Oxytocin and the Bottom Line

by John J. Medina, PhD

Trust can be a scary proposition. Among other characteristics, trusting someone involves the ability to measurably predict a behavior on the basis of nothing more than a memory, an impression, or a whim. For creatures like us, who spend a ridiculous amount of time with unpredictable strangers, brokering trust is an oddly important survival strategy.

Trusting behaviors have fascinated a broad swath of the behavioral research community, from social scientists and evolutionary theorists to cellular and molecular biologists. This community has, over the past few years, acquired insight from unlikely corners of academia, including, of all places, business schools. This month's column is all about an interesting collision between biologists, economists, and the human capacity to rely on the character or integrity of other people.

Those of you who are already familiar with the topic know I am about to discuss one of biology's most ancient neurotransmitters: oxytocin. Its molecular mechanisms have become increasingly well characterized and have strong links to behaviors that involve the seemingly subjective experience of trust. Oxytocin has even been hypothesized to influence economic decisions. Can it?

The purpose of this column is to answer that question. I will start with the basic biology of this small molecule, briefly discuss its multifaceted role in animal behavior, and then move to data involving human subjects and their monetary decisions. As you shall see, it is not at all farfetched to include economists as important peers in the greater neurobiological community. We may just need to trust them a little more.

Oxytocin basics

Oxytocin was famously isolated more than half a century ago. Its identification and subsequent characterization earned Vincent du Vigneaud a Nobel Prize in chemistry in 1955.

That discovery turned out to be the easy part. Over the years, oxytocin has proved to be maddeningly difficult to work with for several reasons. Oxytocin is not a big, bulky protein but a little peptide weighing in at a paltry 1007 daltons (9 amino acids). It is produced in minute quantities in the human brain and degrades soon after manufacture (an effective half-life of less than 180 seconds).

Although it is tricky to work with, great strides have been made in understanding its biology. In the brain, oxytocin functions as a neurotransmitter, exerting its effects through a complex of interconnecting neural pathways. Oxytocinergic neurons display widespread projections throughout the CNS. In these cells, the peptide functions by binding to the oxytocin receptor, which is a fairly nondescript class I G protein–coupled receptor linked to phospholipase C. Specific brain nuclei that are mostly involved in emotional regulation possess dense fields of these receptors, mediating many of oxytocin's behavioral effects. These regions include the septum, hypothalamus, brain stem, and amygdaloid complex.

Oxytocin can also enter non-CNS tissue, functioning not like a neurotransmitter but like a hormone. Suckling, stress, and parturition all can stimulate oxytocin release from the posterior pituitary into peripheral circulation. Predictably, oxytocin receptors exist in many regions of the body outside the CNS, including in the uterus and breast. The peptide is involved in the dilation of the cervix before birth and can cause uterine contractions in the terminal stages of labor. It is also involved in the so-called letdown reflex in lactation, causing milk to gather into the breast's collecting chambers.

Oxytocin also has effects on some truly complex animal behaviors. In female rats, the administration of oxytocin antagonists after they give birth eradicates the animals' maternal behaviors. Virgin female sheep begin to exhibit maternal behavior toward unrelated lambs when oxytocin is exogenously supplied to their cerebrospinal fluid. Oxytocin in prairie voles helps to maintain monogamous pair-bonding behavior when released into the brain of females during periods of sexual activity. These are not unusual findings. Oxytocin mediates bonding social behaviors in a wide variety of species. In humans, oxytocin appears to assist in the formation and maintenance of sexual arousal.

The breadth of oxytocin-mediated behaviors has caught the attention of researchers who are interested in human social interactions—including trust. To talk about the effects of oxytocin on trust-associated behaviors, I turn to the work of Paul Zak, Ernst Fehr, and their colleagues, who have created experimental paradigms (games, actually) in which the seemingly subjective experience of trust competency can be reliably measured. I discuss the design of one of these games and the interesting role oxytocin plays in it next.

The game

Paul Zak designed the "trust game," which is based on the work of John Dickhaut and Kevin McCabe. The game always involves 2 people, the "subject" and the "stranger"—a person the subject has never met. It also involves money.

In Zak's version, the subject is said to trust the stranger if the subject withdraws money from a fictional (or actual) account and then gives some of it to the stranger. The subject has been informed that on receipt of the funds, the stranger will reciprocate, returning either the same amount or an even greater amount of money, at a later date.

The trust game is divided into several steps, as described below (**Figure**). Because reactions to other people can be easily influenced by physical appearance, perceived affect, and even clothing, it is important that neither participant has face-to-face contact. Both the subject and the stranger are thus seated at computers away from each other. They are both given $10 for participating in the study.

Step A. The experiment begins when the subject is told by the computer to make a monetary decision. The subject is asked whether he or she would like to send all or a portion of his $10 to the stranger. The computer tells the subject that if he decides to part with some of the money, the stranger's account will receive triple the amount that the subject donated. If the subject chooses to send $5, the stranger's account will be credited with $15, plus the $10 the stranger already has. This is a pretty good deal for the stranger, who now has $25!

Step B. The computer now informs the stranger about the subject's decision, and then asks the stranger, "Would you like to return some of the subject's money?" The stranger is informed that he does not have to return any of the money. Even if the stranger decides to be generous, the "tripling" effect will not occur in the subject's account. All decisions will remain confidential, no deception is ever allowed, and real money is at stake.

How do people react? The game has been performed numerous times in many countries, sometimes with breathtaking amounts of real money. Results from Zak's laboratory are typical. About 85% of subjects give at least some money to the stranger. The stranger who receives the money almost always gives some of it back to the subject (about 98% return money).

Although the behavioral work is interesting, the really compelling findings concerned the levels of oxytocin in the participants' brains, the results of which eventually led to an "intervention" experiment. The researchers found that the strangers' brains produced bucketloads of oxytocin when they received their free monetary gift from the subjects. The interpretation was that they were "trusted."

The effect was dose-dependent. The more money the strangers received, the more oxytocin was released in their brains. There was no increase in the level of this peptide in control groups who received monetary gifts in a random, nonpartner-dependent fashion.

Interestingly, strangers with higher baseline levels of oxytocin before the experiment almost always gave more money back to the subject as the experiment unfolded than did strangers with lower levels. That was not true of the subjects. Elevated levels of oxytocin in these participants did not predict higher initial monetary "gifting." Clearly, there was a relationship between trusting behaviors and oxytocin levels. It was almost as if the establishment of trust-competent situations had to be inaugurated to coax oxytocin levels to come out of their neurological dens.

Or was it the other way around?

The data seemed to suggest that the recognition of trust-competent social interactions was being mediated by oxytocin release. However, because association never means causation, the next experiments involved intervention protocols. What if oxytocin levels were artificially supplied to the participants? Would their behavior change? If that were true, supplying oxytocin to the subjects might increase the percentage of giving to the strangers on the computer.

Oxytocin was formulated to work as an inhalant, and 200 subjects in the experimental group were exposed to the peptide. Consistent with the hypothesis (although perhaps in contradiction to previous baseline findings), there was an increase in the amount of money the subjects gave to their cognate strangers (about 17% more). An unexpected finding also emerged. A large number of oxytocin-treated subjects (almost half) gave their entire cash amounts to their partners! This was very different from the controls and may have been the most revealing part of the experiment. With apologies to Fritz Perls, it appeared that elevated levels of oxytocin in the brain produced a background "trust gestalt" in the subjects that made them much more willing to part with their money.

Conclusion

These are certainly interesting results, but before we encourage grocery store managers to pretreat their stores with aerosolized oxytocin (air-soluble oxytocin, at least as configured by the researchers, is very easy to detect, by the way), a few cautions might be in order.

The effects, while dramatic in some participants, had no noticeable effects on other members of the group. Elevating oxytocin levels in these unresponsive populations was simply not enough to coax them to project positive faith into their social interactions. This unevenness suggests that feelings of trust have many complex components, and oxytocin, while prominent, may not be a one-size-fits-all explanation for everyone's trusting behaviors. Moreover, it was not the absolute levels of oxytocin that predicted the trusting behavior but the rise in levels from a baseline. This is an important insight because, if you recall, initial baseline levels in the subjects did not predict their generosity—the acute change did.

There are also environmental issues to consider that were suggested by this change-over-baseline finding. There is evidence that people have oxytocin "set points"—a thermostat-esque mechanism that can be deeply influenced by environmental issues, including stress. How stressed you are may thus profoundly influence your ability to rise from your baseline. Because the peptide normally interacts with a wide variety of biochemicals throughout the body (levels can fluctuate on an hourly basis), your ability to trust may depend on the time of day. There may even be sex considerations. Estrogen increases the uptake of exogenously supplied oxytocin to specific tissues in the body. If you are female, your ability to trust may not only depend on the time of the day but also on the time of the month.

Finally, there are definitional issues to consider. Most economists believe that 2 different events are being measured in these experiments. Only the subject's behavior involves measurable trust, at least by current definitions. The stranger's behavior is classified differently; he is exhibiting what is being termed "trustworthiness." Are these the same? Are they different? Are they parts of a continuum? Semantics? Both subject and stranger seemed to respond to oxytocin, but exactly what that means is not necessarily straightforward.

None of these comments are dealbreakers, of course, but simply represent the growing edge of some really fascinating findings. The data also predict something about the future way of thinking about things and even a new academic unit. The man most responsible for these findings, Paul Zak, is not a brain scientist at all. He is an economist, founding director of the Center for Neuroeconomics Studies, at Claremont Graduate University (he was trained in neuroimaging while in a postdoctoral fellowship at Harvard University).

As a brain scientist who has spent many years navigating the gap between basic research and business, I might be suspicious of such a background. However, his findings and those of his colleagues are compelling stuff. On a distrustful day, perhaps I can borrow one of Paul's inhalants.

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Figure

The mechanics of the "trust game"

Shown below is the operational structure of the trust game that was used to investigate the effects of oxytocin in human behavior. Divided into 4 steps, the game proved valuable in determining the role the peptide plays in the presence of anticipated monetary reward. The experiment involved 2 persons, a "subject" and "stranger," each of whom were given a certain amount of money for participating in the experiment.