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STUDIES EXPAND OXYTOCIN'S ROLE BEYOND "CUDDLE HORMONE"

Research has implications for relationships, addiction, psychiatric disorders, advertising, and more

SAN DIEGO — New human research suggests the chemical oxytocin — dubbed the “cuddle hormone” because of its importance in bonding between romantic partners and mothers and children — also influences feelings of well-being and sensitivity to advertising. Additional animal research shows that oxytocin may relieve stress and anxiety in social settings and may be more rewarding than cocaine to new mothers. The findings were presented at Neuroscience 2010, the Society for Neuroscience’s annual meeting and the world’s largest source of emerging news about brain science and health.

Oxytocin is best known for its vital role in childbirth and breastfeeding, and animal studies have shown that it is also important in monogamous social relationships. Recently, economic research in humans implicated oxytocin in trust and empathy.

Today’s new findings show that:

- Oxytocin is linked to happiness and well-being. When trusted with money from a stranger, women who showed the greatest increase in oxytocin also reported being more satisfied with their lives, resilient to adverse events, and less likely to be depressed (Paul Zak, PhD, abstract 387.18, see attached summary).
- Oxytocin increases sensitivity to advertising. Researchers found that after sniffing oxytocin, people were more empathetic toward public service announcements and more likely to donate to their causes (Paul Zak, PhD, abstract 387.21, see attached summary).
- In the presence of their newborns, rat mothers’ brains did not respond to learned cues associated with addictive drugs. This suggests that maternal bonds — a function of oxytocin — profoundly influence brain activity and behavior, with important implications for drug-addicted mothers (Martha Caffrey, abstract 888.22, see attached summary).
- Oxytocin reduces anxiety in stressed animals, but only if they recover in the presence of a friend. It is less effective at relieving stress for isolated animals, suggesting that social contact is an important factor in its ability to reduce anxiety (Jason Yee, PhD, abstract 190.7, see attached summary).

Other recent findings discussed show that:

- Oxytocin is important in evaluating social signals and may be as rewarding as drugs of abuse in some monogamous animals. The findings have important implications for designing novel treatments for several psychiatric disorders that affect social interactions, including autism spectrum disorders and schizophrenia (Larry Young, PhD, see attached speaker’s summary).

“Converging evidence from different research studies indicates oxytocin and other hormones have a profound influence on value judgments, shaping emotions and behaviors in humans and other animals,” said press conference moderator Margaret M. McCarthy, PhD, from the University of Maryland School of Medicine, an expert on the effects of hormones on the developing brain.

This research was supported by national funding agencies, such as the National Institutes of Health, as well as private and philanthropic organizations.

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Abstract 387.18 Summary

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Trust Hormone Associated with Happiness *Human study suggests new role for oxytocin*

The hormone oxytocin, which is known to be important in trust, may also be involved in a sense of well-being. According to new research, women who show large increases in oxytocin when they are trusted also report being more satisfied with life and less depressed. The study was presented at Neuroscience 2010, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

"Our findings reveal that the biological basis for social connections — oxytocin — is part of the brain mechanisms that serve to make us happy," said Paul Zak, PhD, at Claremont Graduate University in California, the senior author of the study.

Zak and his colleagues drew blood from study participants before and after they received a \$24 gift from a stranger. The participants could then return to the stranger a portion of the money they received. Before any money changed hands, participants completed surveys assessing their general attitudes and dispositions.

The researchers found that the women who showed the greatest increases in oxytocin after receiving the gift were more satisfied with their lives, showed greater resilience to adverse events, and were less likely to be depressed, according to their survey responses. In addition, the women who shared the most money with the stranger were happiest, had stronger attachments to others, and trusted others more.

Although the study suggests new roles for oxytocin, it remains unclear whether oxytocin makes people happy, or if happy people release more oxytocin when trusted.

Research was supported by the John Templeton Foundation.

Scientific Presentation: Monday, Nov. 15, 9–10 a.m., Halls B–H

387.18, Oxytocin and happiness

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TECHNICAL ABSTRACT: What makes people happy? The biological basis for happiness is only beginning to be studied. This research examined if the release of the peptide oxytocin (OT) was associated with greater subjective well-being. We designed a neuroeconomics experiment with a standard task, the "trust game," that has been shown to increase OT levels. Using a female college student sample (N=60), we obtained blood samples before and after the trust game and assayed OT, estradiol, cortisol, and ACTH. We also assessed satisfaction with life, resilience, depression, sexual activity, and attachment styles. We found that an individual's change in OT predicted greater resilience ($p < .05$), lower depression scores ($p < .05$), and greater satisfaction with life ($p < .05$), when controlling for estradiol and number of sexual partners. People who returned more money to a stranger who had trusted them in the experiment were also happier ($p < .05$), had better attachment to others ($p < .01$), trusted others more ($p < .01$), and were less focused on money ($p < .01$). Those who were happier had more sex ($p < .05$) with fewer partners ($p < .05$), scored lower on depression ($p < .001$), and were more resilient ($p < .001$). Our findings indicate that happiness is associated one's connections to other people, and that greater OT release appears to help sustain these social connections. In this study we cannot determine if happy people release more OT when trusted, or if greater OT causes people to be happier. But, we have found that OT, the hormone that promotes maternal bonding and romantic relationships, is also connected to one's satisfaction with life.

Abstract 387.21 Summary

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Oxytocin Increases Advertising's Influence

Hormone heightened sensitivity to public service announcements in human study

The hormone oxytocin makes people more susceptible to advertising, according to new research presented at Neuroscience 2010, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health. The findings suggest that advertisements may exploit the biological system for trust and empathy.

The researchers, directed by Paul Zak, PhD, at Claremont Graduate University in California, found that people treated with oxytocin donated 56 percent more money to causes presented in public service announcements. Study participants who received oxytocin also reported that the advertisements made them feel more empathetic.

After sniffing a spray of oxytocin or a placebo, participants viewed short public service announcements that had aired on television in the United States and the United Kingdom. The advertisements presented the dangers of smoking, alcohol, reckless driving, and global warming. Participants then reported how they felt about the people and issues presented in the advertisements. They were also given an opportunity to donate a portion of the money they had earned from participating in the experiment.

“Our results show why puppies and babies are in toilet paper commercials,” Zak said. “This research suggests that advertisers use images that cause our brains to release oxytocin to build trust in a product or brand, and hence increase sales,” he said.

Research was supported by Claremont Graduate University.

Scientific Presentation: Monday, Nov. 15, 8–9 a.m., Halls B–H

387.21. Oxytocin increases the influence of advertising

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TECHNICAL ABSTRACT: Background: Advertising is a billion dollar industry in the U.S. meant to persuade us to care about and purchase a product or service. This study examined the mechanism of advertising by examining its effect on the brain. Because oxytocin (OT) release is associated with empathy and trust [1] we hypothesized that OT would affect how people respond to advertisements. We also hypothesized that OT would have a larger effect for ads that had more social content. Method: A sample of 41 male participants were given either 40IU of oxytocin or saline intranasally and after a one hour loading period watched 16 public service advertisements, including issues in global warming, smoking, drunk driving and speeding. The ads lasted 30 - 60 seconds each. Participants were asked to assess how much they cared about the people in the ads and how much self-concern each ad elicited for themselves. They were given an opportunity to donate money to the cause in the ad using money they earned from the experiment. Results: Participants receiving OT donated significantly more than those on placebo, $t(587) = -2.652$, $p = .008$, Cohen's $d = .22$, $N = 589$. Additionally, using a non-parametric gamma we obtained the relationships between donation amount and concern for self/others for each individual. Their gamma values were used as the dependent variable in a 2x2 ANOVA yielded a significant interaction effect between OT and concern for others/self, $F(1, 21) = 10.577$, $p = .004$, $\eta^2 = .335$, $N = 23$. Those given OT donated more to the cause in the ads they viewed. Subjects donated more when the ads induced a concern for others. This study confirms previous research that oxytocin can increase individuals' empathetic inclinations, and it further shows that empathetic tendencies will have greater behavioral implications when social contexts allow people to express empathy. Our findings may help people resist the effect of advertisements designed to play on our emotions. They also explain why babies and puppies, potent oxytocin releasers, are so common in commercials.

Abstract 888.22 Summary

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Mother's Young Alter Brain's Response to Drugs

Rat brain shows different response to drug cue depending on the presence or absence of pups

The presence of a mother's young changes the way her brain responds to drugs, according to new animal research. The study was presented at Neuroscience 2010, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health. The findings suggest new avenues of treatment for mothers who are recovering drug abusers.

Researchers at Northeastern University used brain imaging techniques to test mother rats a few days after they gave birth. The animals had been exposed to cocaine prior to pregnancy and learned to associate a peppermint scent with drug use.

In the absence of the new pups, mother rats responded normally to the peppermint scent, showing activation in brain regions associated with drug association and craving. However, when the pups were physically present, the mother rats' brains showed an altogether different pattern of activation, suggesting that the pups themselves changed the way the brain responds to drug cues.

"Drug relapse is especially problematic for recovering drug users who are mothers," said graduate student Martha Caffrey, who led the study. "Maternal care has a profound influence on the offspring's long-term outcome, and insufficient or inappropriate maternal care leads to detrimental changes in their neural structure, and may lay the groundwork for dysfunction in future generations," she said.

Research was supported by the National Institute on Drug Abuse.

Scientific Presentation: Wednesday, Nov. 17, 2–3 p.m., Halls B–H

888.22, Pup presence differentially modulates maternal brain response to a cocaine-paired cue
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TECHNICAL ABSTRACT: Responding to a drug-paired cue plays a prominent role in initiating drug craving and seeking in humans as well as within animal models. Administration of cocaine to virgin rats leads to a variety of behavioral and neurobiological changes, and presentation of a drug-paired cue elicits reinstatement of drug seeking in virgin rats even after prolonged periods of abstinence; however, this effect has not been tested in the maternal brain. Furthermore, pregestational cocaine administration alters maternal care as well as maternal brain responsiveness to both pup related and non pup related stimuli. Due to these differences in maternal brain responsiveness, it is unknown how the maternal brain will respond to a cocaine-paired cue, and whether the presence of her pups will alter that responsiveness. In order to test this, virgin female Long Evans rats were administered 15 mg/kg cocaine or saline vehicle IP for 10 consecutive days, and each injection was paired with an olfactory cue and a contextual cue. Following drug administration, all animals were tested for development of conditioned place preference as a measure of the rewarding properties of cocaine. After a 5 day drug wash-out period the animals were bred, and on postpartum day 2-4 imaged awake for their BOLD fMRI response to the drug-paired olfactory cue. The previously paired drug cue and a neutral saline-associated cue were presented to the animal within the magnet during imaging in the presence of her pups, and repeated with the pups absent. One day after imaging, maternal behavior in the presence of the drug-paired olfactory cue was collected. When the pups were absent, significant positive BOLD increases were observed within the orbital, infralimbic and prelimbic regions, and the anterior nucleus of the thalamus. When the pups were present, there was no significant difference in activation within these regions; however, there was an alternate pattern of activation within the maternal brain in regions such as the hippocampus, somatosensory cortex, cingulate, and hypothalamus. These results suggest that while in the absence of pups the maternal brain responds to the drug-paired cue much like a virgin brain, in the presence of pups she does not show increased activity in cue-related brain regions when presented with the cue. Rather, the maternal brain shows a separate pattern of response, indicating that the pups' presence is modulating the maternal brain response to the olfactory drug cue.

Abstract 190.7 Summary

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Oxytocin and Social Contact Reduce Anxiety

Hormone may be less effective at relieving stress for isolated animals

Oxytocin reduces anxiety in stressed animals, according to new research, but only if they recover in the presence of a friend. The study was presented at Neuroscience 2010, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

“Work in the last two decades has propelled oxytocin toward the top of a list of potentially effective stress- and anxiety-reducing agents, largely due to its positive associations with mental health,” said Jason Yee, PhD, a postdoctoral fellow in the laboratory of Sue Carter, PhD, at the University of Illinois at Chicago.

To explore oxytocin's effectiveness in relieving stress, Yee and his colleagues treated voles with oxytocin and then placed them in a wet cage, a stressor that mimics a flooded burrow the voles might experience in the wild. Then the researchers allowed the voles to recover in a dry cage, either by themselves or with another vole.

Most of the voles tried to escape the dry cage — an anxious behavior. However, the voles that received oxytocin and recovered with a companion showed less escape behaviors. These voles had high levels of oxytocin in their blood. In contrast, oxytocin was less effective at reducing anxious behaviors in voles that recovered by themselves. These voles had lower levels of oxytocin in their blood.

“When animals receive oxytocin and are given an opportunity to recuperate in the presence of a familiar partner, their bodies may release extra oxytocin, which in turn appears to facilitate a less anxious pattern of behavior,” Yee said. The findings suggest that social contact is an important factor in oxytocin's ability to reduce anxiety.

Research was supported by the National Institute of Mental Health and the National Institute on Aging.

Scientific Presentation: Sunday, Nov. 14, 10–11 a.m., Halls B–H

190.7, Oxytocin alters the behavioral, cardiovascular, and hormonal responses to a mild daily stressor

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TECHNICAL ABSTRACT: The mammalian neuropeptide hormone, oxytocin (OT), plays a critical role in the facilitation of many positive social and biological functions, including sex, birth, lactation, parenting, and general affiliation. OT is thought to facilitate these functions partially by buffering responses to stress. Previous studies in the lab have demonstrated that daily injections of OT ameliorate the behavioral, hormonal, and cardiovascular changes associated with chronic social isolation. This study investigates the neural mechanisms involved in OT's ability to dampen the stress response. Same-sex pair-housed prairie voles (*Microtus ochrogaster*) were pretreated with intraperitoneal injections of oxytocin (10µg/100µL/vole), oxytocin antagonist (10µg/100µL/vole), or saline. Thirty minutes following injection voles were removed from the home cage and exposed to a flooded-cage stressor in which they were placed into a cage that contained ~1cm of water (~22oC) so that their feet (but not bodies) were submerged. Voles were returned to their home cage after 5 minutes of exposure to the flooded cage, and allowed to recover for at least 60 minutes. One subset of voles was sacrificed at this point to collect plasma and tissue for analysis. Another subset was previously implanted with radiotelemetric transmitters to record heart rate, heart rate variability (including respiratory sinus arrhythmia), temperature, and general activity. Preliminary findings support the role of OT in buffering the stress response. OT-treated voles engaged in fewer escape-related behaviors. Furthermore, OT injection resulted in lower heart rate and higher respiratory sinus arrhythmia during recover from the stressor, consistent with its proposed function in buffering the cardiovascular response to stress. Identification of activated neurons using immunohistochemical detection of the immediate early gene product, c-Fos, will be presented for brain areas implicated in the cardiovascular and hormonal responses to stress, including the ventrolateral septum, hypothalamic paraventricular nucleus, amygdala, and dorsal vagal complex of the brainstem. Supported by NIH Grants AG035627 (JRY) and MH72935 (CSC).

Speaker's Summary

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Special Lecture: **Neurobiology of Social Bonding and Monogamy: Implications for Autism Spectrum Disorders**
(716)

Wednesday, Nov. 17, 8:30–9:40 a.m., San Diego Convention Center, Ballroom 20

Studies in monogamous prairie voles are revealing the brain mechanisms involved in the formation of social relationships, and have important implications for designing novel treatments for psychiatric disorders with disruption in social function, such as autism. Prairie voles, like humans, are highly social and form long-lasting pair bonds between mates. This is in contrast to 95 percent of all mammalian species, which do not appear capable of forming long lasting social bonds between mates. Studies examining the brain and genetic mechanisms underlying pair bonding have revealed an important role for a few key chemicals in the brain in establishing social relationships. Oxytocin and vasopressin appear to focus the brain's attention to the social signals in the environment. During pair bond formation, these chemicals interact with the brain's reward system (e.g. dopamine) to establish an association between the social cues of the partner and the rewarding nature of mating. So why are some species capable of forming social bonds while others are not? Research comparing the brains of monogamous and non-monogamous species reveals that it is the location of the receptors that respond to oxytocin and vasopressin that determines whether an individual will be capable of bonding. For example, monogamous male prairie voles have high concentrations of vasopressin receptors in a ventral forebrain reward center that is also involved in addiction. Non-monogamous meadow voles lack receptors there. However, if receptors are inserted into this reward center in the non-monogamous meadow vole, these males suddenly develop the capacity to form bonds. These studies also suggest that pair bonding shares many of the same brain mechanisms as addiction. Genetic studies have revealed that DNA sequence variation in the gene encoding the vasopressin receptor affect the level of receptor expression in certain brain regions and predict the probability that the male will form a social bond with a female.

Recent studies in humans have revealed remarkable similarities in the roles of oxytocin and vasopressin in regulating social cognition and behavior in vole and man. Variation in the DNA sequence of the human vasopressin receptor gene has been associated with variation in measures of romantic relationship quality. In humans, intranasal delivery of oxytocin enhances trust, increases gaze to the eyes, increases empathy and enhances socially-reinforced learning. Indeed it appears that stimulating the oxytocin system in humans increases the attention to social cues in the environment. These findings have important implications for developing novel therapeutic approaches to enhance social cognition in psychiatric disorders such as autism spectrum disorders. For example several studies have reported improved social function in individuals with autism following oxytocin treatment. Future drug development targeting the oxytocin system may be particularly useful when combined with behavioral therapy approaches to reduce social deficits in autism.