Enhanced Knowledge in Sciences and Technology Vol. 2 No. 2 (2022) 487-497

EKST

Homepage: http://publisher.uthm.edu.my/periodicals/index.php/ekst
e-ISSN : 2773-6385

Oxytocin Role S in Neurodegenerative Disorders and Treatment

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DOI: https://doi.org/10.30880/ekst.2022.02.02.052
Received 1 January 2022; Accepted 30 September 2022; Available online 23 November 2022

Abstract : Oxytocin is a nonapeptide that is incorporated in the cell bodies by the supraoptic (SON) nuclei and hypothalamic paraventricular (PVN). Magnocellular oxytocin neurons of these nuclei innervate different forebrain regions and release oxytocin into the blood from the posterior pituitary. Like other neuropeptides, Oxytocin has been determined to work a critical role in the regulation of many behaviors connected with neuropsychiatric disorders, including social memory response to social stimuli, social interactions, feeding behavior, decision making in the context of social interactions, emotion alloreactivity, etc. Oxytocin may additionally exert important leadership in hippocampal synaptic plasticity, circadian rhythms, autonomic responses, antinociception, and motoneuron excitability. Accordingly, there is a medical care in its potential oxytocin therapeutic use for the treatment of neurodegenerative diseases associated with fear, anxiety, depression, memory and learning and social dysfunctions, posttraumatic stress disorder, generalized anxiety disorder, and social anxiety disorder, as well as autism, Parkinson disease, Alzheimer disease, and schizophrenia. In this review, the researchers

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highlighted many recent studies about oxytocin play essential roles in neurodegenerative diseases and potential therapy.

Keywords: Neurodegenerative disorders, Oxytocin, Behavior, Dopamine, Therapy.

1. Introduction

Oxytocin is a mammalian neurohypophysial chemical. It was named from the Greek words oxys, and tokos, which mean quick birth. This chemical demonstration chiefly as a neuromodulator in the cerebrum, serving generally as an inhibitory synapse that instigates many cycles in the body. OXT is a neurohormone made out of nine amino acids that has orchestrated inside the brain structure and emitted by the back pituitary organ, which is the essential wellspring of oxytocin in the blood[1]. OXT is additionally made in numerous elements of the body, and also the receptors are located in the digestive tube, heart, testes, uterus, placenta, amnion, ductless gland, thymus, adipocytes, pancreas, and kidneys[2].

Neurodegenerative disorders cause the brain and nerves to degenerate over time, they can change the personality and confuse [3]. Neurodegenerative disorders influence millions of people worldwide. Alzheimer's disease and Parkinson's disease are of several common species, including in excess of 5,000,000 Americans being with Alzheimer's illness, and somewhere around 500,000 Americans living among Parkinson's illness, albeit a few evaluations are a lot higher[4]. Neurodegenerative illnesses happen when nerve cells inside the brain or peripheral nervous system miss the function over time and eventually die[5]. Recently, behavioral impacts of oxytocin have obtained much attention due to studies determining that modifications in its function might carry neuropsychiatric diseases, for example autism, anxiety and mood disorders [6, 7, 8]. Genetic differences in the oxytocin receptor gene (OXTR) have been associated with abnormal social behaviors such as aggressive behavior [9]. So, oxytocin has been estimated as a potentially appropriate medicine for and communication lacks and maintaining social in neuropsychological and neurodevelopmental disorders [10, 11]. Although treatments may assist reduce some of the physical or mental symptoms associated with neurodegenerative disorders, there is presently no way to slow illness progression and no known medicines. Treatment usually involves the use of medicines to control symptoms. In this review the researchers first consider the normal structure and physiological function of oxytocin, then the researchers summarized data on the impacts of oxytocin on neurodegenerative disorders.

2. Molecular Structure and Functions of oxytocin

Oxytocin is a nonapeptide (i.e., nine amino acids; see (**Figure 1**) that is synthesized in the hypothalamus emitted by the back-pituitary organ, which is the significant wellspring of OXT in the blood [1]. They have variable hormonal activities in the periphery, and the center nerves system， OXT is coded by homologous genes that are thought to have risen out of a quality duplication occurrence before vertebrate divergence[12]. The human gene for oxytocin-neurophysin I encoding the oxytocin pre-propertied is mapped to chromosome 20 p.13[13]. Assorted capacities this hormone completes, two frameworks have been perceived; the focal Oxytocin framework and the fringe Oxytocin framework. The fringe activities of Oxytocin, for the most part, reflect discharge from pituitary gland [14]. Oxytocin will affect bonding, sexual behavior, maternal care, and also the capability to make social attachments[15]. Oxytocin, the questionable 'love hormone,' has been joined to several social behaviors, as well as saliency, empathy, bonding, maternal behavior, and sexual behaviors [16, 17].

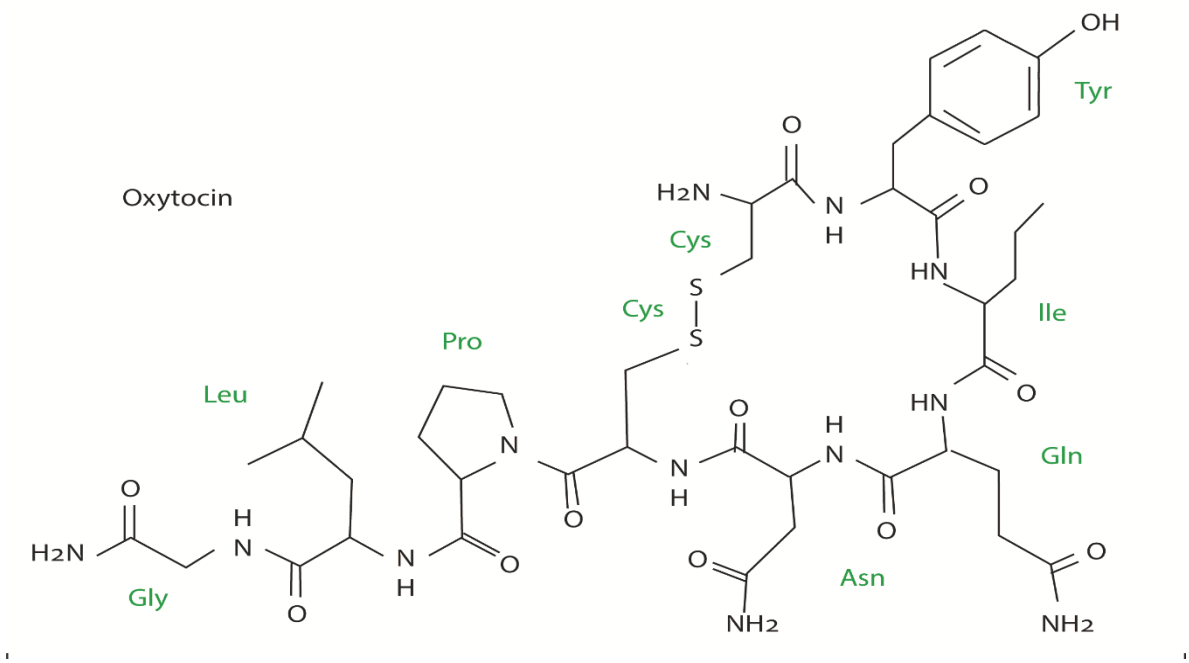

Figure 1: Structures of oxytocin

Oxytocin has the chemical formula C43H66N12O12S2. It is being composed of only nine amino acids (a nonapeptide). The sequence is cysteine - tyrosine - isoleucine - glutamine - asparagine - cysteine - proline - leucine - glycine.

3. Physiological effects of oxytocin

There are a lots of Physiological effects of endocrine such as Lactation and giving birth, Social Behavior, Stress-Related Behavior, Memory and Learning, and Sexual Behavior **Figure 2**).

3.1. Social Behavior

The role of OXT in Social Behavior a vital role within the initiation and maintenance of complicated social behaviors[18, 19].

1- **The pairs Attachment:** the neural distribution of OXT receptors describes the first salient distinction between the two species: the grassland voles' demonstration OXT receptors in those brain areas related to the reward system, like the nucleus accumbency and prelimbic cortex whereas signifying that OXT might need reinforcing possessions by selection in these species[20].
2- **Parental Attachment:** it has been incontestable that OXT injection within the lateral ventricles of nulliparous ovariectomized rats could induce maternal behaviors[21]. This proof, as well as the fact that, once a feminine has become maternal, OXT antagonists have not any result, could indicate that OXT is essential for the onset, however not for the upkeep of those behaviors[22].
3- **Infant Attachment:** OXT is considered to be one in every one of the potential up-and-comers worried inside the transduction of early encounters (birth technique, breastfeeding and various parts of parent-newborn child associations) into physio-(patho-) coherent changes, as well as cerebrum development, later pressure reactivity and female inward regenerative organ issues[23].

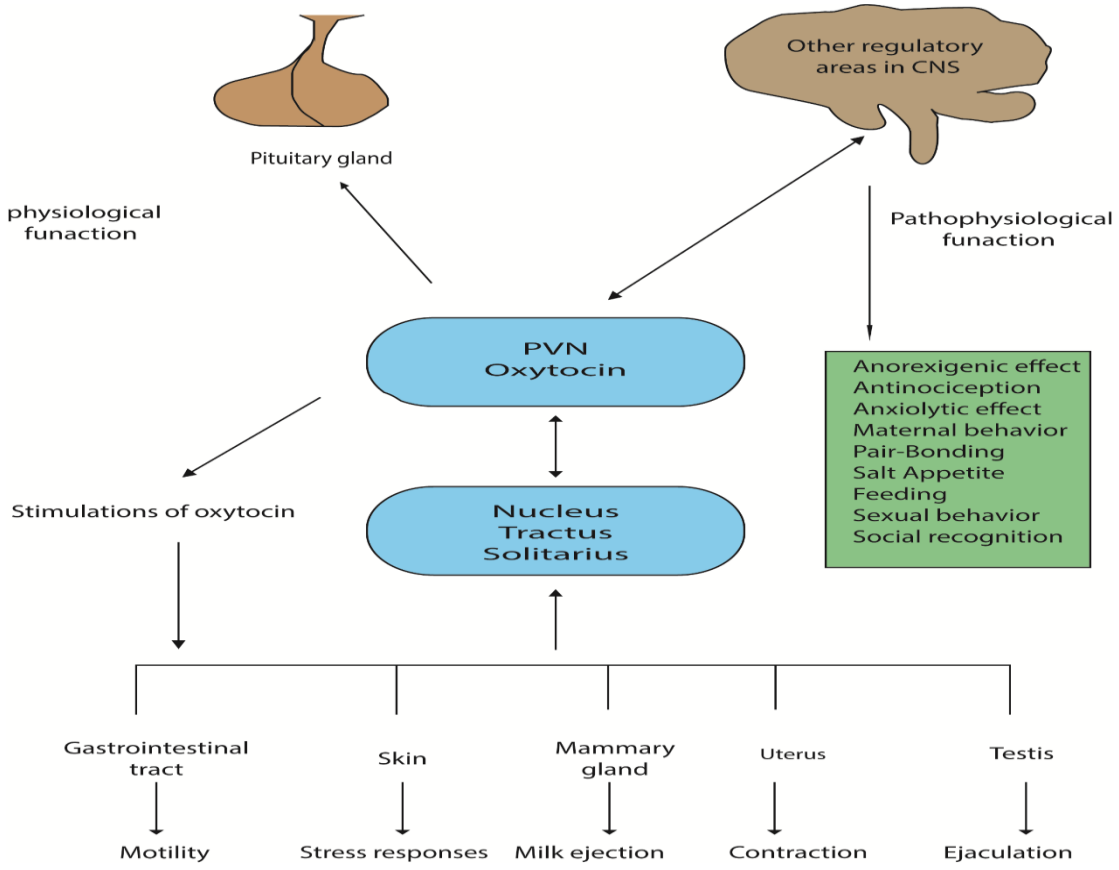

Figure 2: Schematic illustration showing the physiological and Pathophysiological function of oxytocin

Oxytocin has peripheral (hormonal) actions, and also has activities in the brain, such as milk ejection, uterine contraction, antinociception, anxiety, feeding, social recognition, orgasm, pair bonding and stress responses. And how afferent nerves from different parts of the body.

3.2. Stress-Related Behavior

OXT is liberated from the endocrine in light of totally unique difficult upgrades, as well as torment, molded concern and openness to novel conditions; noradrenergic neurons containing prolactin-delivering amide have all the earmarks of being, at least somewhat, responsible for the pressure related OXT emission into the flow[24]. OXT-mRNA levels, whereas each forced swimming and shaker stress aggravated an increase of median and plasma OXT concentrations. OXT would work with the enactment of the hypothalamic-pituitary-adrenal pivot by expanding the chemical release. What is more, some girls with an anxiety disorder are incontestable to expertise a discount of their anxiety symptoms throughout lactation [25].

3.3. Memory and Learning

OXT is concerned in many psychological feature functions, wherever OXT has reduced learning processes and memory. In creatures, OXT was incontestable to work with the termination of dismissal response and to constrict the capacity of verbal memory. In refined neurons, OXT is in a situation to downsize the action of N-methyl-D-aspartic corrosive receptors, that are one in every one of the primary fundamental substrates for the enlistment of learning and memory[26].

3.4. Sexual Behavior

OXT has been powerfully associated with sexual behavior and purposes in mammals, as well as humans. Plasma OXT levels begin to extend throughout arousal and are considerably higher throughout consummation than at baseline in each man and ladies [19, 27]. In men, magnified mean plasma OXT rose concerning five-fold throughout ejaculation and came back to basal concentrations at intervals half-hour[28]. In male rats, OXT will stimulate penial erection [29], whereas in females it is secreted throughout channel stimulation [30]. In each man and ladies, the number of muscular contractions throughout consummation was extremely correlated with OXT plasma levels, whereas suggesting that many OXT effects could rely on its capability to stimulate smooth muscles contraction within the genital-pelvic space [20].

4. A potential role of oxytocin in neurodegenerative disorders

Neurodegenerative disorders cause the brain and nerves to degenerate over time, they can change the personality and confuse[3]. They can also destroy your brain's tissue and nerves, all through the previous decade, critical advancement has been accomplished in understanding the procedure of cell death [31]. The side effects and the intensifications of these issues are vastly different as indicated by their particular pathways of cell demise and having their instruments of cell passing prompts novel restorative systems[5]. A portion of the more common indications of the neurodegenerative issue includes memory, forgetfulness, loss, agitation, Anxiety, apathy, mood changes and a loss of inhibition.

4.1. Eating disorders

Eating disorders are branded by strange eating practices, self-perception adjustments, drive and state of mind unsettling influences, and also by a few neuroendocrine disfunctions, counting those of the hypothalamic-pituitary hub [32]. As examined, OXT and AVP have been exhibited to impact bolstering conduct [33], and a couple of information indicate fundamental changes of OXT and AVP in dietary issues [34, 35, 36].

4.2. Social Recognition Disorder

Most studies on the effects of OXT on social recognition and behavior have been conducted in rodents, wherever social recognition depends primarily on olfactory cues[37]. The brain focuses on these impacts incorporate the olfactory embellishment system, lateral septum, amygdala, bed nucleus of the stria terminalis, and core accumbent [14, 38, 39]. OXT has complementary neuromodulator function in this circuit, increasing neuronal action at various levels[37].

4.3. Post-Traumatic Stress Disorder

OXT lessens memory solidification and recovery, encourages the eradication of an actuated shirking reaction and diminishes uninvolved evasion conduct[40]. The intranasal OXT organization was appeared to lessen the memory recovery and adapted retort in patients with post-horrendous pressure issue (PTSD)[41]. It appears that changes of the OXT framework succeeding severe early pressure and misuse encounters may meddle with the mental health and increment the ensuing danger of treating PTSD and, more as a rule, mental scatters[42].

4.4. Anxiety and fear Disorders.

OXT has effects on the behavioral aspects of anxiety and fear related to social recognition; OXT exerts an anxiolytic and antidepressant force [37, 38, 43]. Pharmacologic and social examinations in transgenic mice lacking either OXT or the OXTR bolster the contribution of the brain OXT system in the reduction of anxiety [38, 44]; One area that may mediate the effects of OXT on anxiety is the CeA, which has an

essential role in initiation of autonomic, endocrine, and motor responses associated with fear[45]. The differential distribution of OXT receptors in the CeM and CeL may contribute to their opposite effect on anxiety and fear responses[37].

4.5. Depression

Since OXT has been appeared to diminish pressure reaction and nervousness levels, and additionally to balance personal capacities and advance positive social connections, a few manifestations of misery, specifically, social withdrawal, intellectual weakness, hunger alterations and stress reactivity[46], have been identified with OXT[47]. The main examinations completed in CSF demonstrated no distinction in OXT levels among discouraged patients and control topics[47, 48], while an expanded thickness of AVP-and OXT-communicating neurons was recognized in the PVN core after the death of patients with both significant unipolar and bipolar melancholy[48].

4.6. Schizophrenia

Little is recognized on the connection among the OXT framework and schizophrenia or, all the more, for the most part, psychoses because just a couple of information is accessible. One investigation demonstrated that OXT levels were expanded in schizophrenic patients, as contrasted and solid controls, especially in those taking neuroleptics and that, in medication-free patients, they were fundamentally higher following three weeks of treatment[49]. Furthermore, a morphometric assessment of neuropsychic immunoreactivity in the cerebrum of raw schizophrenic patients proposed the nearness of adjusted OXT work[50].

4.7. Autism and Related Illnesses

OXT and AVP appear to be embroiled in social aptitudes[18, 19, 50, 51] and anomalies of their neural pathways have been proposed to underlie a few parts of chemical imbalance including tedious practices, intellectual and social shortfalls, early beginning, and hereditary stacking[52, 53]. It has additionally been suggested that the focal direction and articulation of OXT and AVP may add to the higher pervasiveness of the confusion in male subjects. OXT appears to have impacts including diminished nervousness, unwinding, development, and reclamation. Then again, OT, which is estrogen-subordinate and is higher in female subjects, particularly amid new improvement, might be defensive[54].

4.8. Other neurodegenerative disorders.

Several morphometric studies have addressed the involvement of the AVP or OXT neurons in neurodegenerative disorders. OXT has lately been involved in mediating mesolimbic DA pathways through drug addiction and abandonment. SO, the loss of OXT neurons in the PVN led Parkinson disease[55] and loss of parvocellular with preservation of magnocellular AVP neurons in multiple system atrophy[56].

4.9. Treatment of Anorexia/Bulimia

Given the job of central OXT in anxiety, fear and craving control, just as it is known cooperation with DA in different CNS diseases, oxytocin ought to be tended to add later on as an inherent part of treatment for these conditions. As shown above, it is very much perceived that anorexia/bulimia and other different conduct problems are related with coextrusion of nervousness or melancholy like side effects [57].

4.10. Treatments for Depression

OXT is definitely not a pharmacological objective at this point, despite the fact that intranasal OXT treatment has the potential for lessening misery related indications in men. [58]. Since the present principle medicates treatment for depression, specific serotonin reuptake inhibitors are not successful in a more significant part of patients or have just a deferred impact in improving symptoms[59], maybe the collaboration between OXT-serotonin, or OXT– DA-serotonin could be misused further in growing new medicines for significant depression [57, 60].

In our last study we found oxytocin promoted neuronal survival, ameliorated motor dysfunctions, and prevented oxidative damage. Also, oxytocin improved behavioral deficits, alpha-synucleinopathy, and the reduced dopaminergic neuron loss that was induced by neurotoxicity (**Figure 3**) [60].

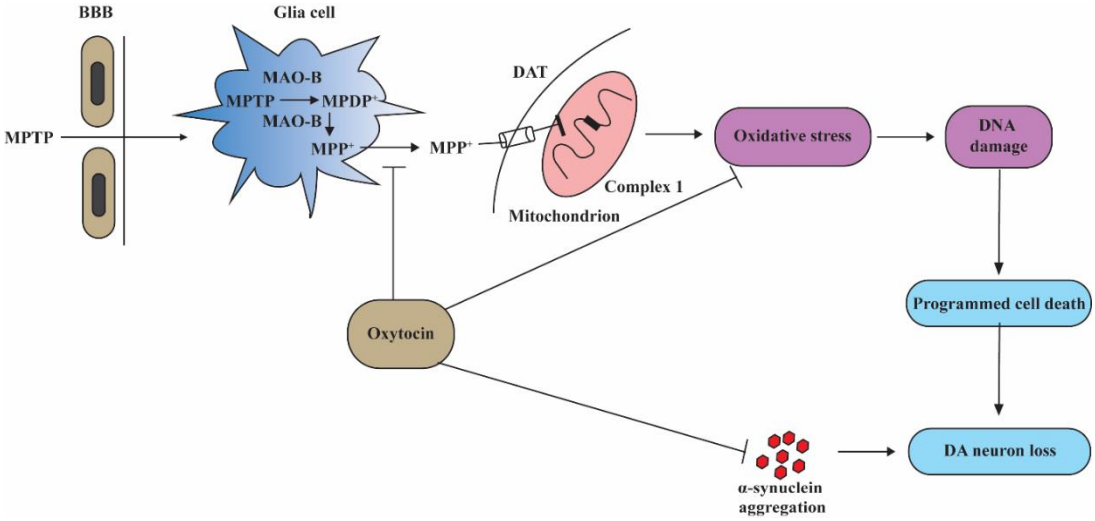

Figure 3: Oxytocin treatment of neurotoxicity

Oxytocin treatment could improve the MPTP-induced damage by either preventing the conversion of MPTP to its neurotoxic metabolite MPP+ and it could be preventing DNA damage, programmed cell death through antioxidation, maybe attenuates the hyperphosphorylation and aggregation of α-synuclein and improve dopaminergic neurodegeneration.

5. Conclusion

In summary, increased translation in the animal research and clinical studies in males and females, jobs of OXT on the neurodegenerative issues can possibly invigorate quick expansion in the improvement of compelling medicines for pressure related messes, including PTSD, melancholy, and nervousness, and habit, learning progressed mental errands and memory, as well as issues which remember shortages for association, such as autism, AD, PD, and another neurodegenerative disorder. These treatments may include pharmacological attacks, modifications to modern practices, social interventions, or a combination of approaches. In this review, the researchers have discussed the physiological and pathophysiology pieces of evidence of oxytocin in different brain actions and the possibility of the existence of this communication in neurodegenerative disorders. Current therapy using oxytocin is an emerging field because of its part in promoting positive social behavior and stress regulation, as well as its potential as a therapeutic medication to treat different features of psychiatric disorders and neurological disease. Despite, oxytocin is understood for its extensive impacts on social and reproductive rules, and recent data on intranasal administration in humans have led to hope for therapeutic use in autism, schizophrenia, and other neurodegenerative disorders. Finally, many studies

shall be done to confirm this hypothesis or to find out other possible mechanisms that would help us to understand such roles oxytocin in neurodegenerative disorders.

Acknowledgement

The authors would like to thank the Faculty of Applied Sciences and Technology, Universiti Tun Hussein Onn Malaysia for its support and provide basic facilities to carry out this present research work.

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