

UNDER THE INFLUENCE

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A magnified view of the hormone oxytocin, which has been dubbed the 'moral molecule'

Friendlier and more generous, or gloating and envious? New research is revealing how the hormone oxytocin makes you all of these and more, finds **Clint Witchalls**

YOU ONLY HAVE to think back to your teenage years to know how much of an effect hormones can have on you. These biological messengers carry instructions around your body, commanding you to eat, sleep, reproduce and more. In fact, their sphere of influence stretches far beyond our baser needs. In particular, one hormone's uncanny ability to affect our judgement has drawn the attention of scientists in recent years: oxytocin. Yet just as scientists have learned to harness its positive effects, a darker side to the hormone has demolished conventional wisdom about emotions.

For decades, the hormone was best known for assisting labour by causing uterine contractions. (Indeed, oxytocin is Greek for 'quick birth'). But today, the ring-shaped molecule is implicated in everything from orgasms to xenophobia.

"Almost every month there is a new paper on oxytocin with exciting findings," says Dr Carsten De Dreu,

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➔ an oxytocin researcher and professor of psychology at the University of Amsterdam. “In the past three years, it’s really exploded.” Arguably, the experiment that kicked it all off was one conducted by Dr Cort Pedersen at the University of North Carolina at Chapel Hill in the late 1970s. Dr Pedersen wanted to know where the mothering instinct in female rats came from. Put a pup near a virgin female rat and she’ll ignore it, bury it alive or eat it. But something happens in the rodent’s brain during pregnancy or labour that transforms her from an infanticidal maniac to a nurturing mum.

It was well known at that time that the endocrine system releases floods of oxytocin into the bloodstream during labour. The molecule then latches onto the oxytocin receptors in the uterus and causes contractions. But Dr Pedersen wondered if oxytocin might also be doing something in the brain. So he injected the hormone into the brains of virgin female rats. This time, instead of killing pups placed near them, they began to nurture them. Dr Pedersen had shown, for the first time, that oxytocin plays a role in the brain and that the role has something to do with the nurturing instinct.

Subsequent experiments, involving sheep, prairie voles and humans showed that oxytocin, in addition to being a nurturing hormone, is also involved in social bonding, co-operation, trust and altruism. More recently, neuroeconomist

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and oxytocin researcher Paul Zak, even went as far as describing the hormone as ‘the moral molecule’ after his experiments found that a dose of the stuff made people more trusting with their money.

The experimental floodgates really opened with the arrival of brain imaging technology, particularly functional magnetic resonance imaging (fMRI), and gene sequencing. Dr De Dreu also puts the recent surge in research activity down to a trend to use biology to understand human behaviour.

MEDICAL TREATMENT?

A hot area of research right now is oxytocin and autism spectrum disorder (ASD). ASD is a developmental disorder that affects about one in 100 people.



In this experiment at the University of Zurich, couples who took oxytocin via a nasal spray were shown to have increased empathy towards each other

Some of the features of the disorder are social difficulties, problems with communication and a lack of empathy.

According to Dr Larry Young, chief of the Yerkes Division of Behavioural Neuroscience and Psychiatric Disorders at Emory University, Atlanta, oxytocin seems to play a role in the processing of social information. This is a key skill that people with autism struggle with. “People with ASD tend not to look at the eyes. They tend not to be able to read emotions,” he says.

Some studies have shown that people with autism have reduced levels of oxytocin, and other studies

have found differences in the genes related to oxytocin. A number of trials are now underway to see if boosting oxytocin in people with ASD might improve some aspects of their social functioning (see ‘An autism cure?’, right).

Dr Young’s earlier work with prairie voles revealed how oxytocin is involved in linking social encounters with the reward centres of the brain. Not only does oxytocin make social situations pleasurable, it makes the brain pay attention to the ‘fine details’ of the person they are interacting with.

Researchers reason that if people with autism are given oxytocin, perhaps it will make social situations more rewarding for them. “Over time, it may improve how they interact with others and how well they can read emotions,” says Dr Young.

FACE BLINDNESS

An important part of bonding with other human beings involves paying attention to the fine details, including the details of a person’s face. Recognising faces is one thing people can do much better than computers and the study of oxytocin is now shedding light on a rare condition called prosopagnosia. People with this condition can’t remember faces. They can’t recognise their partner’s face, their children’s faces, and even their own face. It’s socially debilitating, to put it mildly.

Dr Young discovered that if you disrupted the oxytocin receptor in mice they can no longer recognise other mice they previously encountered. But mice recognise each other through smell, not sight. Dr Young and his colleague at University College London, Professor David Skuse, wondered if the oxytocin

AN AUTISM CURE?

Brain scans have revealed that oxytocin increases activity in affected areas of the brain

AREAS OF INCREASED ACTIVITY

- Making social judgements
- Making non-social judgements

PLACEBO

OXYTOCIN-AFFECTED BRAIN

Medial prefrontal cortex (decision-making and social judgement)

Precuneus (memory and consciousness)

Cingulate cortex (cognitive and emotional behaviour)

PEOPLE WITH AUTISM spectrum disorder (ASD) suffer from impaired social abilities, and the hormone oxytocin has been mooted as a means to improve their interactions. A large-scale study by the Yale School of Medicine has shown that oxytocin increases the brain function of children with autism.

To find out if the hormone would have any beneficial effects, the team gave a dose of oxytocin in a nasal spray to children and adolescents with ASD. An MRI scanner was then used to see how the hormone affected their brains when looking at human eyes and vehicles – a social and non-social judgement respectively. Placebos were also given to act as a control. The scientists found that oxytocin increased activity in areas of the brain that deal with social information.

BOOSTING THE PLACEBO EFFECT

A mysterious effect of oxytocin is puzzling scientists and could lead to better pain relief

SCIENTISTS IN GERMANY have discovered that oxytocin can boost the placebo effect. Researchers at the University of Hamburg took 80 male volunteers and applied identical, inert creams to two sides of the participant’s forearm. The volunteer was told that the cream on one side of his forearm was a powerful painkiller, like lidocaine, and on the other side an inert control cream. Of course, in reality, both sides were treated with inert control creams.

Pain was then applied, in the form of heat, to both sites on the forearm using a device called a thermode. “What typically happens



Oxytocin has the ability to enhance the effect of a placebo cream

is that, at the side where you tell the participant that this will be the lidocaine, they experience reduced pain,” says Ulrike Bingel, one of the researchers. “And we did this for every subject, but in 50 per cent of the subjects we applied oxytocin intranasally [via nasal spray] half an hour before the procedure was performed. The other 50 per cent received a saline spray via the same device.”

The researchers found that volunteers who received oxytocin experienced stronger pain reduction at the site where they expected the lidocaine to be, compared with those who received a saline spray.

“The next step will be to figure out exactly how oxytocin enhances the placebo pain relief and how we can exploit this clinically,” says Dr Bingel.

Dr Larry Young with a prairie vole, an animal that has revealed how oxytocin links social interactions with reward centres in the brain



→ receptor gene also played a role in face recognition, so they enrolled 198 families from the UK and Finland to take part in a face-recognition study. Each family had one child with autism, a condition that, like prosopagnosia, involves difficulty understanding faces. The researchers found that a small difference in the oxytocin receptor gene – whether in the parents, the child with autism or the siblings without autism – had a significant impact on their ability to recognise faces. And this small difference in the oxytocin receptor gene is found in about one-third of the general population. The figures so astounded Professor Skuse that at first he thought it must be a chance finding, so he ran the numbers, carefully correcting for false positive results. But the figures were correct. The findings suggest that oxytocin plays an important role in social information processing and might even suggest new avenues for developing treatments for people who are ‘face blind’.

TOO MUCH OF A GOOD THING?

The evidence for oxytocin’s role in making us social creatures is building day by day, but the solution to reversing social deficits in people with autism, schizophrenia, social phobia or depression might not be as clear cut as spritzing oxytocin mist up their noses. The reason is that you might become desensitized to its effects.

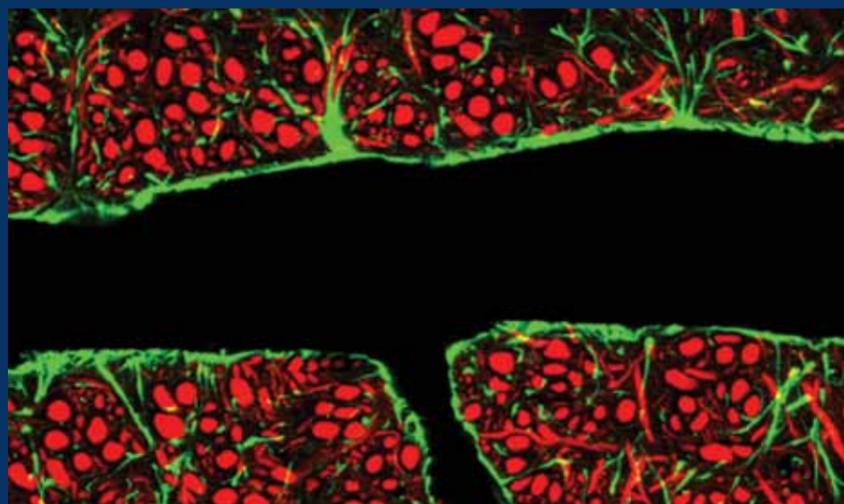
A paper published by Karen Bales, a professor in biological psychiatry at the University of California, Davis, showed that if you give male prairie voles low or medium doses of oxytocin every day for an extended period of time, it decreases their ability to form pair bonds with their mates later in life.

Prairie voles are known for their life-long monogamy. Professor Bales thinks that this effect could be due to ‘down-regulation of the oxytocin receptors’ or because the vole’s brain simply stops producing as much oxytocin as it should.

OXYTOCIN MYSTERY

Is the hormone even able to make it into the brain?

NOBODY KNOWS IF oxytocin taken via a nasal spray actually reaches the brain. The blood-brain barrier, a layer of cells that stops harmful substances getting into the brain, may prevent it from entering. “The big question is: are the effects of intranasal oxytocin actually due to the effects of it acting in the brain, or is it peripheral effects?” asks Dr Larry Young. There are many organs that are rich in oxytocin receptors, including the heart, kidneys and the womb. “Oxytocin could be acting in the body and then indirectly affecting the brain,” ponders Dr Young.



A cross-section of a blood vessel in the brain (black) is surrounded by glial cells (green), which provide structure for the neurones (red). The vessel is lined with endothelial cells that form the blood-brain barrier

IS IT OKAY TO BUY OXYTOCIN ONLINE?

Buying the hormone is a risky business while the long-term effects are still unknown

IT IS ILLEGAL to sell oxytocin in the UK without a prescription, but that hasn’t stopped unscrupulous vendors selling bottles of liquid that claim to be oxytocin. The blurb for the fake oxytocin usually mentions the product’s ability to attract mates and enhance sexual desire. A product called OXYTOCIN, made by Maxam Nutraceuticals, doesn’t contain oxytocin but ‘a proprietary blend of amino acids’. A different product, sold by HBC Protocols, is a homeopathic ‘oxytocin accelerator’. Neither is cheap. Ordering over the internet is a waste of money, but there are stories of parents of children with autism obtaining legitimate prescriptions for the drug from their family doctor.



Buyer beware: bottles labelled with the name oxytocin are sold online, but taking the hormone could be dangerous

However, given that the only preparation of oxytocin that has been given a licence in the UK is Syntometrine – an intravenous form of the drug – it seems unlikely that these stories are true. According to the Royal Pharmaceutical Society, intranasal oxytocin products have yet to receive marketing authorisation in the UK.

But even if you are able to purchase legitimate oxytocin, Dr Carsten De Dreu says you should be very cautious. “Scientists have no idea about the long-term effects of repeated usage,” he says. “So if you give it to your child on a regular basis, you may introduce adverse long-term effects.”



However, Dr Young is sceptical. “We know that when you engage with your child or hug your child you stimulate oxytocin release,” he says. “I don’t think that if you hug and engage with your child every day that you’re causing deficits.”

Even if Dr Young is right, there may be problems carrying out future work. New research, conducted by the Institute of Neuroscience, Chinese Academy of Sciences, and published in *Nature Neuroscience*, found that oxytocin doesn’t just act in the brain (as a neurotransmitter). It acts on the brain. It’s involved in the development of an area called the sensory cortex. “Administering any treatment that might affect the development of children needs to be handled with extreme caution, because if development goes awry, the consequences can be very far reaching,” says Xiang Yu, one of the authors of the paper.

Recent research has also revealed that oxytocin has a dark side. Dr De Dreu found that oxytocin seems to promote ethnocentrism. He conducted five experiments with Dutch students who

took either oxytocin or a placebo (they didn’t know which). In one experiment, the students were shown a pair of words on a computer screen. One word had either positive or negative connotations,

“I don’t think that if you hug and engage with your child every day that you’re causing [oxytocin] deficits”

Dr Larry Young, Emory University, Atlanta



and the other word was a Dutch, German or Arab name. To the students, Dutch people would be part of their ‘in-group’, but Germans and Arabs would be part of the ‘out-group’.

The researchers measured the speed at which the key was pressed. When the

students were given oxytocin, they were much faster (compared with those given a placebo) at assigning a positive word to their in-group than to the out-group. With out-group name, though, oxytocin had little effect. It didn’t make people slower or faster. There was only limited evidence that students had a negative reaction to the out group. But still, nepotism and favouritism aren’t exactly behaviours we should be encouraging.

Other studies have found that oxytocin increases emotions such as gloating, envy and taking pleasure from other people’s misfortune. Oxytocin doesn’t just affect how you treat others, it can worsen your own mood too. A recent study published in the journal *Emotion*, involving healthy young adults, found that oxytocin makes people emotionally over-sensitive.

If anyone was thinking that it might be a good idea to pump oxytocin vapour through the air vents at the UN General Assembly, they’d better think again. ■

CLINT WITCHALLS is a health and science writer and the author of *How Cool Stuff Works*