

TREAT WITH CARE

With around 40 clinical trials under way using oxytocin to treat conditions such as autism and schizophrenia, there is a lot of optimism that the hormone could help people by boosting trust and reducing social anxiety. However, there is also a growing realisation that under certain circumstances oxytocin can make people more antisocial (see main story). Understanding these subtle effects could mean the difference between helping someone and making things worse.

"From the early data, it's very clear that oxytocin alone will do nothing," says Markus Heinrichs at the University of Freiburg, Germany. "If you sit at home with a social phobia and someone prescribes a nasal oxytocin spray, I bet that the only effect you'd get would be a dripping nose." The trick is to work out when and in whom oxytocin would be expected to improve social behaviour, undermine it, or do nothing. For example, people might respond

differently depending on how much of the hormone naturally courses through their blood, their emotional state at the time of inhalation, or which version of a gene called *OXTR* they have. Combining treatment with counselling should help get the best results, provided people identify with their therapist and so are likely to experience the positive side of oxytocin's effects.

Researchers are addressing these issues, but meanwhile oxytocin sprays are readily available online. "We know people are buying it off the internet and trying to use it to treat children with autism," says Sue Carter at the University of Illinois, Chicago.

In most cases, the amount of hormone in the sprays is so low that they cannot be effective. Still, Carter points out that no one knows the long-term consequences of inhaling oxytocin, or what happens when you give it to young children. "This is very worrying," she says.

(*Journal of Biological Psychiatry*, vol 66, p 864). When volunteers played a gambling game, those who inhaled the hormone gloated more when they beat other players. They also felt sharper stabs of jealousy when the tables were turned. Clearly, oxytocin can produce antisocial as well as social behaviour.

That's not all. The hormone also has sharply contrasting effects depending on a person's disposition. Jennifer Bartz from the Mount Sinai School of Medicine, New York, found that it improves people's ability to read emotions, but only if they are not very socially adept to begin with (*Psychological Science*, vol 21, p 1426). Her team also showed that oxytocin actually reduces trust and cooperation in people who are particularly anxious or sensitive to rejection (*Social Cognitive and Affective Neuroscience*, vol 6, p 556). It can even alter our memories in different ways. It gives people fonder recollections of their mothers, but only if they are secure in their personal relationships. If they are socially anxious, oxytocin makes them remember their mums as being less caring and more distant (*Proceedings of the National Academy of Sciences*, vol 107, p 21371).

The effects of oxytocin can also depend on a person's culture. Although we have yet to fully unravel the complex biochemical pathways by which this hormone shapes behaviour, we do know that it starts off by docking onto a protein found throughout the nervous and reproductive systems, one encoded by the *OXTR* gene. A change in one of the gene's DNA letters, from A to G, makes people more socially sensitive. G-carriers tend to be more empathetic and less lonely. They are also more likely to turn to their friends in times of trouble, but only if they live in a culture where it is customary to seek companionship when distressed. Heejung Kim of the University of

California, Santa Barbara, found that in South Korea – where it is often a faux pas to burden friends with your problems – G-carriers are no more likely, and may in fact be slightly less likely, to seek solace from their social circles than A-carriers (*Proceedings of the National Academy of Sciences*, vol 107, p 15717). So a single trait, social sensitivity, plays out in radically different ways against the backdrops of different cultures.

Another discovery is that oxytocin's effects vary depending on who we interact with. Carolyn DeClerck of the University of Antwerp, Belgium, found that people under the hormone's influence become more



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cooperative only if they have some information about their partner. When paired with anonymous strangers, they become less cooperative. Meanwhile, Carsten de Dreu at the University of Amsterdam in the Netherlands discovered that oxytocin-sniffers show more trust and cooperation towards their compatriots, but not people of other nationalities (*Science*, vol 328, p 1408). They also showed favouritism: Dutch men became quicker to associate positive words with Dutch names than with German or Arabic ones, for example. De Dreu says that oxytocin promotes a “tend and defend” response, one that drives people to care for those in their

social circles and protect them from outside dangers. “It’s what we call the mama-bear effect,” he says. So, rather than promoting blanket goodwill, oxytocin strengthens biases.

There were signs of these subtleties from the start. Bartz has recently shown that in almost half the existing studies, oxytocin held sway only over certain individuals or in particular circumstances (*Trends in Cognitive Sciences*, vol 15, p 301). Where once researchers ignored such findings, now a more nuanced understanding of oxytocin’s effects is propelling investigations down new lines.

To Bartz, the key to understanding what the hormone does lies in pinpointing its core

function rather than in cataloguing its seemingly endless effects. There are several hypotheses, which are not necessarily mutually exclusive. Oxytocin could help to reduce anxiety and fear. Or it could simply motivate people to seek out social connections, which would account for a rise in trust and cooperation, but also explain why oxytocin-sniffers gravitate towards others resembling themselves, and why people who fear social rejection are not necessarily better off with more of the hormone.

For her part, Bartz favours the social salience hypothesis. The idea here is that oxytocin acts as a chemical spotlight that shines on social cues – a shift in posture, a flicker of the eyes, a dip in the voice – making people more attuned to their social environment. This would explain why it makes us more likely to look others in the eye and improves our ability to identify emotions. For people with autism who are less able to pick up on social cues, oxytocin could bring those subtle signs into sharp focus (see “Treat with care”, left). But it could make things worse

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for people who are overly sensitive and prone to interpreting social cues in the worst light. “People may become more empathic or protective, but they may also become more vigilant or competitive,” says De Dreu. “It depends on who they are and the other people that they’re dealing with.”

Perhaps we should not be surprised that the oxytocin story has got more complicated. The hormone is found in everything from octopuses to sheep, and its evolutionary roots stretch back half a billion years. “It’s a very simple and ancient molecule that has been co-opted for many different functions, from lactation to social behaviour,” says Sue Carter at the University of Illinois, Chicago, who did many of the early studies in animals. “It affects primitive parts of the brain like the amygdala, so it’s going to have many effects on just about everything.” Bartz agrees. “Oxytocin probably does some very basic things, but once you add our higher-order thinking and complex behaviours and social situations, these basic processes could manifest in different ways depending on individual differences and context.” ■

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