The review by Depue & Morrone-Strupinsky (D&M-S) covers so much ground that inevitably there are areas that suffer relative neglect. The purpose of this response is to expand on how social interactions can be influenced by serotonin, a topic covered only in a two-sentence paragraph in the article. As stated at the end of the penultimate paragraph of section 6.1.3, serotonin "may also promote calm, prosocial interactions, such as allogrooming in vervet monkeys and positive social interaction in young adult humans." The authors point out at the start of their Concluding Remarks (sect. 9) that "there is a great paucity of *human* neurobiological research on traits that comprise the broad domain of interpersonal behavior." Serotonin may not be more important than any of the other neurotransmitters mentioned in the article. However, there is a small but growing literature on the role of serotonin in human social interaction, and specifically in behaviors that are involved in affiliation.

The discovery that drugs that potentiate serotonin function have therapeutic effects in various psychiatric disorders led to extensive animal work on the role of serotonin. The traditional view of one aspect of serotonin's role is that it inhibits response to a number of different stimuli (Spoont 1992), and there is an extensive literature on the role of serotonin in aggression. Aggression, particularly inappropriate aggression, can lead to social isolation, which, as the authors discuss in section 3.2.3, can lead to an early death in nonhuman primates. Inappropriate aggression, social isolation, and excessive mortality are related to low serotonin levels in rhesus monkeys (Higley et al. 1996). In humans, selective serotonin reuptake inhibitors (SSRIs) can decrease aggression (Coccaro & Kavoussi 1997). Furthermore, SSRIs enhance prosocial behavior in patients with depression (Dubini et al. 1997) and social anxiety disorder (van Vliet et al. 1994). One important question is whether these actions of SSRIs are secondary to the treatment of a disorder, such as pathological aggression, depression, or social anxiety disorder, which disrupts normal social interactions, or whether they have a direct role in the promotion of prosocial behavior. In vervet monkeys, enhancing serotonin function not only decreases aggression but also promotes approach and grooming of other animals (Raleigh et al. 1980), suggesting that serotonin is not just inhibiting response to a stimulus. Recent human placebo–controlled experimental studies suggest that enhanced serotonin function may also promote prosocial behavior in humans.

In studies on healthy volunteers, acute enhancement of serotonin function with either the SSRI paroxetine (Knutson et al. 1998) or with a dietary source of the serotonin precursor tryptophan (Attenburrow et al. 2003) enhanced detection of facial expressions of fear and happiness. Accurate detection of others' moods might contribute to affiliative social interactions. Several studies have shown that enhancing serotonin function also influences social behavior in healthy volunteers. One week of treatment with paroxetine increased affiliative behavior in a dyadic puzzle task (Knutson et al. 1998). In a study of another SSRI, citalopram, given to participants for two weeks, participants were perceived as less submissive by their flatmates and sent more cooperative messages while playing a game with a stranger (Tse & Bond 2002).

The results mentioned thus far were primarily based on observations made in the laboratory or during artificial interactions structured by the investigator. However, advances in methodology have made it possible to study human social interaction in everyday life using an event-contingent recording procedure. This method was developed to examine the multiple occurrences of individuals' social behaviors and their affect in their natural environments rather than in the laboratory. Participants complete a one-page form about their social behaviors immediately after each significant social interaction throughout the day. Abundant evidence has accumulated demonstrating the considerable reliability and validity of this kind of method for assessing interpersonal behavior (Csikszentmihalyi & Larson 1987; Moskowitz 1994). The method developed by Moskowitz (1994) provides assessments of interpersonal behavior corresponding to the two-dimensional model presented in Figure 1 by D&M-S. In this model, interpersonal behaviors are assessed along two dimensions, dominant–submissive and agreeable–quarrelsome, with the extreme end of quarrelsome behavior corresponding to aggressive behavior. In an event-contingent methodology, these behaviors can vary greatly from one interaction to another, but the reliability of measures aggregated across days increases considerably (Brown & Moskowitz 1998). Using this method, the effect of tryptophan, a nutritional supplement that enhances serotenergic activity, was studied in healthy volunteers using a crossover design during nine days of tryptophan supplementation and nine days of placebo administration (Moskowitz et al. 2001). Tryptophan decreased quarrelsome behaviors and increased dominance. In another study of similar design conducted with participants who had higher than average levels of irritability and hostility, tryptophan not only decreased quarrelsome behaviors but also increased agreeable behaviors (aan het Rot et al. 2004). Under some circumstances it also increased the perception of agreeableness in others. The participants were apparently unaware of these changes, as they were not able to guess better than chance when they were on tryptophan and when on placebo.

The studies described suggest that serotonin has a role in promoting affiliative behaviors in human adults in everyday life. This effect is probably not only a result of the ability of serotonin to inhibit aggressive responses but also a result of the ability of serotonin to facilitate prosocial behavior. Serotonin is probably not more important than a variety of other neurotransmitters in regulating social behavior, but the variety of pharmacological and dietary tools available to manipulate serotonin function in humans have helped the study of the role of serotonin to progress.

D&M-S specifically raise the issue of psychobiological processes underlying affiliative bonding. Whether serotonin affects bonding is not yet known. However, animal studies suggest that repetitive, rhythmic, oral buccal motor activity, such as occurs during breast-feeding, activates central serotenergic neurons and serotonin release (Jacobs & Fornal 1995; Rueter et al. 1997), which raises the possibility that activation of serotonin neurons during feeding helps infants bond to their mothers.

The ability of serotonin to enhance recognition of faces as well as alter actual social behavior suggests that serotonin may be acting through more than one mechanism to influence social behavior. Following suggestions of D&M-S, it may be informative to examine further the role of serotonin in changes in the perceptions of others as an incentive for affiliative behaviors and changes in the value and arousal level of rewards associated with affiliative behavior, so as to better understand the complex psychobiological underpinnings of affiliative behavior.

Trust: A temporary human attachment facilitated by oxytocin

Paul J. Zak

Center for Neuroeconomics Studies, Claremont Graduate University, Claremont, CA 91711-6165; Department of Neurology, Loma Linda University Medical Center, Loma Linda, CA 92354; and Gruter Institute for Law and Behavioral Research, Portola Valley, CA 94028. **paul.zak@cgu.edu**
http://fac.cgu.edu/~zakp

Abstract: Trust is a temporary attachment between humans that pervades our daily lives. Recent research has shown that the affiliative hormone oxytocin rises with a social signal of interpersonal trust and is associated with trustworthy behavior (the reciprocation of trust). This commentary reports these results and relates them to the target article's findings for variations in affiliative-related behaviors.

Depue & Morrone-Strupinsky's (D&M-S's) remarkable review of the neurobiology of affiliation lacks only in the paucity of direct human evidence. This commentary reports new findings support-

ing their primary contention that affiliation is an essential human trait.

My lab has been studying the physiology of a temporary human attachment, interpersonal trust. Trust is so frequent in quotidian activities that we hardly notice it. Trust among family members and friends is unsurprising because of the value of repeat bidirectional cooperation. What is surprising is that humans trust unrelated strangers quite easily and often with substantial resources. Consider how many strangers you trust to fly an airplane safely, to prepare your food, and to invest your hard-earned money. A conditional psychology supporting interpersonal trust is essential for humans to live among large numbers of unrelated others in modern societies (Pedersen 2004; Zak 2003; Zak & Knack 2001).

Zak and colleagues hypothesized that this conditional psychology would utilize the neuroendocrine architecture for affiliation and social recognition (Zak et al. 2004). In this study, trust and trustworthiness were operationalized using a paradigm from experimental economics using monetary transfers. Money is used so that participants' decisions to trust others or to be trustworthy have personal costs and benefits, seeking to mimic why humans trust others outside the laboratory. In each experimental session, 12 to 16 subjects from a large California public university earned $10 for showing up at the lab, were randomly assigned to the role of decision-maker 1 (DM1) or decision-maker 2 (DM2), and were placed in DM1–DM2 dyads through proprietary software. Subjects were informed that their own decisions and those of the other DM in the dyad affected how much money they earned during the experiment, but they were unable to communicate directly with the other DM. There was no deception of any kind.

During the experiment, DM1s were queried by the software to send an integer amount of their $10 show-up compensation, including zero, to the DM2 in their dyad. Both DMs were advised that whatever DM1 sent to DM2 would be tripled in DM2's account. After DM1s' decisions, the software reported to DM2s the tripled amount that the DM1 in their dyad sent them and the total in their account. DM2s were then prompted to send some integer amount, including zero, to the DM1 in their dyad. Researchers in experimental economics agree that the transfer from DM1 to DM2 is a signal of trust; relatedly, the amount DM2 returns to DM1 is an index of trustworthiness (Smith 1998). Here's the logic: DM1 sacrifices some of his or her show-up earnings by transferring them to an unknown DM2 to signal that the "pie" just got bigger and that the DM1 trusts DM2 to share some of this largess. DM1 can send a stronger trust signal only by sacrificing more of the show-up amount. Similarly, DM2 can only reciprocate trust by taking money out of his or her account – every dollar transferred to a DM1 reduces DM2's earnings one-to-one (and is not tripled).

Each participant was told that he or she would make a single decision and would do so serially. Immediately following each DM's decision, 28 ml of blood was drawn from an antecubital vein. After all decisions, subjects were privately paid their earnings in cash. Each experimental session began at 1:00 p.m., a time of minimum diurnal hormone variation. We conducted two experimental conditions. In the Intention condition, the trust social dilemma just described was implemented; in the Random Draw condition, a separate group of DM1s publicly pulled a numbered ball from an urn. The urn contained 11 balls numbered 0, 1, . . . 10, corresponding to the set of choices that DM1s could make in the Intention condition. The Random Draw condition removes the intentional signaling element from DM1's decision while maintaining the other aspects of the experiment. This allows an identification of the behavioral and endocrine effects of the trust signal.

DM2s who received an intentional trust signal had nearly twice the oxytocin (OT) levels as DM2s in the Random Draw condition (Intention mean OT = 340.87, SD = 130.50 pg/ml; Random Draw mean OT = 197.75, SD = 165.23 pg/ml; F-test, one-tailed, $N = 38$, $p < .004$), even though the monetary transfers received by DM2s in both conditions were on average identical (F-test, two-tailed, $p > .87$). The two conditions also resulted in different

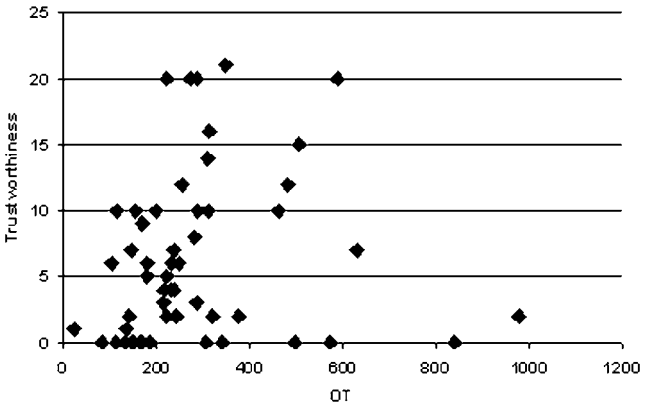

Figure 1 (Zak). OT levels and trustworthy behavior (dollars returned by DM2 to DM1 after tripled transfer from DM1 to DM2) for DM2s receiving an intentional signal trust.

behaviors. DM2s who received an intentional trust signal returned an average of 53% of the amount they received from the DM1 in their dyad. In the Random Draw condition the mean DM2 return to DM1 was zero (t-test, two-tailed, $p > .45$).

OT levels in DM2s were also related to their behavior in the Intention condition. Using a multiple regression model, the percentage that DM2s returned to DM1s (relative trustworthiness) was statistically related to OT(+) and OT^2 (–) (one-tailed t-test, $p < .035$), and an indicator of ovulation (progesterone > 3 ng/ml; one-tailed t-test, $p < .036$), including age, gender, and a fainting indicator ($N = 3$) as covariates. Our finding that ovulating women were statistically less trustworthy is consistent with evidence that progesterone inhibits OT receptor binding (Grazzini et al. 1998). It provides evidence that oxytocin facilitates trustworthiness directly, rather than indirectly. None of eight other hormones assayed were related to DM2s behaviors directly or indirectly through their effect on OT.

These results support the role of affliative hormones in responding to an experimental state. We also have evidence supporting D&M-S's assertion that affiliation is a human trait using an extensive social and affect survey. Trustworthy behavior by DM2s was related with three measures of calm affect ($p < .04$), but not robustly with any of the other 189 survey questions. Figure 1shows a positive relationship between OT and trustworthy behavior in the Intention condition ($N = 77$), with five DM2s who had high OT (> 400 pg/ml) after a trust signal, but were not very trustworthy (return transfer ≤ 7). We investigated traits that differentiated these five "usual" participants from the others and found that they exhibited labile affect on four self-report measures, were usually sexually active, said that they thought others were trustworthy, and evaluated themselves as very trustworthy. They also stated that accumulating wealth while others lived in poverty was acceptable. Though these results are based on a small sample and should be taken with caution, they suggest that a lack of trustworthiness after receiving a signal of trust is associated with identifiable personality traits.