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Botulinum toxin as an innovative treatment for depression and anxiety disorders: a review of clinical evidence and mechanisms of action

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ABSTRACT

MDD is currently the leading cause of disability worldwide, affecting approximately 5% of the general population. A great clinical problem is that nearly one-third of patients do not improve despite standard pharmacotherapy and psychotherapy, which we call treatment-resistant depression. This circumstance requires the search for new, unconventional therapeutic approaches, such as BoNT-A. This study intends to investigate the mechanisms of action of BoNT-A and to evaluate its value and success in the treatment of depression and other affective disorders. This paper reviews current clinical evidence and scientific research on the use of BoNT-A in psychiatry and neurology. The analysis includes both clinical studies involving humans and animal model studies explaining the neurobiological basis of the toxin's effects. The present paper searched the literature on electronic databases, including PubMed, using the keywords: "BoNT-A"; "MDD"; "Anxiety disorders"; "NMDA receptors". The effects of BoNT-A are wide and not limited only to muscle relaxation. The most important mechanism is the Facial Feedback Hypothesis - a paralysis of the "sadness muscles" that interrupts the transmission of negative proprioceptive signals to the amygdala and improves mood. At the molecular level, the toxin modulates NMDA receptors, increases BDNF expression, and affects monoaminergic systems. Clinical evidence confirms a significant reduction in depressive and anxiety symptoms. BoNT-A may help treat affective disorders. It may affect brain areas involved in emotions. Current studies show promising results, but more research is needed to understand how it works and whether it is effective in the long term.

Keywords: BoNT-A, MDD, Anxiety disorders, Facial Feedback Hypothesis, NMDA receptors

1. INTRODUCTION

Chronic lifestyle diseases represent one of the greatest challenges to modern public health. Among them, major depressive disorder (MDD) is recognized as the leading cause of disability worldwide (Gambini et al., 2025; Rodríguez-Cerdeira and

Eckhardt, 2024; Wollmer et al., 2022, 2012; Zhang et al., 2021). It is estimated that between 264 and 280 million people globally currently suffer from depression, affecting about 5% of the general population (Ceolato-Martin et al., 2024; Makunts et al., 2020; Rodríguez-Cerdeira and Eckhardt, 2024; Wollmer et al., 2022). Statistics indicate clear gender differences, as women are nearly twice as likely to develop the condition as men (Ceolato-Martin et al., 2024; Gambini et al., 2025; Wabbels and Liebertz, 2025). Depression rarely occurs in isolation, and we know that it increases the risk of developing other serious chronic lifestyle diseases. These include heart disease, stroke, diabetes, asthma, and chronic pain syndromes (Gambini et al., 2025).

A serious clinical problem remains the fact that despite the use of established treatment methods, such as psychotherapy or pharmacotherapy (primarily SSRI and SNRI medications), approximately one-third of patients show no improvement. This is defined as treatment-resistant depression (Ceolato-Martin et al., 2024; Gambini et al., 2025; Makunts et al., 2020; Rodríguez-Cerdeira and Eckhardt, 2024; Zhang et al., 2021). This therapeutic gap compels modern medicine to seek new, unconventional treatment pathways that take into account, among other things, the regulatory feedback between the body and the mind (Gambini et al., 2025; Rodríguez-Cerdeira and Eckhardt, 2024; Wollmer et al., 2022). Botulinum toxin type A (BoNT-A) is the most commonly used type of botulinum toxin in medicine. It is widely known as Botox. Several strains of the anaerobic bacterium Clostridium botulinum produce the toxin (Dhengare et al., 2022; Gambini et al., 2025; Milev, 2015; Rodríguez-Cerdeira and Eckhardt, 2024). Although it is highly toxic and can be fatal in large doses, botulinum toxin is used in medicine to cause temporary muscle paralysis (Dhengare et al., 2022; Milev, 2015).

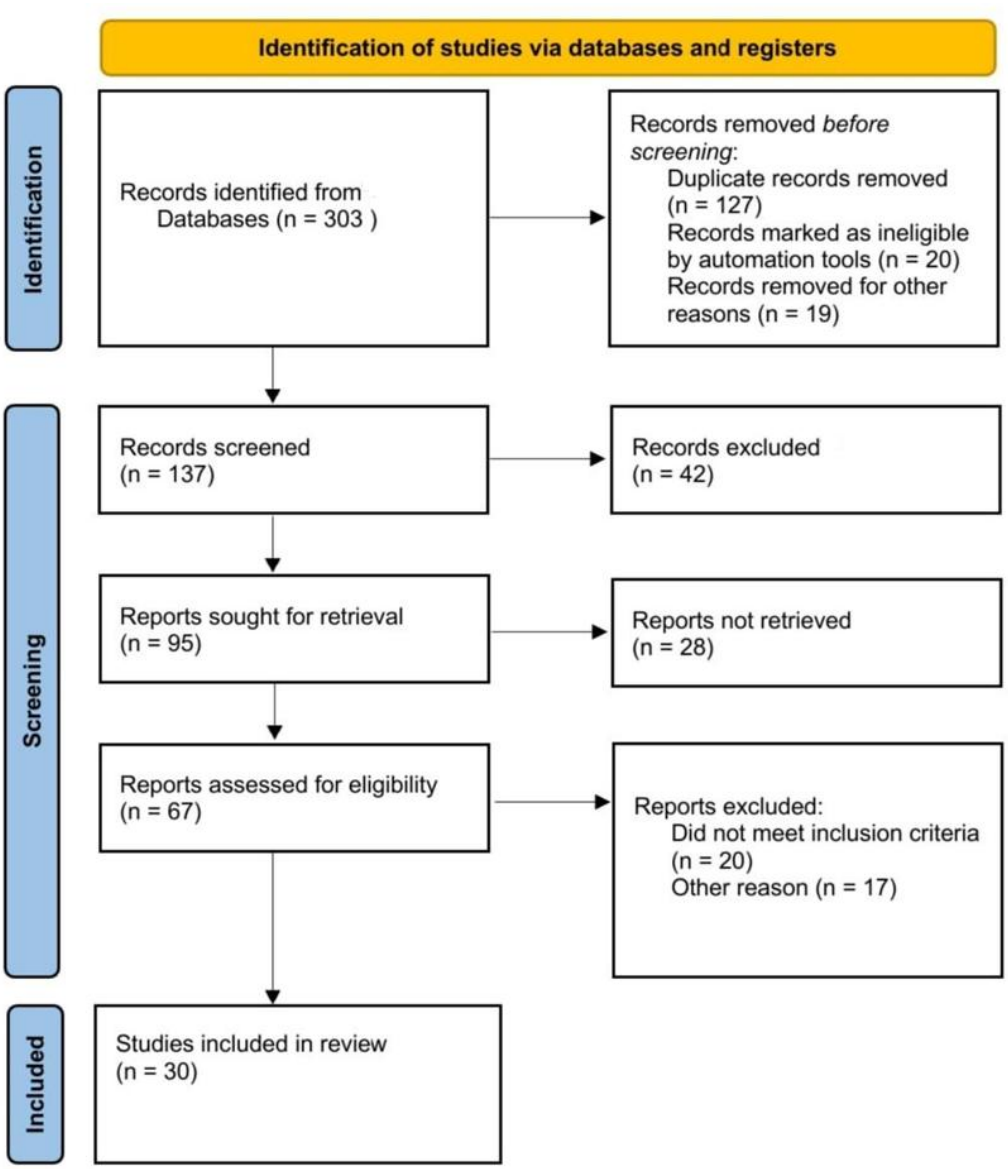

Figure 1. PRISMA 2020 flow diagram of study selection.

2. REVIEW METHODS

The literature reviewed in this paper was identified through searches of the PubMed, Scopus, and Google Scholar databases. Keywords used in the search included: "botulinum toxin type A"; 'major depressive disorder"; "anxiety disorders"; "Facial Feedback Hypothesis"; "NMDA receptors." Only peer-reviewed studies on the mechanisms of action and clinical use of BoNT-A in depression and anxiety disorders were included. Clinical and experimental studies, as well as systematic reviews and meta-analyses, were considered if they reported the antidepressant or anxiolytic effects of BoNT-A. Articles focused only on cosmetic use, conference abstracts, editorials, letters to the editor, and non-peer-reviewed publications were excluded. The included studies were reviewed qualitatively. Particular attention was given to the proposed mechanisms underlying the central effects of BoNT-A, including the facial feedback hypothesis, modulation of limbic system activity, retrograde transport, changes within neurotransmitter signaling, neuroplasticity, and anti-inflammatory effects, as well as to clinical findings in patients with depression and anxiety disorders. In total, 30 publications met the inclusion criteria and were included in the review (Figure 1).

3. RESULTS AND DISCUSSION

Mechanism of Action of Botulinum Toxin Type A

Neuromuscular mechanism

The basic mechanism of action of botulinum toxin, particularly the most commonly studied type A toxin, is to block communication between nerves and muscles and to modulate signals sent to the brain (Gambini et al., 2025; Rodríguez-Cerdeira and Eckhardt, 2024; Wollmer et al., 2022). Its main action is to block the release of acetylcholine from nerve endings into the synaptic cleft (Affatato et al., 2021; Gambini et al., 2025; Makunts et al., 2020). Acetylcholine is a neurotransmitter that is necessary for muscle contraction (Affatato et al., 2021; Gambini et al., 2025; Zhang et al., 2021). BoNT-A enters the nerve cell after binding to receptors on the nerve ending (Li et al., 2023; Zhu et al., 2021). It then breaks down SNAP-25, a protein involved in acetylcholine release (Gambini et al., 2025; Gilman Kuric et al., 2026). This blocks the release of acetylcholine (Gambini et al., 2025). This blocks neural transmission to the muscle, producing temporary muscle relaxation and paralysis at the injection site (Gambini et al., 2025; Milev, 2015; Zhang et al., 2021).

Central effects and amygdala modulation

The effects of botulinum toxin go beyond its peripheral action, which relaxes muscles, and may include a direct effect on brain structures (Dudzic et al., 2025; Gambini et al., 2025; Makunts et al., 2020; Wollmer et al., 2022). BoNT-A may affect the amygdala, which could explain its effects in depression and other affective disorders. The amygdala helps process fear and other negative emotions (Demchenko et al., 2024; Finzi, 2023; Gambini et al., 2025; Kruger et al., 2022). Studies with brain imaging suggest that BoNT-A lowers the response to negative emotions. On the other hand, in patients with borderline personality disorder, a specific reduction in the activity of the right amygdala was observed during the processing of negative emotions (Kruger et al., 2022). Injection into the muscles of the glabella (corrugator and procerus) initiates a signal transmitted via the proprioceptive fibers of the ophthalmic branch of the trigeminal nerve. This signal travels to the midbrain nucleus and then to the amygdala and the ventromedial prefrontal cortex (Finzi, 2023; Gambini et al., 2025). These structures form a loop that regulates emotions (Finzi, 2023). An injection into this area leads to paralysis of the 'grief muscles' (Finzi, 2023; Makunts et al., 2020; Wollmer et al., 2022; 2014) This reduces the negative signals sent to the brain, which may help improve mood.

Facial Feedback Hypothesis

This mechanism is based on the Facial Feedback Hypothesis. This is a key theory explaining the toxin's effect on the psyche and its antidepressant action. The main premise of the hypothesis is that facial expressions not only convey emotions, but also regulate, amplify, and sustain them through proprioceptive signals sent to the brain (Ceolato-Martin et al., 2024; Gambini et al., 2025; Lehnert et al., 2023; Rodríguez-Cerdeira and Eckhardt, 2024; Wollmer et al., 2022; 2014). This process is significant in the treatment of depression. Restricting the physical ability to furrow the brow reduces feelings of sadness, anxiety, and anger, as well as negative emotions (Kruger et al., 2022; Lehnert et al., 2023; Wollmer et al., 2022; 2014; 2012). Studies suggest that this treatment may work best in patients with high psychomotor activity, including increased facial muscle movement. The amygdala is connected to the hypothalamus and brainstem, so changes in its activity can also affect blood pressure, heart rate, and breathing (Finzi, 2023; Gambini et al., 2025). Restoring its normal activity may improve somatic responses to stress (Gambini et al., 2025).

Neurobiological Mechanisms in the Central Nervous System

NMDA receptors and neuroplasticity

Studies in animals suggest that BoNT-A injections into facial muscles can influence brain activity related to movement and stress. Botulinum toxin type A affects NMDA (N-methyl-D-aspartate) receptors by increasing the expression of their key subunits in brain structures responsible for mood, which is a key component of the substance's antidepressant mechanism. Preclinical trials in stressed mice have shown that a single injection of BoNT-A substantially increases the expression of the NR1 and NR2B subunits of the NMDA receptor in the hippocampus. An increase in the number of these subunits is directly related to promoting synaptic plasticity and augmenting neuronal resilience (Gambini et al., 2025). This is key to reversing synaptic deficits caused by chronic stress. Changes in NMDA receptors occur in parallel with increases in brain-derived neurotrophic factor (BDNF) levels and activation of ERK-CREB signaling pathways. These biochemical processes are considered to be the central mechanisms of action of modern antidepressants (Gambini et al., 2025).

The toxin briefly increases the activity of ERK and CREB, two proteins that help the brain respond to treatment (Gambini et al., 2025; Rodríguez-Cerdeira and Eckhardt, 2024; Zhang et al., 2021). BoNT-A is injected into the muscles, but it also affects NMDA receptors in the hippocampus. This suggests it may influence the brain, either by moving into the central nervous system or by altering the signals sent to it (Gambini et al., 2025). Whilst ketamine therapy acts as an NMDA receptor antagonist, botulinum toxin normalizes its function by modulating subunit expression, leading to a long-lasting improvement in mood (Gambini et al., 2025; Young, 2013). BoNT-A may increase BDNF in several brain regions, including the hippocampus, amygdala, and prefrontal cortex (Ceolato-Martin et al., 2024; Gambini et al., 2025; Li et al., 2023; Wollmer et al., 2022; Zhang et al., 2021). This supports neuronal regeneration and synaptic plasticity. It also promotes increased neuronal resilience along with the repair of emotional circuits (Gambini et al., 2025; Wollmer et al., 2022). The modulatory effect is closely linked to the toxin's action on muscles. Studies show that after the effects of BoNT-A wear off (usually after 3–4 months), amygdala activity returns to normal and depressive symptoms may come back. The temporary effects of BoNT-A on emotional processing in the brain may help explain the improvement in mood (Finzi, 2023). Research suggests that BoNT-A may travel through nerve fibers and reach the central nervous system, where it can affect brain signaling (Gambini et al., 2025; Gilman Kuric et al., 2026; Lehnert et al., 2023; Makunts et al., 2020; Wollmer et al., 2022; 2012). This is a key synaptic transmission system in the CNS that regulates mood, sleep, motivation, and emotions.

BoNT-A can be taken up by nerve endings and carried back along the nerve to the neuron cell body. It may then affect other connected neurons, so its effects may not be limited to the injection site (Gambini et al., 2025). Studies show that after being injected into the body, BoNT-A can reach the central nervous system and remain active (Gambini et al., 2025; Gilman Kuric et al., 2026) One identified target of retrograde transport in humans is the Renshaw cell, i.e., an inhibitory interneuron in the spinal cord. Research on spasticity suggests that BoNT-A changes the activity of these cells (Gambini et al., 2025; Makunts et al., 2020). This suggests that it may also affect motor pathways in the central nervous system (Gambini et al., 2025).

Neurotransmitter modulation

BoNT-A may change serotonin (5-HT) and dopamine levels in the brain. These changes may contribute to its antidepressant effects (Ceolato-Martin et al., 2024; Gambini et al., 2025). Facial injections in mice led to a large increase in serotonin (5-HT) levels in the hippocampus and hypothalamus (Gambini et al., 2025; Zhang et al., 2021). It has been suggested that BoNT-A may affect the release of dopamine and noradrenaline by acting on cholinergic neurons or interneurons in the central nervous system. Studies in rats found that BoNT-A injected into the face increased brain noradrenaline levels, suggesting it may affect multiple neurotransmitter systems. In Parkinson's disease, BoNT-A can improve depressive symptoms without affecting dopamine production. This suggests that other neurotransmitters, such as serotonin, may be involved. Overall, BoNT-A can affect the brain after being injected into the muscles (Li et al., 2023).

Anti-Inflammatory and Analgesic Mechanisms

Pain mediators and chronic pain

Among the mechanisms underlying the action of botulinum toxin, its anti-inflammatory plus analgesic properties should also be highlighted. These mechanisms influence the treatment of depression through direct biochemical modulation of the nervous system and the elimination of somatic factors that place a burden on the psyche. The action goes beyond muscle relaxation and includes complex processes in both the peripheral and central nervous systems (Dudzic et al., 2025; Gilman Kuric et al., 2026). Botulinum toxin

inhibits the release of pain mediators from nerve endings, such as substance P, glutamate, and calcitonin gene-related peptide (CGRP) (Affatato et al., 2021; Dhengare et al., 2022; Gilman Kuric et al., 2026). By blocking these substances, BoNT-A reduces the hypersensitivity of pain receptors, i.e., peripheral sensitization (Affatato et al., 2021; Gilman Kuric et al., 2026).

Blocking the release of substance P may reduce inflammation caused by nerve activity and help relieve chronic pain (Dec-Ćwiek et al., 2024; Dhengare et al., 2022; Gilman Kuric et al., 2026). It may also improve mood by reducing excess glutamate activity in the brain (Li et al., 2023). Inhibiting the release of CGRP from nociceptive neurons is a key mechanism in migraine prevention (Affatato et al., 2021; Dhengare et al., 2022; Gilman Kuric et al., 2026). It also limits the amplification of pain signals in the brain and spinal cord, i.e., central sensitization (Affatato et al., 2021; Gilman Kuric et al., 2026). Chronic pain is one of the main triggers of anxiety and depression. It provides effective relief from toxins in conditions such as dystonia or migraine and directly improves the patient's emotional state (Dudzic et al., 2025; Gilman Kuric et al., 2026). In conditions such as cervical dystonia, relaxing tense muscles can decompress compressed nerve fibers. BoNT-A reduces muscle tension and pain by improving muscle function along with reducing pain signals. It can also change signals sent from muscles to the brain, which may reduce pain (Dec-Ćwiek et al., 2024; Gilman Kuric et al., 2026). BoNT-A reduces glutamate release from nerve cells, which may help decrease pain sensitivity and relieve neuropathic pain (Dec-Ćwiek et al., 2024; Dhengare et al., 2022; Gilman Kuric et al., 2026). By inhibiting excessive glutamate release, the toxin may act as a modern antidepressant by targeting the glutamatergic system, similar to other fast-acting drugs (Li et al., 2023).

Neuroinflammation and microglial activation

Too much microglial activity can damage neurons in diseases such as depression and Parkinson's disease. Normally, microglia protect nerve cells and help them function properly. Under the influence of psychological stress, damage, or a deficiency of monoamines, microglia enter a state of activation. Activated cells increase the volume of their cell bodies and reduce the number and length of their processes, becoming less branched. Microglia can be 'primed' by an initial inflammatory stimulus, thereby making subsequent stress responses stronger and more destructive (Li et al., 2023). BoNT-A may act on TLR2 receptors on microglial cells. Since these receptors are involved in inflammation, the toxin may help reduce inflammation in the nervous system (Finzi, 2023; Li et al., 2023). This leads to lower levels of inflammatory molecules, including TNF-α and IL-1β, which are associated with depression. TLR2 receptors play a role in regulating the immune response. C3 may activate inflammation through TLR2 receptors. BoNT-A may reduce this process, protect brain cells, and improve mood. It may also help reduce anxiety. These findings suggest that BoNT-A acts not only on muscles but also on the brain (Finzi, 2023; Li et al., 2023).

Inflammassociated withokines, serotonin, and the kynurenine pathway

Administration of BoNT-A reduces inflammatory protein levels, including TNF-α (tumor necrosis factor) and IL-1β (interleukin-1β). The suppression of their expression correlates with a rapid improvement in mood and the resolution of behavioral phenotypes typical of depression. Microglia release these substances during stress or brain damage. High TNF-α levels are connected with worse depression symptoms and difficulties in everyday life. TNF-α and IL-1β are inflammatory mediators that may contribute to mood disorders by altering brain function. These proteins are products of immune system activation, and their increased levels are a marker of chronic inflammation (Gambini et al., 2025; Li et al., 2023). These cytokines may damage brain connections by reducing the number of synapses and dendritic spines, especially in the hippocampus (Li et al., 2023).

TNF-α and IL-1β can activate the classical complement pathway, including C1q and C3 proteins, which 'mark' healthy synapses. This causes their erroneous phagocytosis by microglia, resulting in measurable hippocampal atrophy in people with depression. BoNT-A helps reverse this stress-induced process. This prevents the atrophy of brain structures responsible for regulating emotions. Chronic inflammation induced by IL-1β and TNF-α also affects neuroplasticity. As its activity decreases, the brain becomes less able to recover and adapt to stress, which may help maintain depression. Inflammatory proteins may also alter the metabolism of neurotransmitters such as serotonin, thereby reducing their levels in key brain regions. According to the monoamine hypothesis, chronic inflammation may reduce serotonin levels in the brain. Inflammation may disturb the synthesis, transport, and sensitivity of serotonin receptors. Long-term stress and inflammation can reduce serotonin (5-HT) in the brain. In Parkinson's disease with depression, this inflammation is linked to problems with serotonin in the hippocampus. BoNT-A may help patients function better in daily life and make it easier to deal with the effects of the disease (Dudzic et al., 2025; Gilman Kuric et al., 2026). Mood may improve even if movement symptoms do not improve as much. This suggests that BoNT-A may have direct effects on the brain through neuromodulatory and anti-inflammatory mechanisms (Gilman Kuric et al., 2026).

Studies mention the monitoring of the kynurenine pathway in inflammation-related depression. Kynurenine is listed alongside cytokines such as TNF-α and IL-1β as part of an immuno-metabolic panel used to assess patients with treatment-resistant depression. There is a link between chronic immune-inflammatory activation and reduced monoamine availability, including serotonin (5-HT). This mechanism is currently being investigated by monitoring kynurenine levels, which points to a link between these biochemical processes (Gambini et al., 2025). Preclinical studies show that effective inhibition of inflammatory processes in the brain via botulinum toxin administration leads to a significant increase in serotonin levels in the hippocampus, hypothalamus, and prefrontal cortex (Finzi, 2023; Gambini et al., 2025; Li et al., 2023; Rodríguez-Cerdeira and Eckhardt, 2024; Wollmer et al., 2022). This demonstrates that reducing inflammatory cytokines restores normal serotonergic transmission (Gambini et al., 2025; Wollmer et al., 2022). Table 1 shows the main changes linked to BoNT-A treatment.

Table 1. Neurobiochemical Changes Induced by BoNT-A

MARKER/SUBSTANCE	CHANGE INDUCED BY BoNT-A	CLINICAL SIGNIFICANCE
Serotonin (5-HT)	Increased levels in the hippocampus and hypothalamus	Restoration of normal serotonergic transmission, which is crucial for mood regulation
BDNF	Increased expression in the limbic system (hippocampus, amygdala, prefrontal cortex)	Supports neuronal regeneration and the repair of emotional circuits
Pro-inflammatory Cytokines	Significant reduction of TNF-α and IL-1β levels	Prevents stress-induced synaptic loss and hippocampal atrophy
NMDA Receptors	Normalization of function through increased expression of NR1 and NR2B subunits	Reverses synaptic deficits caused by chronic stress

Clinical Evidence in Neurological and Psychiatric Conditions

Movement disorders and psychiatric symptoms

Movement disorders, including Parkinson's disease, cervical dystonia, benign eyelid spasm, and hemifacial spasm, can affect patients' mental health and may lead to depression and anxiety (Dong et al., 2018; Kako et al., 2021; Martino et al., 2025; Wollmer and Krüger, 2021). In Parkinson's disease, altered proprioceptive signals from tense or hypomimetic facial muscles may actively contribute to the development and maintenance of low mood (Wollmer and Krüger, 2021). Patients with BEB and CD have a particularly high incidence of depression, which may result from disturbances within the basal ganglia (Kako et al., 2021). For patients with cervical dystonia, problems such as anxiety and depression may affect their quality of life more than the physical symptoms (Martino et al., 2025). Blepharospasm can lead to career failure, social withdrawal, and even 'functional blindness', which drastically reduces psychological well-being (Hui-Na Zhang, 2024). Facial synkinesis is also associated with increased levels of anxiety and depression, as well as a substantial reduction in self-esteem. Treatment with botulinum toxin type A brings about a significant improvement not only in motor symptoms but also in psychiatric parameters. Studies of patients with Parkinson's disease have shown that botulinum toxin injections are no less effective in treating depression than the traditional antidepressant sertraline (Wollmer and Krüger, 2021). In cases of blepharospasm and hemifacial spasm, BoNT-A therapy results in a marked reduction in scores on the anxiety (SAS) and depression (SDS) scales (Dong et al., 2018). Treatment of facial synkinesis improved quality of life and reduced anxiety symptoms for more than three months. These effects may last longer than the toxin's direct action (Adegboye et al., 2025). Most of the important information contained above is included in Table 2.

Table 2. Clinical Evidence for BoNT-A Efficacy

CONDITION	OBSERVED PSYCHOLOGICAL IMPACT
Treatment-Resistant Depression	BoNT-A offers a promising alternative for the approximately one-third of patients who do not improve with standard pharmacotherapy or psychotherapy.

Parkinson's Disease	Injections are as effective in treating depression as the traditional antidepressant sertraline.
Cervical Dystonia	Relaxation of tense muscles leads to significant improvements in quality of life, often exceeding the degree of motor symptom resolution.
Blepharospasm and Hemifacial Spasm	Therapy results in a marked reduction in scores on the anxiety and depression scales.

Appearance-Independent Antidepressant Effect

Studies show that a patient's appearance is not a key factor in emotional improvement, as individuals without visible wrinkles also experience remission of depression following toxin administration. The severity of expression lines before treatment does not predict the strength of the antidepressant response, which refutes the theory that patients feel better simply because they look more attractive (Reichenberg et al., 2016). It is also worth noting that women commonly show greater levels of anxiety and depression at the start of treatment, yet at the same time constitute a group that is highly responsive to the therapeutic effects of botulinum toxin (Dong et al., 2018).

This review analyzes the use of botulinum toxin type A in depression and anxiety disorders. Given the limited efficacy of standard therapies, such as pharmacotherapy (SSRIs, SNRIs) and psychotherapy, particularly in patients with treatment-resistant depression, it is necessary to search for alternative treatment strategies that take into account the multifarious interactions between the somatic system and the central nervous system (Ceolato-Martin et al., 2024; Demchenko et al., 2024; Gambini et al., 2025; Gilman Kuric et al., 2026; Rodríguez-Cerdeira and Eckhardt, 2024; Wollmer et al., 2022; 2014). The available evidence shows that BoNT-A acts in several ways and does more than block nerve signals to muscles (Dudzic et al., 2025; Gambini et al., 2025; Gilman Kuric et al., 2026; Wollmer et al., 2022). BoNT-A may also affect the limbic system, especially the amygdala.

According to the facial feedback hypothesis, alterations in facial expressions can influence emotions (Affatato et al., 2021; Ceolato-Martin et al., 2024, 2024; Demchenko et al., 2024; Finzi, 2023; Gambini et al., 2025; Gilman Kuric et al., 2026; Kruger et al., 2022; Lehnert et al., 2023; Makunts et al., 2020; Milev, 2015; Qian et al., 2020; Rodríguez-Cerdeira and Eckhardt, 2024; Wollmer et al., 2022; 2014; Zhu et al., 2021). The main proposed mechanisms underlying the antidepressant and anxiolytic effects of BoNT-A are summarized in Table 3.

Table 3. Mechanisms of Action of BoNT-A in Affective Disorders

MECHANISM	DESCRIPTION AND IMPACT ON THE PATIENT
Facial Feedback Hypothesis	Paralysis of "sadness muscles" interrupts the transmission of negative proprioceptive signals to the amygdala, leading to mood improvement.
Amygdala Modulation	BoNT-A injections reduce the amygdala's hyperactivity to negative emotional stimuli; the amygdala is a center for processing fear and negative emotions.
Neuroplasticity Support	The toxin increases BDNF expression and modulates NMDA receptors, promoting synaptic plasticity and neuronal resilience.
Anti-inflammatory Action	BoNT-A inhibits microglial overactivity and blocks signaling pathways, reducing pro-inflammatory cytokines such as TNF-α and IL-1β.

BoNT-A also affects the central nervous system. It influences NMDA receptor function, BDNF expression, and the serotonin and dopamine systems (Affatato et al., 2021; Ceolato-Martin et al., 2024; Demchenko et al., 2024; Finzi, 2023; Gambini et al., 2025; Li et al., 2023; Rodríguez-Cerdeira and Eckhardt, 2024; Wollmer et al., 2022; Young, 2013; Zhang et al., 2021). BoNT-A may also improve psychological psychological health through reducing inflammation in the nervous system and relieving chronic pain (Affatato et al., 2021; Dhengare et al., 2022; Finzi, 2023; Gambini et al., 2025; Gilman Kuric et al., 2026; Li et al., 2023; Rodríguez-Cerdeira and Eckhardt, 2024). The results of the clinical studies presented in this review suggest that the use of BoNT-A may lead to a considerable reduction in

symptoms of depression and anxiety, including in patients with neurological disorders such as Parkinson's disease, dystonia, or migraine. The effects of BoNT-A are not only related to augmented appearance but also to biological changes (Finzi, 2023; Gambini et al., 2025; Lehnert et al., 2023; Makunts et al., 2020; Reichenberg et al., 2016; Wollmer et al., 2022). Because the effects of BoNT-A are temporary, further studies are needed to determine how often treatment should be repeated and how effective it is over the long term.

4. CONCLUSION

Overall, botulinum toxin type A may help treat affective disorders. It should be emphasized, however, that a full understanding of the mechanisms of action of botulinum toxin and its permanent place in the therapeutic arsenal requires further research. Nevertheless, the scientific findings to date in this area, presented in this study, support the formulation of a theory regarding the efficacy of botulinum toxin in treating a range of diseases.

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Data and materials availability

All data associated with this study will be available based on the reasonable request to corresponding author.

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