

# Neuroendocrine

BRIEFING

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## SUMMARY

Since the 2010s, oxytocin has captured popular attention as a “love drug”, with reports that a quick spray of this chemical can radically change behaviour. In reality, oxytocin is a neurohormone with nuanced roles in social behaviour. There is evidence that deficits in oxytocin signalling may influence the likelihood of autism and depression, and that increasing oxytocin levels may be of therapeutic value – although this is highly dependent on the individual and the social context.



## Is oxytocin therapy a credible treatment for autism and mental health conditions?

### Oxytocin: the social neurohormone

Of all the hormones known to influence social behaviour, none has attracted as much interest as oxytocin. Early studies reporting that oxytocin enhanced trust, emotion recognition, and empathy led the media to describe it as a “love drug” or “liquid trust”, with speculation that oxytocin could help people with conditions that influence social interactions and communication. Before delving into whether there is any truth to such claims, we first must understand what makes oxytocin such an interesting hormone!

In contrast to neurotransmitters that act in the central nervous system, hormones like oxytocin have distinct effects in the body and the brain — which is why oxytocin is often called a neurohormone. Importantly, the effects in the body and brain are often complementary. For example, increases in oxytocin in the blood trigger smooth muscle contractions necessary for birth and lactation, while increases in oxytocin in the brain promote the formation of strong bonds between mothers and their babies. Oxytocin plays this role in mother-offspring bonding in all mammals, and studies have shown that increases in oxytocin levels also play a role in the formation and maintenance of other relationships, including romantic relationships, friendships, and even bonds between people and pets!

### The link between oxytocin levels and neurological conditions

Given the crucial role of oxytocin in social relationships, an obvious question is what happens when something goes wrong with the oxytocin system? Researchers tested this in sheep using an oxytocin receptor antagonist – a drug that prevents oxytocin from binding to oxytocin receptors in the brain – and found that the antagonist prevented ewes from bonding with their newborn lambs.

*“There is some evidence of changes in the oxytocin system in people with neurodevelopmental and psychiatric conditions”*

There is also some evidence of changes in the oxytocin system in people with neurodevelopmental and psychiatric conditions that involve changes in social behaviour and cognition. Studies report lower blood/saliva oxytocin levels in autistic people (particularly children) compared to the general population (although some studies report no significant differences, which may indicate a publication bias), and lower oxytocin levels in people with schizophrenia and depression. However, critics of these studies note that oxytocin is notoriously difficult to measure and that a single measurement in blood or saliva is unlikely to be a reliable indicator of levels in the brain.

## Oxytocin genes and human social behaviour

It is possible that the relationship between oxytocin and social behaviour in humans is not as simple as low oxytocin levels. Instead, the important factor might be the ability of oxytocin to bind to receptors in the brain. Because examining receptors in living human brains is difficult, studies have examined variation in the human oxytocin receptor gene (OXTR), as genetic variants are expected to influence the structure and density of the receptors. Single nucleotide polymorphisms (SNPs) in OXTR, particularly rs53576, are associated with higher empathy in the general population, whereas other OXTR SNPs are associated with the likelihood of autism, schizophrenia and depressive symptoms. However, it must be noted that the influence of oxytocin-related genes on complex traits and states is likely very small and early “candidate gene” studies focusing on OXTR used smaller sample sizes than current genetic research.

## Can inhaling oxytocin improve social skills?

If low oxytocin levels do contribute to neurological conditions, could increasing oxytocin levels be a valuable treatment option? The development of intranasal oxytocin inhalation – a method proposed to allow oxytocin molecules to cross the blood-brain barrier and enter the brain – allowed researchers to test this possibility.

Initial studies using this method reported that oxytocin had broadly pro-social effects in the general population, leading to high expectations for its therapeutic potential for people with autism. Early studies administering oxytocin to autistic people reported promising results, such as increased recognition of others’ emotions, increased eye contact during a conversation, and increased enjoyment when they participated in a social game. However, these studies tended to use small sample sizes, include only male participants, administer oxytocin only once, and did not

look at real-world outcomes. More recent long-term studies involving hundreds of autistic people have generally found no difference in symptom scores and severity between participants given oxytocin and those given placebo, suggesting oxytocin does not have the ability to enhance social skills in autistic people.

There are also doubts around whether intranasal oxytocin results in a meaningful amount of oxytocin entering the brain. While studies in humans and non-human primates indicate that intranasally administered oxytocin enters the central nervous system (reflected by increased oxytocin in the cerebrospinal fluid), a substantial amount of oxytocin-spray does drip down from the nose into the throat and enter the bloodstream. Thus, any effects of oxytocin on behaviour could arise from peripheral, rather than central effects. To address this, researchers are working on improved oxytocin delivery methods and the possibility of combining intranasal oxytocin with antagonists to block any peripheral effects.

## What’s next for oxytocin research?

Despite the variable findings on the therapeutic potential of oxytocin, research in this area remains a flourishing field. With the realisation that oxytocin is not a “one-size-fits-all” strategy for enhancing social skills across all domains, researchers are refining their questions. Understanding how individual factors (e.g. sex, age) influence responses to oxytocin, the mechanisms through which oxytocin influences social behaviour (e.g., by reducing social stress, by increasing attention to social stimuli) and methods to stimulate endogenous oxytocin release in the brain, will provide critical information for determining who (if anyone) is likely to benefit from oxytocin treatment and under what conditions.

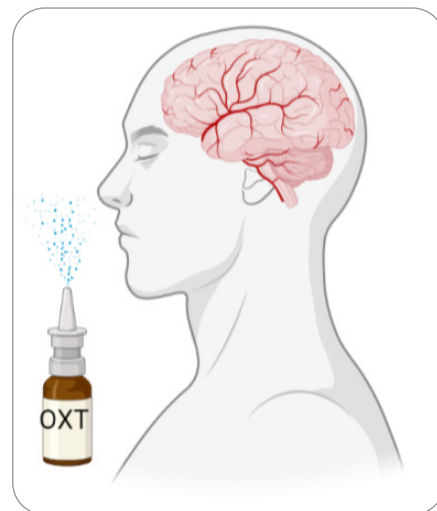


Figure 1. Inhaling a nasal spray containing oxytocin can influence social behaviour. Made with BioRender.



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