The Weak Science Behind the Wrongly Named Moral Molecule

No matter what all the articles, books, and TED talks say, Oxytocin isn't a “hug hormone.”

Kim Hong-Ji / Reuters

Ten years ago, *Nature* published a paper with a simple title: *Oxytocin increases trust in humans*.

The paper described an experiment carried out by Swiss scientists, who asked volunteers to entrust money in an anonymous partner. This anonymous partner could either repay their trust by reimbursing them, or betray them by keeping the cash. Amazingly, the volunteers entrusted more money to their partner if, before playing the game, they inhaled a hormone called oxytocin.

For years, scientists had shown that oxytocin matters for social interactions in animals. It prompts sheep and rats to show motherly care to their newborn babies, and it strengthens the bond between monogamous voles. But the *Nature* paper claimed that oxytocin “causes a substantial increase in trust among humans,” which really cemented the chemical's fame as a molecular totem of human virtue.

In the decade since, other groups have shown that sniffing oxytocin makes people more generous, cooperative, empathetic, and constructive. Commentators have suggested using the hormone during couples therapy, or to

promote social behaviors in kids with autism. Journalists can't seem to write about it without calling it a “hug hormone” or “cuddle chemical.” And the third author of that *Nature* paper has repeatedly and misleadingly promoted the substance as a “moral molecule,” in interviews, a book, and a TED talk.

But recently, several scientists have shown that this tower of evidence for oxytocin's positive influence is built on weak foundations.

Gideon Nave at the California Institute of Technology found five other papers where researchers had used similar trust games to those in the original *Nature* experiment. None of these found that a sniff of oxytocin could significantly boost trust. And when the team combined the results of all six studies, they couldn't find an effect either. “We were interested in whether the foundational finding that got this research focus going was firm,” says Michael McCullough at the University of Miami, who was involved in the work. “And the odds that it's true are rather low.”

Ernst Fehr from the University of Zurich, who led the original *Nature* study, notes that none of the other studies cleanly replicated his own. Each introduced tweaks, and sometimes flaws, that would have changed the results. Still, he says, “What we're left with is a lack of evidence. I agree that we have no robust replications of our original study, and until then, we have to be cautious about the claim that oxytocin causes trust.”

“The field's in its adolescence, where there's a growth spurt and not a lot of prefrontal control.”

Nave's team also criticize the methods used in the tidal wave of human oxytocin studies. For the hormone to exert an influence on behavior, it presumably needs to reach neurons in the brain, and dock at proteins called oxytocin receptors. No one knows if the nasal sprays that have been the bedrock of human studies can actually deliver oxytocin to those neurons. The hormone certainly enters the body in large amounts, but it barely crosses the barrier that separates our blood supply from our brain—a view supported by another recent review.

These criticisms don't just apply to studies on trust, but to those on altruism, cooperation, and other behaviors that oxytocin supposedly boosts. When Larry Young from Emory University analyzed a wealth of past studies using oxytocin nasal sprays, he found that they are very statistically underpowered. Statistical power refers to the odds that a study will find an effect, provided one exists. Ideally, scientists aim for a statistical power of at least 80 percent, giving a 4 in 5 chance of finding an effect. But Young showed that studies with oxytocin nasal sprays were so small that they had an average power of just *16 percent*. So, the fact that most of them reported statistically significant effects becomes suspicious, given how unlikely they were to find any.

Indeed, Young has personally talked to people who tried oxytocin-sniffing experiments, failed to find anything, and never published their results—a common problem that plagues many areas of science. “The field's in its adolescence, where there's a growth spurt and not a lot of prefrontal control,” says Young. “The best decisions aren't always being made.”

These problems will only get worse as psychologists come to grips with oxytocin's subtler effects. As I've reported before, the hormone is highly contextual in its influence. It can trigger positive behavior in some settings, but negative ones like distrust, favoritism, envy, and schadenfreude in others. Biologically, this makes sense. Experimentally, it's a pain in the ass.

If scientists blindly run experiments, by complete chance, they'll find some condition in which oxytocin seems to be doing something—perhaps only in men, or in anxious people, or in anxious men. This is the sharpshooter fallacy, named after an imaginary Texan gunman who fires many rounds at the side of a barn and then paints a target around the biggest cluster of holes.

The best way to avoid this fallacy, says McCullough, is to start off with a strong theory—a solid idea about what oxytocin does, and what kinds of effects you *expect* to see. Fortunately, that's exactly what people like Young are building. Rather than searching for cute, TED-friendly psychological effects, they're working on the hard neuroscience of oxytocin, and working out exactly what this hormone does in the brain.

Young's team is giving oxytocin to human volunteers who sit in a brain scanner, to see how the hormone influences the communication and coordination between different regions of the brain, including areas involved in social information and reward. They have also mapped the location of oxytocin receptors in the brains of monkeys, and are looking at how those receptors affect the animals' behavior.

Others have done landmark studies in mice. In 2013, Richard Tsien at New York University Langone Medical Center found that the hormone improves the clarity of signals in the brain, by reducing the background buzz of neurons and causing those that fire to do so more sharply. A month later, Robert Malenka from Stanford University found that oxytocin and serotonin interact in a part of the brain called the nucleus accumbens, and together make social information more rewarding.

Just this year, Robert Froemke from New York University showed that oxytocin tunes the brains of mother mice to the cries of their pups, by acting on regions involved in hearing. And way back in 2001, Young found something similar: Mice can't tell each other apart if they can't make their own oxytocin, but they regain that ability if you inject the hormone into a brain region called the amygdala.

All of these results support the growing idea that oxytocin makes animals pay more attention to social information in particular, like the call of a youngster or the smell of a stranger. Psychologists imagine a spotlight that shines upon these social cues and makes them more salient. But neuroscientists are defining that process in terms of regions of the brain, the activity of neurons, and the actions of hormones.

“I'm President of the Society for Social Neuroscience, and we're split half-way down the middle between social psychologists who do human work and neuroscientists who do animal work,” says Young. “The goal is to bring these fields together so that the theoretical constructs can meet the neural mechanisms.”

This will be especially important if clinicians want to use oxytocin to help people with autism to form stronger social bonds with their peers. That's a theoretically sound idea, but clinical trials have found mixed effects. In some, children with autism become more socially responsive after inhaling the hormone; in others, nothing happens. These differences probably reflect the hormone's contextual nature, which becomes incredibly important when thinking about how to use it.

“Say a child with autism takes oxytocin before they get on a school bus, and a kid on the bus makes fun of him,” says Young. “If oxytocin increases the salience of social stimuli, that's not going to make him better. That's going to increase the salience of [the bullying.] But if you combine oxytocin with therapy that encourages appropriate social behavior, the child might pay more attention to the therapist and their reward system might be more activated. That might make the therapy more effective.”

Then, there's a question of dose. Last year, an Italian team showed that mice become *less* sociable if they inhale oxytocin regularly, for long periods of time. It seems that over-stimulating the brain's oxytocin receptors can be worse than not stimulating them at all. So, what would happen if children took daily doses of the hormone in an attempt to improve their social behavior?

This is why the neuroscience of oxytocin is so important. The inaccurately named “moral molecule” is still more of a mystery molecule, despite decades of work. And that mystery needs to be solved before it finds its way into the clinic.

"