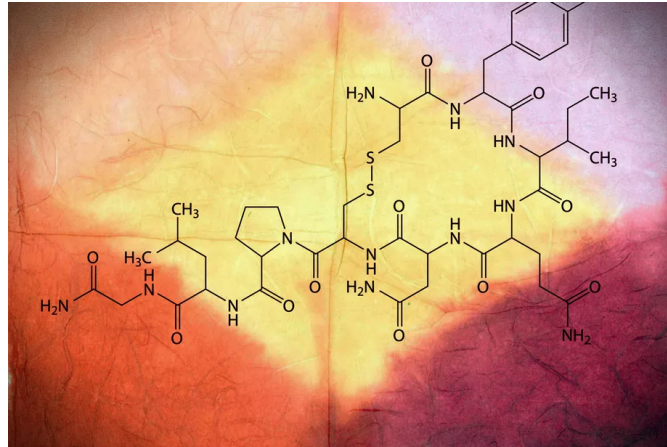


How scientists fell in and out of love with the hormone oxytocin

Scientists believed a whiff of the chemical could increase trust between humans. Then they went back and checked their work.

By Brian Resnick | @B_resnick | brian@vox.com | Apr 4, 2016, 11:40am EDT



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Would you trust a stranger with a packet filled with notes detailing your sexual secrets?

In 2010, psychologist Anthony Lane and his colleagues at Catholic University of Louvain in Belgium **assumed** most people would not. But they had a hunch about how to manipulate levels of trust with oxytocin, a neurochemical best known for its ability to induce labor. Just one whiff of it, they thought, might make people less anxious about a stranger — in this case, the researcher running the experiment.

They gave participants a survey inquiring about their bedroom habits and fantasies — everything from bondage to toys. After the survey was complete, the experimenters gave half the participants the oxytocin. The other half got a placebo.

Next came the real test: The researchers gave their participants an envelope to seal their secrets in, and told them they would not look at participants' questionnaires. The participants had the option of closing their envelopes and adding sticky tape.

Sixty percent of the oxytocin sniffers decided to not seal their envelopes, while only 3 percent of the placebo group did the same. It appeared the placebo group was particularly anxious too: 80 percent not only sealed the envelope but added the tape.

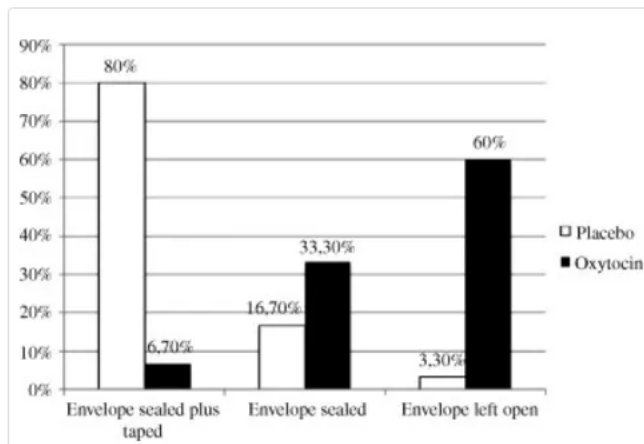


Fig. 1.

Percentage of participants displaying each behavior in the placebo and oxytocin condition.

Lane's study saw stark differences between participants who received oxytocin and those who did not. | *Biological Psychology*

From this simple but compelling study, Lane and his colleagues concluded that oxytocin does make people more trusting of others. "We thought the hormone was a kind of magic one," Lane tells me.

At the time, the "envelope task" was just the latest study adding fuel to an increasingly hot line of psychology research into oxytocin.

For many decades in the 20th century, scientists had studied the effect of the chemical in animals. They knew it was important in inducing labor but also in mother-infant bonding and lactation, and even relationships beyond mother and child. In the soup of chemicals that constitute animal life, oxytocin seemed to be the one that bonded individuals together.

In 2005, scientists took this knowledge and made a leap. If oxytocin seemed to make animals care about one another, what would happen to if you gave it to humans — who can be quite cold-hearted at times — an extra dose?

A *Nature* **paper** found that people who got a blast of oxytocin nasal spray became more trusting of others in a money-sharing game. Experiments that followed — including Lane's — showed that a whiff of oxytocin could make people more willing to **open up** and share painful stories with strangers. Others suggested it could help people recognize emotion in others. It made people more charitable, more empathetic. It showed promise in helping people with autism connect with others.

All the results seems to point in the same, very promising direction: Perhaps oxytocin could be widely deployed to soften the world's coldest hearts.

That's what Paul Zak, one of the authors on the original *Nature* paper, has argued to the public. In a 2011 **TED talk** he brandished a syringe filled with oxytocin, dubbing it "the moral molecule." The video has since been watched more than 1.4 million times. He told the audience, "It's so easy to cause people's brains to release oxytocin." His favorite method? Hugging. "Eight hugs a day," he said, to be specific. "You'll be happier, and the world will be a better place. Of course, if you don't like to touch people, I can always shove this up your nose."

But lately, doubt has seeped into the theory that a dose of oxytocin could be used to promote trust and gooey feelings between people.

Now even the chemical's leading researchers are doubtful of the extent of its powers. Here's **one conclusion** from a 2015 statistical overview of oxytocin research: "[M]ost of the reported positive findings regarding how OT [oxytocin] affects human behavior are likely to be false-positives."

Psychologists can chase wrong conclusions for years

That most of the positive findings on oxytocin may be false positives is actually something Lane has concluded after undertaking a critical reevaluation of his lab's work on oxytocin.

He tells me that in 2010, he and his colleagues had produced experiment after experiment like the envelope task that confirmed the link between oxytocin and trust. "We didn't think it was possible to fail with oxytocin," Lane says. "We were maybe a bit naive."

"OXYTOCIN DOES NOT DESERVE TO BE KNOWN AS A MIRACLE ANYMORE"

But after 2010, fewer and fewer of their lab's experiments yielded data that confirmed the oxytocin could reliably increase levels of trust. Lane says the first few misses just seemed like bad luck. That's just science: Sometimes experiments fail on chance alone. But there was a point where the bad luck became more consistent than the good. "There wasn't a real point where the doubt just explodes," Lane says.

The doubts crested in 2014 when Lane and his colleagues couldn't replicate their own envelope study. They had conducted a modified version of the test, changing the design from a single-blind test (the experimenter knew who received the oxytocin but the subjects did not) to a double-blind test (no one knew who got what). And they found nothing.

"Our results question the purported size of [oxytocin's] effect on trust and emphasize the need for replications," their resulting paper in *PLOS* **stated** in summary.

The lab was able to publish this negative finding, but Lane felt a larger problem was lurking. Labs are judged on the strength of their published work. And Lane's published portfolio on oxytocin just wasn't representative of their work anymore. They still had five papers showing promise for oxytocin, and only one casting doubt.

In a new paper published March in the **journal** *Neuroendocrinology*, Lane and his colleagues go through their "file drawer" of studies, and conclude the whole of their work yields an inconclusive result on the power of oxytocin spray to change behavior. They looked at 25 different tests their lab conducted. Only six of the 25 tests yielded significant results. In aggregate, the difference between the oxytocin sniffers in their studies and placebo groups "was not reliably different than zero," the paper found.

When they tried to submit their null findings, they "were rejected time and time again," the paper reports.

Publication bias puts perverse pressure on scientists

This is a great illustration of what's known as publication bias: the tendency for journals to favor publishing results that confirm hypothesis, and neglect inconclusive data.

Publication bias puts a perverse pressure on scientists to cherry-pick their results to skew positive. After all, prominent citations are an academic's lifeblood. It's often called "**publish or perish**," and it's a real threat researchers feel.

The result of publication bias: Whole textbook chapters of psychological theories may be resting on overly sunny data. Experiments — even classic ones, with hundreds of supporting citations — are failing under systematic

retests. Psychologists are calling it a **"replication crisis."** The cure, many believe, is a call for a **new age of transparency** in psychology.

Lane openly wonders if his lab, on the whole, shows an inconclusive result for oxytocin "that may be the case in many labs around the world," he says.

It may be. In February, Larry Young, a neuroscientist at Emory, **published a report** on the statistical methods used in oxytocin research on humans. He and his co-authors found that overall, the field is underpowered. Statistical power is the likelihood a study will produce a result, provided one exists.

High power is the result of sample size. The more people who participate in the study, the more likely a scientist can find differences wrought by an experimental design. (Lane admits this was a problem in his lab's work: Most of their studies only had around 30 participants per condition.)

It's weird when many labs report positive findings with low statistical power. Young determined that the average oxytocin study had a 16 percent chance of finding an effect. Yet most of them did. Evidently, more labs — like Lane's — were only choosing from the top of the file drawer.

"I do believe that some of the effects reported in the literature are true effects," Young writes me in an email. "But I am afraid that in some of the more psychological literature the best research practices may not always be followed, and people are doing post hoc analyses on lots of variables and cherry-picking those that are significant to report."

So what do we really know about oxytocin today?

Even Ernst Fehr, a neuro-economist at the University of Zurich who was an author on the original 2005 oxytocin paper in *Nature*, says the "real" effect of oxytocin nasal spray on trust may be very small. If the effect were strong, he says, it wouldn't be so fragile under slight changes in study design.

"There are few studies who really had a design similar to ours, which means that the jury is still out," Fehr writes. It could be oxytocin works, but only in small and very specific instances.

Other work has suggested that the effects of oxytocin **are a lot more complicated than simply, "It makes us more trusting."** Jennifer Bartz, a McGill psychologist, says she's found in her experiments that the effect of oxytocin depends on personality and context.

"It's unlikely that it is having this universal effect of having people be more trusting," she tells me. "People with a lot of interpersonal insecurities — whether they have prior experiences with negative relationship, or even in borderline personality disorder, where you have extreme concerns about being abandoned by others — in those individuals, oxytocin actually amplifies those interpersonal fears and concerns."

Knowing this, she says, it makes sense labs like Lane's have a lot of inconclusive findings in their drawers. A small study could be skewed by personality effects alone.

Overall, the new consensus on oxytocin is that it draws our attention to personal relationships but doesn't necessarily direct the emotions of them. (It's important to note that the animal research on oxytocin is more conclusive: When scientist block oxytocin all together in the brain, they **become uninterested** in their mates.)

Still, scientists say they haven't given up on studying the chemical, particularly when it comes to treating autism. **Elissar Andari**, a postdoctoral fellow in Young's lab at Emory, has conducted tests on the use of oxytocin in people with autism and found it may help them interact with others. She says it's important to continue research, because severely autistic people don't have many options for treatment.

Even if oxytocin only works narrowly, it's worth finding out if that narrow effect applies to this population. (That's not to say parents of autistic children should go out and buy oxytocin sprays on Amazon. These products are highly **suspect**.)

The bigger point, Lane argues, is that scientists really don't know the nuts and bolts of how intranasal oxytocin works. And that has to come before any theory on how a spray might help people. "The problem with oxytocin research is that too many people have been focusing on cataloging what it does (at least in some situations), rather than how it works," Ed Yong, a science journalist, **wrote** on the state of the science in 2012, in Slate.

Before scientists try to predict what effects it can produce, they need to shore up details like how much oxytocin from the sprays actually reach the brain, and how much of a dose is needed to see changes in behavior.

"There are a lot of moderators that can modify the reaction after the administration of an intranasal oxytocin," Lane says. "People at the moment are carrying on assessing variables without knowing the mechanism. Without having a strong reliable theory, it's worthless."

For now, he says, "oxytocin does not deserve to be known as a miracle anymore."