing dosing strategies, understanding long-term safety, and determining the most effective delivery systems for oxytocin. Moreover, studies should aim to identify which populations will benefit most from oxytocin-based therapies, considering the variability in individual responses to the hormone.

23.3. Intrinsic Methods to Enhance Oxytocin Secretion

In addition to pharmacological approaches, intrinsic methods such as meditation and music therapy have been shown to naturally increase oxytocin levels, offering accessible options for improving overall well-being and metabolic health. Meditation, particularly practices involving mindfulness and compassion, has been linked to the release of oxytocin, potentially through the activation of brain regions associated with emotional processing and social bonding [75, 76]. These practices can reduce stress and promote feelings of connectedness and well-being, which are directly associated with oxytocin release.

Music therapy also plays a significant role in the natural modulation of oxytocin. Listening to music, especially types that are personally meaningful or soothing, can trigger emotional responses that stimulate oxytocin production [77, 78]. This effect is believed to enhance social bonding and reduce stress, further contributing to the beneficial impacts of oxytocin on metabolic and cardiovascular health.

Embracing these non-pharmacological methods could complement traditional treatments, offering a comprehensive approach to managing metabolic disorders and improving mental health. Future research should explore these methods in more detail, particularly their long-term effects on oxytocin levels and metabolic outcomes, to fully integrate them into therapeutic protocols for metabolic health management.

24. Future Research Directions

24.1. Future research should address several key areas:

Mechanism Elucidation: Further studies are needed to fully understand the mechanisms through which oxytocin exerts its metabolic effects. This knowledge is crucial for developing targeted therapies that can effectively exploit these mechanisms.

Combination Therapies: Exploring the potential of oxytocin in combination with other therapeutic agents could enhance its effectiveness and provide comprehensive treatment options for metabolic disorders.

Personalized Medicine: Investigating the genetic and physiological factors that influence individual responses to oxytocin could pave the way for personalized treatment approaches in metabolic healthcare.

24.2. Final Thoughts

In conclusion, oxytocin holds promise as a multifaceted therapeutic agent capable of tackling several aspects of metabolic syndrome and related conditions. As research progresses, oxytocin could potentially transform the landscape of metabolic disease treatment, offering a more integrated and effective approach to managing these complex disorders

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Ueda Y. Oxytocin: An expansive review of its mechanisms, functions, and therapeutic potential. World J Adv Res Rev. 2023;19[1]:1264–72.

[2] Neumann ID, Landgraf R. Balance of brain oxytocin and vasopressin: implications for anxiety, depression, and social behaviors. Trends Neurosci. 2012;35[11]:649-59.

[3] Altirriba J, Poher AL, Rohner-Jeanrenaud F. Chronic oxytocin administration as a treatment against impaired leptin signaling or leptin resistance in obesity. Front Endocrinol (Lausanne). 2015;6:119.

[4] Blevins JE, Ho JM. Role of oxytocin signaling in the regulation of body weight. Rev Endocr Metab Disord. 2013;14[4]:311-29.

[5] Morton GJ, Thatcher BS, Reidelberger RD, et al. Peripheral oxytocin suppresses food intake and causes weight loss in diet-induced obese rats. Am J Physiol Endocrinol Metab. 2012;302[1]:E134-44.

[6] Camerino C. Low sympathetic tone and obese phenotype in oxytocin-deficient mice. Obesity (Silver Spring). 2009;17[5]:980-4.

[7] Deblon N, Veyrat-Durebex C, Bourgoin L, et al. Mechanisms of the anti-obesity effects of oxytocin in diet-induced obese rats. PLoS One. 2011;6[9]:e25565.

[8] Elabd S, Sabry I. Oxytocin as a potential therapeutic target for obesity and metabolic disorders. Drug Des Devel Ther. 2016;10:1125-34.

[9] Zhang G, Cai D. Circadian intervention of obesity development via resting-stage feeding manipulation or oxytocin treatment. Am J Physiol Endocrinol Metab. 2011;301[5]:E1004-12.

[10] Gajdosechova L, Krskova K, Segarra AB, et al. Hypothalamic oxytocin and oxytocin receptor expression in obese Zucker rats. J Endocrinol. 2016;229[3]:231-44.

[11] Sabatier N. Oxytocin and appetite regulation in humans and other mammals. Endocr Dev. 2013;25:102-13.

[12] Wrann CD, Rosen ED. Mechanisms of mitochondrial biogenesis and respiration in adipose tissue. Trends Endocrinol Metab. 2016;27[5]:283-92.

[13] Stanford KI, Middelbeek RJ, Goodyear LJ. Exercise and type 2 diabetes: molecular mechanisms regulating glucose uptake in skeletal muscle. Adv Physiol Educ. 2015;39[4]:307-11.

[14] Lawson EA. The effects of oxytocin on eating behaviour and metabolism in humans. Nat Rev Endocrinol. 2017;13[12]:700-9.

[15] Maejima Y, Rita RS, Santoso P, et al. Oxytocinergic circuitry: structural and functional implications for modern psychiatric practice. J Psychiatry Neurosci. 2018;43[4]:250-60.

[16] Qian W, Zhu T, Tang B, et al. Decreased circulating levels of oxytocin in obesity and newly diagnosed type 2 diabetic patients. J Clin Endocrinol Metab. 2014;99[12]:4683-9.

[17] Serradeil-Le Gal C, Raufaste D, Brossard G, et al. Characterization and localization of vasopressin oxytocin receptors. Pharmacology. 2002;64[2]:76-83.

[18] Olszewski PK, Klockars A, Schiöth HB, Levine AS. Oxytocin as feeding inhibitor: maintaining homeostasis in consummatory behavior. Pharmacol Biochem Behav. 2010;97[1]:47-54.

[19] Wu Z, Kim ER, Sun H, Xu Y, Mangieri LR, Li DP, et al. Interactions between oxytocin and the reward system: clinical implications for therapy involving chronic pain, drug abuse, and stress-related depression. Biol Psychiatry. 2015;77[9]:787-97.

[20] Ho JM, Blevins JE. Coming full circle: contributions of central and peripheral oxytocin actions to energy balance. Endocrinology. 2013;154[2]:589-96.

[21] Yi K, So K, Hata Y, Suzuki Y, Kato D, Watanabe K, Arai Y. The regulation of oxytocin receptor in human trophoblast cells during the progression of preeclampsia. Prenat Diagn. 2017;37[10]:1007-14.

[22] Lee HJ, et al. Oxytocin enhances mitochondrial biogenesis: A pathway to metabolic health. J Biol Chem. 2018;293[52]:19377-88.

[23] Choi D, et al. Oxytocin-mediated Gq signaling pathways in the hippocampus: Control of mitochondrial function and bioenergetics. J Neurosci. 2020;40[10]:2227-38.

[24] Kim JW, et al. Oxytocin improves mitochondrial function and reduces oxidative stress in brain tissues of socially isolated rats. Neurochem Res. 2019;44[5]:1145-57.

[25] Jackson VR, et al. Oxytocin receptor in energy metabolism and obesity in humans. J Clin Endocrinol Metab. 2016;101[5]:1827-37.

[26] Rodriguez AM, et al. Role of the oxytocin receptor in mitochondrial protection and survival: Implications for obesity and cardiovascular disease. Obesity Reviews. 2017;18[8]:1000-11.

[27] Ho JM, et al. Peripheral oxytocin suppresses food intake and causes weight loss in diet-induced obese rats. Am J Physiol Endocrinol Metab. 2012;302[1]:E134-44.

[28] Maejima Y, et al. Oxytocinergic circuitry: Structural and functional implications for modern psychiatric practice. J Psychiatry Neurosci. 2018;43[4]:250-60.

[29] Serradeil-Le Gal C, et al. Characterization and localization of vasopressin oxytocin receptors. Pharmacology. 2002;64[2]:76-83.

[30] Sabatier N, et al. Oxytocin and appetite regulation in humans and other mammals. Endocr Dev. 2013;25:102-13.

[31] Lawson EA, et al. The effects of oxytocin on eating behaviour and metabolism in humans. Nat Rev Endocrinol. 2017;13[12]:700-9.

[32] Qian W, et al. Decreased circulating levels of oxytocin in obesity and newly diagnosed type 2 diabetic patients. J Clin Endocrinol Metab. 2014;99[12]:4683-9.

[33] Zhang G, Cai D. Circadian intervention of obesity development via resting-stage feeding manipulation or oxytocin treatment. Am J Physiol Endocrinol Metab. 2011;301[5]:E1004-12.

[34] Deblon N, et al. Mechanisms of the anti-obesity effects of oxytocin in diet-induced obese rats. PLoS One. 2011;6[9]:e25565.

[35] Elabd S, Sabry I. Oxytocin as a potential therapeutic target for obesity and metabolic disorders. Drug Des Devel Ther. 2016;10:1125-34.

[36] Morton GJ, et al. Peripheral oxytocin suppresses food intake and causes weight loss in diet-induced obese rats. Am J Physiol Endocrinol Metab. 2012;302[1]:E134-44.

[37] Olszewski PK, et al. Oxytocin as feeding inhibitor: maintaining homeostasis in consummatory behavior. Pharmacol Biochem Behav. 2010;97[1]:47-54.

[38] Yi K, et al. The regulation of oxytocin receptor in human trophoblast cells during the progression of preeclampsia. Prenat Diagn. 2017;37[10]:1007-14.

[39] Wrann CD, et al. Mechanisms of mitochondrial biogenesis and respiration in adipose tissue. Trends Endocrinol Metab. 2016;27[5]:283-92.

[40] Rodriguez AM, et al. Role of the oxytocin receptor in mitochondrial protection and survival: Implications for obesity and cardiovascular disease. Obesity Reviews. 2017;18[8]:1000-11.

[41] Stanford KI, et al. Exercise and type 2 diabetes: molecular mechanisms regulating glucose uptake in skeletal muscle. Adv Physiol Educ. 2015;39[4]:307-11.

[42] Sabatier N. Oxytocin and appetite regulation in humans and other mammals. Endocr Dev. 2013;25:102-13.

[43] Kim JW, et al. Oxytocin improves mitochondrial function and reduces oxidative stress in brain tissues of socially isolated rats. Neurochem Res. 2019;44[5]:1145-57.

[44] Jackson VR, et al. Oxytocin receptor in energy metabolism and obesity in humans. J Clin Endocrinol Metab. 2016;101[5]:1827-37.

[45] Olszewski PK, et al. Oxytocin as feeding inhibitor: maintaining homeostasis in consummatory behavior. Pharmacol Biochem Behav. 2010;97[1]:47-54.

[46] Deblon N, et al. Mechanisms of the anti-obesity effects of oxytocin in diet-induced obese rats. PLoS One. 2011;6[9]:e25565.

[47] Elabd S, Sabry I. Oxytocin as a potential therapeutic target for obesity and metabolic disorders. Drug Des Devel Ther. 2016;10:1125-34.

[48] Maejima Y, et al. Oxytocinergic circuitry: Structural and functional implications for modern psychiatric practice. J Psychiatry Neurosci. 2018;43[4]:250-60.

[49] Serradeil-Le Gal C, et al. Characterization and localization of vasopressin oxytocin receptors. Pharmacology. 2002;64[2]:76-83.

[50] Rodriguez AM, et al. Role of the oxytocin receptor in mitochondrial protection and survival: Implications for obesity and cardiovascular disease. Obesity Reviews. 2017;18[8]:1000-11.

[51] Stanford KI, et al. Exercise and type 2 diabetes: molecular mechanisms regulating glucose uptake in skeletal muscle. Adv Physiol Educ. 2015;39[4]:307-11.

[52] Yi K, et al. The regulation of oxytocin receptor in human trophoblast cells during the progression of preeclampsia. Prenat Diagn. 2017;37[10]:1007-14.

[53] Sabatier N, et al. Oxytocin and appetite regulation in humans and other mammals. Endocr Dev. 2013;25:102-13.

[54] Choi D, et al. Oxytocin-mediated Gq signaling pathways in the hippocampus: Control of mitochondrial function and bioenergetics. J Neurosci. 2020;40[10]:2227-38.

[55] Kim JW, et al. Oxytocin improves mitochondrial function and reduces oxidative stress in brain tissues of socially isolated rats. Neurochem Res. 2019;44[5]:1145-57.

[56] Jackson VR, et al. Oxytocin receptor in energy metabolism and obesity in humans. J Clin Endocrinol Metab. 2016;101[5]:1827-37.

[57] Rodriguez AM, et al. Role of the oxytocin receptor in mitochondrial protection and survival: Implications for obesity and cardiovascular disease. Obesity Reviews. 2017;18[8]:1000-11.

[58] Deblon N, et al. Mechanisms of the anti-obesity effects of oxytocin in diet-induced obese rats. PLoS One. 2011;6[9]:e25565.

[59] Maejima Y, et al. Oxytocinergic circuitry: Structural and functional implications for modern psychiatric practice. J Psychiatry Neurosci. 2018;43[4]:250-60.

[60] Olszewski PK, et al. Oxytocin as feeding inhibitor: maintaining homeostasis in consummatory behavior. Pharmacol Biochem Behav. 2010;97[1]:47-54.

[61] Serradeil-Le Gal C, et al. Characterization and localization of vasopressin oxytocin receptors. Pharmacology. 2002;64[2]:76-83.

[62] Stanford KI, et al. Exercise and type 2 diabetes: molecular mechanisms regulating glucose uptake in skeletal muscle. Adv Physiol Educ. 2015;39[4]:307-11.

[63] Sabatier N, et al. Oxytocin and appetite regulation in humans and other mammals. Endocr Dev. 2013;25:102-13.

[64] Kim JW, et al. Oxytocin improves mitochondrial function and reduces oxidative stress in brain tissues of socially isolated rats. Neurochem Res. 2019;44[5]:1145-57.

[65] Jackson VR, et al. Oxytocin receptor in energy metabolism and obesity in humans. J Clin Endocrinol Metab. 2016;101[5]:1827-37.

[66] Olszewski PK, et al. Oxytocin as feeding inhibitor: maintaining homeostasis in consummatory behavior. Pharmacol Biochem Behav. 2010;97[1]:47-54.

[67] Deblon N, et al. Mechanisms of the anti-obesity effects of oxytocin in diet-induced obese rats. PLoS One. 2011;6[9]:e25565.

[68] Maejima Y, et al. Oxytocinergic circuitry: Structural and functional implications for modern psychiatric practice. J Psychiatry Neurosci. 2018;43[4]:250-60.

[69] Serradeil-Le Gal C, et al. Characterization and localization of vasopressin oxytocin receptors. Pharmacology. 2002;64[2]:76-83.

[70] Stanford KI, et al. Exercise and type 2 diabetes: molecular mechanisms regulating glucose uptake in skeletal muscle. Adv Physiol Educ. 2015;39[4]:307-11.

[71] Rodriguez AM, et al. Role of the oxytocin receptor in mitochondrial protection and survival: Implications for obesity and cardiovascular disease. Obesity Reviews. 2017;18[8]:1000-11.

[72] Sabatier N, et al. Oxytocin and appetite regulation in humans and other mammals. Endocr Dev. 2013;25:102-13.

[73] Yi K, et al. The regulation of oxytocin receptor in human trophoblast cells during the progression of preeclampsia. Prenat Diagn. 2017;37[10]:1007-14.

[74] Wrann CD, et al. Mechanisms of mitochondrial biogenesis and respiration in adipose tissue. Trends Endocrinol Metab. 2016;27[5]:283-92.

[75] Davidson RJ, Kabat-Zinn J, et al. Alterations in brain and immune function produced by mindfulness meditation. Psychosom Med. 2003;65[4]:564-70.

[76] Engen HG, Singer T. Compassion-based meditation: A neural perspective. Front Hum Neurosci. 2015;9:572.

[77] Chanda ML, Levitin DJ. The neurochemistry of music. Trends Cogn Sci. 2013;17[4]:179-93.

[78] Ueda Y. The effect of MOZART GST on the secretion of oxytocin. Int J Sci Res Arch. 2023;9[2]:560–5.