Oxytocin and autism

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The capacity to interact with others in complex social situations constitutes one of the key elements of our daily life. Patients suffering from high-functioning autism spectrum disorders (HF-ASDs) are not capable of interacting spontaneously with others in social situations, despite their normal intellectual abilities. They avoid eye contact and have difficulties in understanding the intentions of others. Autism is classified as a pervasive developmental disorder because symptoms emerge early in infancy, or perhaps from birth, affecting many aspects of cognition and behavior. Many studies have investigated autism, covering several domains of research: neuroscience, genetics, neurobiology, and the social sciences. However, there are still no promising cures for autism. Recently, one uniquely mammalian hormone, oxytocin, which probably evolved along with parturition and lactation approximately 200 million years ago, has attracted considerable attention because of its potential use in the treatment of autism. There has been much research exploring the link between oxytocin and autism at the genetic and behavioral levels, especially because researchers reported that children with autism had reduced levels of oxytocin in their plasma as compared to age-matched controls. This has opened an interesting avenue of investigation for the treatment of autism. Thus, what is oxytocin?

Oxytocin as a key facilitator for life

The process of evolution has endowed oxytocin with a remarkable capacity to be released in the blood as well as in the brain. Although best known for its role in birth delivery and breast feeding, oxytocin is also a fundamental mediator for a large range of emotions and behavior. Researchers have found that oxytocin initiates maternal behaviors such as nest building even in virgin animal models. Recently, in humans, it has been shown that the simple presence of the mother's voice represents an impressive support for the child, releasing the child from stress and increasing the child's levels of oxytocin. As such, oxytocin is a mediator of maternal attachment through its action on the reduction of stress and anxiety.

Also best known for its role in sexual activities, oxytocin is related to pair attachment and love bonding. Elegant studies on prairie voles have shown that the distribution of oxytocin's receptors in the brain can predict the degree of social behavior of these rodents. (Unlike most mammalian species, prairie voles form long-term pair bonds and show more oxytocin release during the sex act compared to their relatives, the meadow voles. Thus, the prairie vole is an attractive subject of research on oxytocin.) Administration of oxytocin to social species (such as prairie voles) induced a partner preference formation, and blocking oxytocin prevented formation of pair bonds even after mating. Thus, oxytocin has been associated with sexual activity and approach behavior, and does not only mediate the birth-life process but also promotes the fundamental basis of attachments, affiliation, and social interactions. Overall, a substantial body of research has established that oxytocin increases trust, empathy, eye contact, memory for faces, and generosity in humans.

Oxytocin and social deficits
In the light of the aforementioned findings, scientists have started to explore the implications of oxytocin treatment in patients with autism. For example, researchers have looked at the effect of an intravenous administration of oxytocin on the modulation of repetitive behavior in 14 adults with HF-ASDs. Indeed, these patients also suffer from the development of rigid adherence to routines or rituals and repetitive motor mannerisms, such as stereotypes. It was found that oxytocin decreased the severity as well as the number of different types of these repetitive behaviors (need to know, repeating, ordering, need to tell/talk, self-injury, and touching). In another study, the administration of oxytocin intravenously to 15 adults with HF-ASDs improved their comprehension of the emotional intonation of human voices. Finally, nasal administration of oxytocin in 16 youth patients with HF-ASDs led to improved capacity to recognize emotions expressed by the eyes.

However, because oxytocin plays a key role in social engagement and affiliation, and given that social deficits are significantly higher in patients with HF-ASDs, a key question will be whether oxytocin will improve social interaction in those patients. Will oxytocin improve one of the core deficits in autism, namely the lack of eye contact? Will oxytocin modulate social comprehension in these patients?

**Oxytocin promotes social comprehension**

Research has been carried out to see whether administration of oxytocin can improve the social capacities of patients with HF-ASDs, such as looking toward a face or interacting spontaneously with other people. In one test study, 13 adult patients with HF-ASDs received an intranasal administration of oxytocin (24 IU of synthetic oxytocin spray; three puffs per nostril) or placebo (no treatment). Administration of oxytocin or placebo was randomly assigned and separated by one week. In addition, another group of 13 healthy subjects, who only performed the behavioral experiments, were tested. The patients with HF-ASDs had significantly low plasma oxytocin concentrations, as compared to healthy subjects, before the nasal intake, which was followed by an increase in this hormone at 10 minutes after oxytocin inhalation. Fifty minutes after the nasal intake (the time needed for the molecule to reach the brain), the patients performed two experiments in front of a computer.

First, while patients were asked to detect the gender (male or female) of faces and the gaze direction (direct or averted), their eye movements were recorded by a camera inserted inside the computer. This was done in order to examine how patients looked at faces and to establish which parts of the face (for example, eyes, mouth, or nose) were fixated on more than others. Then, researchers tried to determine how oxytocin affected this perceptual process. The results showed that patients in the placebo condition (without treatment) spent significantly less time looking directly at the faces as compared to healthy subjects. In fact, they looked preferentially outside the face area. Strikingly, patients who were administered oxytocin looked significantly longer at the face region, particularly the eyes, as compared to the placebo condition (Fig. 1). No effects of oxytocin were observed with regard to the other regions of interest (mouth, nose, forehead, and cheeks) [Fig. 1]. Hence, oxytocin can promote a first level of prosocial approach by overturning what constitutes a core deficit of patients with HF-ASDs, namely the lack of eye contact. This is an important observation because eye contact between individuals is a basic element of social aptitude.
Second, how do patients interact with others in a social game where some implicit rules must be captured and learned over time? Will oxytocin play a role in the modulation of the social behavior of these patients? In order to investigate this, patients were asked to use a touch-screen computer to play an animated social ball-tossing game with three fictitious partners, who were depicted by cartoon characters and their corresponding photograph. Each time that the participant received the ball, he had to address the ball to one of the three players by touching the corresponding photograph. Unbeknownst to the participant, the amount of reciprocation exhibited by the three players was predefined. At the start of the game, the participant had an equal probability of receiving the ball from any of the three players. As the game progressed, player profiles diverged such that player A (the good partner) sent 70%, player B (the neutral partner) sent 30%, and player C (the bad partner) sent 10% of its played balls to the participant. Accordingly, healthy subjects sent significantly more balls to the good player than to the bad or neutral player. However, patients under placebo responded in the same manner to all players through all the game. In striking contrast, oxytocin intake led patients to engage more often with the good player and to send significantly more balls to this player as compared to the bad one (Figs. 2 and Fig. 3).

![Fig. 1 Oxytocin increases eye contact. (a, b) Gaze time spent on the face under oxytocin and placebo. (c, d) Gaze time spent on different regions of interest under oxytocin and placebo. (Reprinted with permission from E. Andari et al., Promoting social behavior with oxytocin in high-functioning autism spectrum disorders, Proc. Natl. Acad. Sci. USA, 107:4389–4394, 2010)
Fig. 2 Oxytocin improves social comprehension. (a) Computer ball game showing the amount of reciprocation of each partner toward the participant P (indicated by the tinted arrows). Gray arrows indicate a healthy subject’s performance. (b) Number of balls sent toward each partner during the game for healthy subjects, patients under placebo, and patients under oxytocin. An asterisk indicates significant statistical differences. (Reprinted with permission from E. Andari et al., Promoting social behavior with oxytocin in high-functioning autism spectrum disorders, Proc. Natl. Acad. Sci. USA, 107:4389–4394, 2010)
Interestingly, after oxytocin treatment, patients modified their behavior and responded according to the partner profiles during a time window as healthy subjects did. Following the game, patients estimated their sentiments of trust and preference with respect to the three players using a subjective seven-point rating scale. Whereas feelings expressed toward the three partners did not differ in the placebo condition, patients who received oxytocin reported that they trusted more and showed stronger preference for the good than the bad player. Thus, oxytocin enhanced the ability of patients to process socially relevant cues and acquire their meaning in an interactive context by facilitating learning. These results are consistent with previous studies with animals and healthy subjects that have enlightened the role of oxytocin in social recognition and social memory. Hence, oxytocin improved social interaction in patients with HF-ASDs. Caution though should be exercised in oversimplifying the role of oxytocin in enhancing social engagement. Recent research also indicates that oxytocin may simply amplify affiliative responses, whether positive or negative. For example, a rise in oxytocin was found in women in distressed relationships that was comparable to the rise of the hormone in women in affectionate relationships; and among men who inhaled oxytocin, those who reported being insecure in their current intimate relationship recalled a worse childhood relationship with their mothers, compared to those who reported being more secure in their current relationship.

Nevertheless, the findings on oxytocin’s role in enhancing social behavior in patients with autism highlight a therapeutic potential of oxytocin through its action on core deficits, such as social comprehension, emotion recognition, and repetitive behavior, of patients with HF-ASDs. However, these studies were limited to small samples of patients with high-functioning autism and Asperger disorder. Another interesting question concerns the neural mechanisms activated by oxytocin to facilitate a patient's prosocial behavior. It has been proposed that oxytocin enhances affiliation and attachment partly by reducing the levels of stress and anxiety. It is possible that patients with autism possess latent social skills and that oxytocin may thus favor social engagement behavior by suppressing fear and mistrust. More work will be needed to understand the relationship between changes in social behavior induced by oxytocin administration in individuals with autism and local changes in brain oxytocin metabolism. This could be accomplished using functional imaging techniques (among other methods). Finally, an important goal is to investigate whether a long-term intake of oxytocin may improve the functioning of patients in real social life.

See also: Autism (/content/autism/062850); Cognition (/content/cognition/146800); Developmental genetics (/content/developmental-genetics/189400); Developmental psychology (/content/developmental-psychology/189450); Hormone (/content/hormone/323000); Lactation (/content/lactation/368000); Nervous system (vertebrate) (/content/nervous-system-vertebrate/449300); Neurohypophysis hormone (/content/neurohypophysis-hormone/449900); Neurosecretion (/content/neurosecretion/450200); Stress (psychology) (/content/stress-psychology/660200)

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Links to Primary Literature


M. Kosfeld et al., Oxytocin increases trust in humans, *Nature*, 435:673–676, 2005 DOI: https://doi.org/10.1038/nature03701

**Additional Readings**

[Autism Society](http://www.autism-society.org/)

[National Institutes of Health: Autism Spectrum Disorder (ASD): Overview](http://www.nichd.nih.gov/autism/)

[Oxytocin Central](http://oxytocincentral.com/)