**THE EFFECTS OF OXYTOCIN ADMINISTRATION IN CHILDREN WITH AUTISTIC SPECTRUM DISORDERS**

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**ABSTRACT**

Oxytocin is one of the most researched hormones of the past two decades. Recent studies have proven its involvement in several behavioral patterns, like attachment, assuming risks and social interaction. Furthermore, it has been shown that oxytocin plays an important role in the mother-infant bonding. It also has promising results in various psychiatric conditions. The aim of this review is to summarize the findings regarding the effects of oxytocin administration in children with autistic spectrum disorders.

**Keywords:** oxytocin, autistic spectrum disorders, intranasal administration

**INTRODUCTION**

Oxytocin is a neurohormone released by the posterior hypofizal gland. It was the first artificially synthesized neurohormone, and it is involved in uterine contractions during labor and in milk ejection during breastfeeding, the name coming from the Greek oxy and tokos, which mean “quick birth”. Oxytocin is produced in the magnocellular neurosecretory cells of the paraventricular and supraoptic nuclei of the hypo-thalamus. It is stored in the posterior pituitary, in the axon terminals of hypothalamic neurons, in structures called Herring bodies, from where it is released into the blood. It is believed that the peripheral hormonal actions of oxytocin are due to the fact that these axons have collaterals towards oxytocin receptors in the nucleus accumbens [1]. Some paraventricular nucleus neurons project onto other parts of the brain and to the spinal cord [2].

Other areas of the brain that express oxytocin receptor cells are the amygdala and the bed nucleus of the stria terminalis.

Specific receptors are also found in the hypothalamus, the lateral septal nucleus, the periductal grey matter, Broca’s area, Meynert’s basal nucleus, locus ceruleus, the vagus nerve, the trigeminal nerve and the lateral reticulate formation [3-5]. Given the localization of these receptors, it is easily understandable why oxytocin influences such a wide range of behaviors.

In the past twenty years, the behavioral roles of oxytocin have been intensely researched. This way, it has been proven that this hormone plays an important role in attachment, empathy and social behaviors, being secreted during pleasant social interactions, such as petting and hugging.

Furthermore, it has been found that the deficit of oxytocin induces various psychiatric disorders. Administering oxytocin to psychiatric patients, on the other hand, seems to have promising results for pathologies such as major depression disorder, schizophrenia, autistic spectrum disorder and impaired mother-infant bonding [6].

The aim of this review is to summarize scientific findings regarding the effects of
Oxytocin administration in children with autistic spectrum disorders.

THE RELATIONSHIP BETWEEN OXYTOCIN AND AUTISM

Oxytocin is synthesized as an inactive precursor protein from the OXT gene [7]. Oxytocin might be involved in the etiology of autism, one report suggesting autism might be linked to the deletion of the oxytocin receptor gene (OXTR).

A study conducted on a sample of 57 Caucasian children and adolescents with autism spectrum disorders concluded that there is an association of OXTR with autism [8]. The aberration may be due to an abnormal methylation of OXTR. These results have also been found on samples of Finnish [9] and Chinese Han families children [10].

In animal models, it has been found that the lack of oxytocin induces stereotypical behaviors, such as exaggerated grooming [11]. OXTR knockout mice emit fewer ultrasonic vocalizations in response to social isolation; they have difficulties in distinguishing between known and unknown peers, and demonstrate a more violent conduct than the wild type [12].

In healthy human volunteers, the administration of intranasal oxytocin increases the gazing in the region of the eyes, the predisposition to gamble in an on-line experimental setting, as well as the ability to decipher positive facial emotions [6].

THE EFFECT OF ADMINISTERING OXYTOCIN TO AUTISTIC SPECTRUM DISORDER PATIENTS

So far, there are around 70 clinical studies involving the administration of intranasal oxytocin in clinical trials as an aiding treatment for psychiatric conditions such as schizophrenia, post-partum depression, dementia, autism and anxiety disorders, most of them having promising results. Social deficits, communication difficulties and stereotyped or repetitive behaviors and interests characterize autism spectrum disorders.

In 2012, Hall and his collaborators published a study in which they show that, in ten children with fragile X syndrome, the administration of oxytocin decreases their response to anxyogenic stimuli [13].

In 2010, Guastella and his collaborators showed, on a sample of 16 young men with autism spectrum disorders, that the results at the Reading the Mind in the Eyes test improved for the subjects after the administration of intranasal oxytocin. The test consists of recognizing the emotions expressed by pairs of eyes displayed on a screen. The results suggest that oxytocin might improve the processing of emotions in patients with autistic spectrum disorders [14].

Another study on social understanding was performed by Hollander and his team, in 2007 on a sample of 15 patients with autism spectrum disorders. The subjects were asked to identify the emotional valences of sentences read out loud, after having been injected, IV, with either oxytocin or placebo. The results showed that, after the injection, there were no significant differences between the two substances, the simple injection being enough to increase the performances of the subjects when compared with the baseline level, but, after two weeks from the injection, only the participants who had been injected with oxytocin still maintained their high scores, whereas the ones injected with placebo went back to baseline [15,16].

Regarding the stereotypical behavior of patients with autistic spectrum disorders, the same team published a study in 2002 in which they proved that the administration of intravenous oxytocin reduces these behaviors in children with autistic spectrum disorders.

As promising as these results may be, it is still uncertain how much of the IV administered oxytocin actually crosses the blood-brain barrier, and that is why the intranasal administration is preferred when searching for the behavioral effects [17].

Also in 2010, Andri and his collaborators have reported that the intranasal administration of oxytocin in patients with autism spectrum disorders increases their gazing in the eye region of photo-ographs with unknown persons. Furthermore, after having received an intranasal administration of oxytocin, these subjects were also more discriminative between a friendly and an unfriendly stranger in a computer game. The subjects were asked to pass the ball to one of two players in the game. One was friendly – he
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passed the ball back, and one was unfriendly—
he did not pass the ball back. Before the
administration of oxytocin, the subjects passed
the ball without discrimination, whereas after
the administration of intranasal oxytocin, they
passed it significantly more frequently to the
friendly stranger.

CONCLUSIONS

All the above-mentioned results suggest
that the administration of oxytocin in patients
with autistic spectrum disorders might improve
their social functioning. Also, given the
localization of the oxytocin receptors in areas
associated with language, such as Broca’s area,
it might also im-prove their ability to
develop expressive lan-guage. So far, the
results elicited by intranasal oxytocin
administration in children and adoles-cents with
autism spectrum disorders are encou-raging,
but there is still a great need for more detailed
studies regarding the safety of long term
administration.

Furthermore, it is still uncertain what the
effects of long-term oxytocin administration on
neurodevelopment are, this being a very
important question, especially in the context of
genetic diagnosis, when oxytocin treatment
might become an option in OXTR gene
abnormalities [18].

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