

**Social Buffering in Rats as Measured by Prolactin: A Potential Role for Oxytocin**

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**Abstract**

Prolactin is released in response to stress, and attenuation of prolactin indicates social buffering. In the present study, adult male and female rats were tested in the conditioned emotional response chamber. Animals tested with a conspecific had lower levels of prolactin than those exposed to the stressor alone. In addition, the present research explored oxytocin as a potential mechanism for changes in prolactin levels during social buffering by injecting animals with 2 mg/kg s.c. Atosiban (1-deamino-2-D-Tyr-(OEt)-4-Thr-8-Orn-oxytocin), a specific oxytocin antagonist. Atosiban-treated rats had higher levels of prolactin than no-shock controls, whereas saline-injected rats returned to control levels.

**Key words:** prolactin, oxytocin, Atosiban, social buffering, stress, footshock

**Introduction**

Primarily known for its reproductive role, the hormone prolactin is now known to be released in response to both physical and psychological stressors. Physical stressors are generally painful or extremely uncomfortable and include restraint, forced swimming, and inescapable footshock. Psychological stressors involve the animal's interpretation of the environment as stressful or potentially harmful and include the open field, noise, predation, and a CER paradigm. Physical stressors are stronger than psychological stressors, and levels of intensity within psychological stressors are delineated by levels of prolactin (Kant, Meyerhoff, Bunnell, & Lenox, 1982; Orr, Meyerhoff, Mougey, & Bunnell, 1990). For example, noise is more stressful than a novel environment among rats (Armario, Lopez-Calderon, Jolin, & Castellanos, 1986b). To avoid a circular definition of stress measured by prolactin, humans who reported more stress before a physiology exam than a psychology exam also had higher levels of prolactin in the former condition (Armario, Marti, Molina, de Pablo, & Valdes, 1996). Thus, it is reasonable to assume that slight variations in prolactin across stressors may provide an excellent gauge for emotional arousal (Armario et al., 1986b).

The best animal model for warranted emotional arousal is the CER paradigm because it offers a stressful environment based on negative past experiences. Among rats, training in a CER paradigm reliably increases levels of prolactin in adult males. Three days of conditioning to footshock were sufficient to elicit higher levels of prolactin in experimental than control animals on the day of testing, when no footshock was given (Lorens et al., 1990; Paris et al., 1987; Van de Kar et al., 1985). Behaviors in conditioned animals included urinating, defecating, jumping, and freezing (Van de Kar et al., 1985). These studies indicate that exposure to the psychological stressor of the CER paradigm increases prolactin and induces several behaviors in adult males; however, responses of adult females have not been established.

While most of hormone research has been conducted on stressful environments in which an animal is alone, social situations can also be stressful. Social defensive aggression has been associated with increases in levels of prolactin in male Wistar rats (Dijkstra, Tilders, Hiehle, & Smelik, 1992) and in Siberian dwarf hamsters (Castro & Matt, 1997). Among humans, giving an oral presentation to an audience was rated as stressful and was related to higher levels of prolactin than in the control group (Gerritsen, Heijnen, Weigant, Bermond, & Frijda, 1996). Thus, negative social situations are stressful as measured by prolactin levels; however, social interactions can also be positive in that they reduce emotional arousal generally associated with psychological stressors (for a recent review, see Kikusui,

Winslow, & Mori, 2006).

To date, cortisol has been the primary focus of research available on hormonal responses to positive social interactions such as social support during an otherwise stressful experience. In adult female squirrel monkeys, cortisol levels remained unchanged during exposure to a novel environment with and without a conspecific (Hennessey, 1986). However, when squirrel monkeys were exposed to a conditioned-fear paradigm (CS paired with footshock), those tested in groups had lower cortisol levels than those tested individually (Stanton, Patterson, & Levine, 1985). By the same token, humans receiving social support during a challenging computer task had lower levels of cortisol than participants with no form of social support (Thorsteinsson, James, & Gregg, 1998). Similarly, among human males, psychological stress induced by preparing to speak to an audience was reduced by social support from a girlfriend as measured by lower cortisol levels (Kirschbaum, Klauer, Filipp, & Hellhammer, 1995). Based on these few available studies, social buffering appears to occur in stressful situations such that cortisol levels are reduced (Levine, 1993).

Prolactin has provided evidence of social buffering during stress in at least one human study and two rat studies. When social support was offered to humans during a computer task for which they received false negative feedback, both prolactin and cortisol levels were lower than in a control condition with no support (Biondi et al., 1986). Using rats to test social buffering, Wilson (2000, 2001) placed a same-sex juvenile conspecific in the open field with a juvenile experimental animal and found that prolactin levels decreased significantly below levels of rats tested in the open field alone. Even when rats were habituated to the open field for several days, and prolactin levels decreased, the presence of a conspecific further reduced prolactin (Wilson, 2000).

As the latter two studies were the first to examine the role of a conspecific in reducing the prolactin response to a stressful situation in rats, it is not known if social stress reduction is limited to the relatively mild psychological stressor of a novel environment. The pervasiveness of this effect remains to be examined across diverse psychological stressors, including the CER paradigm.

Regardless of the stressor employed, a potential moderator of social buffering would have to be linked with social interactions as well as prolactin reduction. Oxytocin is associated with social interaction (Carter & Altemus, 1997), with levels likely stimulated by positive social encounters (Uvnas-Moberg, 1998). Uvnas-Moberg (1998) argued that oxytocin stimulates antistress effects which in turn stimulate long-term health benefits. One possible mechanism involved in the benefits of oxytocin during social interaction may involve [attenuation of] prolactin (Panksepp, Nelson, & Bekkedal, 1997). And in fact, lower levels of prolactin have been found in rats tested together under stress than those tested alone (Wilson, 2000). Thus, social buffering may result from the release of oxytocin, which attenuates prolactin release under stress. If this is the case, injection with Atosiban (1-deamino-2-D-Tyr-(OEt)-4-Thr-8-Orn-oxytocin), a specific oxytocin antagonist, should block oxytocin and reduce social buffering. Peripheral injection of this antagonist is common, with a portion crossing the blood-brain barrier for CNS effects (Jones & Robinson, 1982; Uvnäs-Moberg, Bruzelius, Alster, & Lundeborg, 1993).

## **Method**

### **Subjects**

Seventy-eight (38 males and 40 females) adult Long-Evans Hooded rats were used in this study. Lighting was on a reversed 12:12 light:dark schedule, with the light phase beginning at 6:00 p.m. under 75 watts of white light. Temperature was maintained at 21°C, and humidity was 50%. Water and rat chow were available *ad libitum*. Rats were obtained by breeding animals from Harlan Sprague Dawley Laboratories. The day of birth was considered postnatal day (PD) 0. Litters were culled to 10 pups, and they remained with dams in Plexiglas cages (45.7 cm L x 23.5 cm W x 21 cm H) with pine bedding until weaning. On PD 21, juveniles were weaned and group-housed with same-sex littermates in the same type of Plexiglas cages until testing in adulthood. Weights on the day of testing ranged from 310 g to 540 g for males ( $M = 418.29$ ,  $SEM = 7.74$ ) and from 250 g to 310 g for females ( $M = 277.53$ ,  $SEM = 2.42$ ). All animals were acquired, maintained, and tested in accordance with the *National Institutes of Health Guide for the Care and Use of Laboratory Animals*.

### **Testing Procedure**

Between PD 96 and 109, rats were single housed in Plexiglas cages (25.4 cm L x 22.9 cm W x 21 cm H) with pine bedding and randomly assigned to testing conditions. Beginning on the day of isolation and continuing for a period of three days, 18 rats (10 males and 8 females) were individually exposed to a chamber with no shock (control group), and 60 rats (28 males and 32 females) were individually exposed to the same chamber with scrambled footshock for 10 sec at the end of a 10 min session. The chamber (Med Associates, Inc.) was made of metal on two sides with a Plexiglas front and back for viewing (25.4 cm L x 30.5 cm W x 29.2 cm H) and steel grid flooring through which 1 mA scrambled footshock was delivered. On the day of testing (the fourth day of isolation), no animals were shocked; they were merely exposed to the chamber for 10 min prior to trunk-blood collection. All animals that never received shock were placed in the control group and injected with 1 ml/kg physiological saline 1 hr prior to testing. A second group of rats (who had been shocked) were placed in the chamber alone 1 hr after saline injection. A third group of rats was injected with saline and tested with a conspecific injected with 2 mg/kg s.c. Atosiban (generously provided by Ferring Pharmaceuticals, Denmark) 1 hr prior to testing. Atosiban-treated animals comprised the fourth group. Of each pair, one rat was randomly chosen to be marked with blue ink to facilitate behavioral scoring. All testing occurred between 11:00 a.m. and 2:00 p.m. under 200 watts of red light.

Behaviors were scored to ensure that shock exposure indeed caused stress relative to controls, and instances of freezing were recorded using Etholog software. The most striking behavior in this study was a long freeze that generally occurred in the second half of testing and may have indicated that rats were fearful of impending footshock. Thus, the longest freeze duration per animal and the latency to this freeze were recorded. Animals in the paired condition always had identical freeze duration and latency; therefore, paired animals comprised one group to assess social buffering relative to the alone condition. If an animal did not freeze during testing, a score of 600 sec was given to quantify the entire testing period. For duration of longest freeze and latency to longest freeze, inter-rater reliability was .97 and .96, respectively. Observers were blind to treatment condition other than whether or not animals were alone or with a conspecific.

Within 1 min after testing ended, each rat was decapitated. In the social condition, trunk blood from both rats was collected within 2 min of testing, with the order of Atosiban- and saline-treated animals counterbalanced.

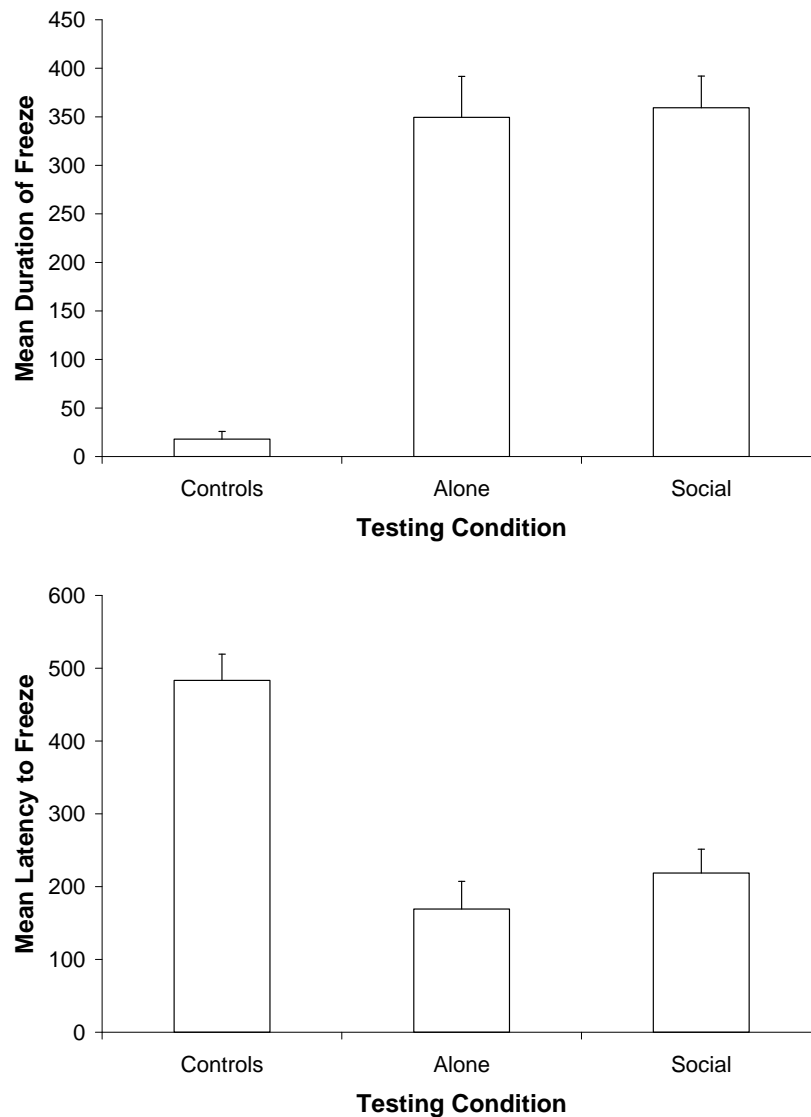
### **Hormonal Assays**

All assays followed the methodology prepared by Cayman Chemical for their EIA kits. The limit of detection for this kit is 0.2 ng/ml. All components of the assay were run in duplicate, with intra- and inter-assay variability averaging 10% and 14%, respectively.

### **Results**

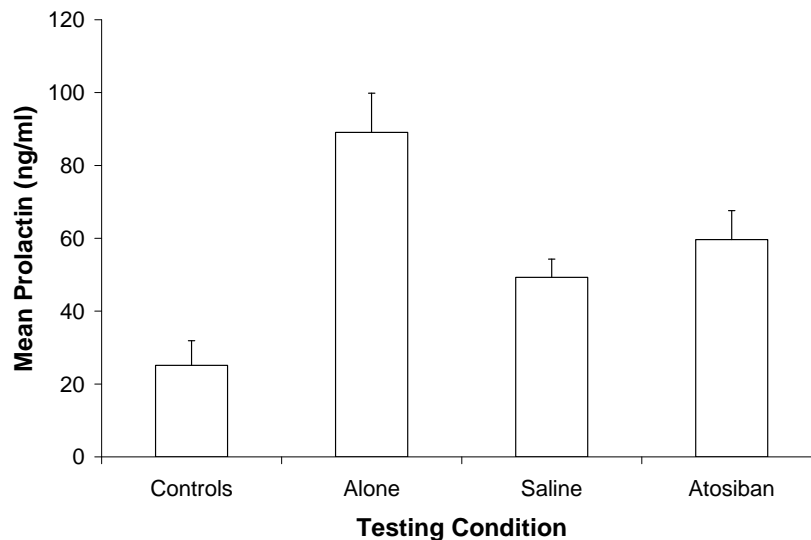
The behaviors of duration of the longest freeze and latency to that freeze were correlated,  $r(76) = -.76$ ,  $p < .001$ ; therefore, both behaviors were analyzed in a 2 x 4 MANOVA of sex and testing condition, with Tukey's *post hoc* tests for specific mean comparisons ( $p < .05$ ). Duration of the longest freeze in a testing session was related to sex,  $F(1, 72) = 5.08$ ,  $p = .027$ ,  $\eta^2 = .066$ , with males freezing for a longer bout ( $M = 324.92$ ,  $SEM = 38.26$ ,  $n = 38$ ) than females ( $M = 234.17$ ,  $SEM = 33.59$ ,  $n = 40$ ). Latency to the longest freeze was also related to sex,  $F(1, 72) = 8.05$ ,  $p = .006$ ,  $\eta^2 = .101$ , but in an opposite pattern. Males began their longest freeze more quickly ( $M = 226.18$ ,  $SEM = 34.24$ ,  $n = 38$ ) than females ( $M = 308.53$ ,  $SEM = 32.97$ ,  $n = 40$ ). As depicted in Figure 1, condition affected duration of longest freeze,  $F(2, 72) = 27.98$ ,  $p = .000$ ,  $\eta^2 = .437$ , with no-shock controls freezing for a shorter period of time ( $M = 18.02$ ,  $SEM = 7.98$ ,  $n = 18$ ) than rats tested alone ( $M = 349.54$ ,  $SEM = 42.16$ ,  $n = 18$ ) or in a social condition ( $M = 359.46$ ,  $SEM = 32.54$ ,  $n = 42$ ). Figure 1 also illustrates that latency to the longest freeze was affected by testing condition,  $F(2, 72) = 20.37$ ,  $p = .000$ ,  $\eta^2 = .361$ , with control animals having a longer latency overall ( $M = 483.29$ ,  $SEM = 36.15$ ) than the remaining two groups: rats tested alone ( $M = 169.22$ ,  $SEM = 38.24$ ) and those in a social condition ( $M = 218.83$ ,  $SEM = 32.77$ ).

**Figure 1.** When the longest bout of freezing per tested session was assessed, no-shock controls froze for less time than the remaining groups ( $p < .05$ ). For latency to the longest bout of freezing, no-shock controls had a longer average latency to freeze ( $p < .05$ ).



A 2 x 4 (sex x testing condition), between-groups ANOVA was used to analyze prolactin, and Tukey's *post hoc* comparisons revealed significant mean differences across testing condition ( $p < .05$ ). Sex was related to prolactin levels,  $F(1, 70) = 5.58, p = .021, \eta^2 = .074$ , with male levels of prolactin ( $M = 63.37$  ng/ml,  $SEM = 7.05, n = 38$ ) higher than female levels ( $M = 48.39, SEM = 7.66, n = 40$ ). Testing condition also affected prolactin levels,  $F(3, 70) = 11.76, p < .001, \eta^2 = .335$ . *Post hoc* comparisons revealed that control animals had lower levels of prolactin ( $M = 25.11, SEM = 6.75, n = 18$ ) than rats tested alone with shock ( $M = 89.11, SEM = 10.73, n = 18$ ) and those injected with Atosiban ( $M = 59.64, SEM = 7.98, n = 21$ ) prior to exposure to the chamber with a conspecific (see Figure 2). However, control animals and saline controls ( $M = 49.29, SEM = 5.03, n = 21$ ) did not differ. Animals tested alone with shock had significantly higher levels of prolactin than saline controls and those injected with Atosiban (see Figure 2). Sex and testing condition did not interact ( $p > .05$ ).

**Figure 2.** No-shock control animals had lower levels of prolactin than rats tested alone with shock and those injected with Atosiban ( $p < .05$ ). Further, rats tested alone with shock had higher levels of prolactin than saline controls and Atosiban animals ( $p < .05$ ).



## Discussion

In the present study, the CER paradigm was used to create a stressful environment based on negative past experiences. Evidence for stress was based on increased duration of freeze and decreased latency to freeze in conditioned rats. In humans, this paradigm could model increases in the experience of stress based on learning. Because the CER paradigm provides a strongly cognitive appraisal of the environment, it could be considered the most “psychological” type of the stressors. Although the animal is not truly in danger on the day of testing, the animal’s interpretation of the environment as life-threatening provides an opportunity to study prolactin responses to this strong psychological stressor.

Results of the present study extend research on prolactin responses to the CER paradigm to include female animals. Females in this study showed the same pattern of results found in males, with both sexes having higher levels of prolactin when tested alone under stress relative to those tested in the absence of CER stress. Females were allowed to cycle freely to increase mundane realism in this experiment. Although Gala (1990) has shown that stress responding in females is moderated by estrus phase, the strong stressor of conditioned fear elicited higher levels of prolactin across females overall.

The present study revealed that males had higher levels of prolactin than females. The most parsimonious explanation is based on weight; males weighed more than females, and greater weight is associated with higher levels of prolactin (Wilson, McKinley, & Young, 2000). As an alternate explanation, males may have perceived more stress than females. In addition to higher levels of prolactin overall, males froze for a longer period of time when their longest bout of freezing was assessed, and latency to that bout was shorter. Freezing is expected in the CER paradigm and has been associated with increased stress (Mast, Blanchard, & Blanchard, 1982). Thus, behavioral and hormonal data from the present study support the explanation that male rats were more reactive than females to the CER stressor.

Support for social buffering was found in males and females based on prolactin. Social buffering occurred for both saline-control and Atosiban-treated rats relative to animals shocked alone in the chamber. This result marks the first report of buffering in adult rats as measured by prolactin levels. Prior research on rats involved juveniles only (Wilson, 2000, 2001), and hormonal immaturity coupled

with low levels of prolactin limited the extent to which results could be generalized to adult animals. Further, prior research on social buffering and prolactin responses in rats exposed to stressors has relied exclusively on the open field (Wilson, 2000, 2001), the mildest of the psychological stressors (Armario et al., 1986b) and perhaps not consistently interpreted as a threat. In fact, Biondi and Picardi (1999) have suggested that neuroendocrine responses to stress may be dictated, at least in part, by our interpretations of the event, and social support may offer a buffer against psychological stress. However, the CER paradigm was a situation known to be dangerous based on prior experience; the threat was unambiguous. Even so, the presence of a conspecific reduced stress responding, indicating that social buffering may be a pervasive phenomenon not restricted to situations of questionable threat.

One alternative explanation for lower prolactin among rats tested in pairs is that animals in the social condition were not trained to expect shock in the presence of a conspecific. Therefore, it could be argued that what appeared to be social buffering was merely exposure to a new, less predictable environment on the day of testing. Future research might address this explanation by introducing a toy as a condition to see if mere distraction on the day of testing will reduce prolactin levels. A second possibility would be to train animals with shock in the presence of a conspecific, with the obvious drawback of stressing both animals. In fact, recent research indicates that a shocked conspecific increases stress responding of the target rat rather than offer social buffering (Kiyokawa, Kikusui, Takeuchi, & Mori, 2004).

If prolactin levels indeed reflected social buffering, this effect was not reflected in the behaviors assessed in the present study. Duration of freeze and latency to freeze were not different between rats in the alone condition and those in the social condition. This separation of effects is not uncommon in the stress and prolactin literature (e.g., Courvoisier, Moisan, Sarrieau, Hendley, & Mormède, 1996; Seggie, 1983; Windle et al., 1997) and might be explained by timing of hormonal vs. behavioral responses. Abel (1993) reported a peak in prolactin levels after 5 min of forced swim, but immobility peaked for animals forced to swim for 25 min. The current study was designed to maximize prolactin responses to stress, which peak at approximately 10 min after the onset of stress (Armario, Lopez-Calderon, Jolin, & Balasch, 1986a; Telner, Merali, & Singhal, 1982; Yelvington, Weiss, & Ratner, 1984). The present study also reflected large within-group variability in behaviors across treatment conditions, reducing the possibility of revealing subtle between-group differences that might be related to social buffering. Although differences in behaviors did not reach significance, prolactin in fact was positively correlated with duration of freeze,  $r(55) = .45, p = .000$ , and negatively correlated with latency to freeze,  $r(55) = -.38, p = .002$ .

A potential moderator of social buffering is oxytocin, a hormone that has been hypothesized to increase following social interactions (Uvnäs-Moberg, 1998) and one that has been shown to attenuate prolactin (Freeman, Kanyicska, Lerant, & Nagy, 2000). In the present study, injection of the oxytocin antagonist Atosiban caused higher levels of prolactin relative to controls, providing evidence that Atosiban blocked social buffering. Further, saline-treated rats did not have higher levels of prolactin than no-shock controls, signifying that social buffering returned prolactin to control levels in animals with available oxytocin. Although comparison with controls indeed indicates social buffering in saline-treated animals and attenuation of buffering in Atosiban-treated rats, it should be noted that Atosiban rats did not have significantly higher prolactin than saline controls.

The most parsimonious explanation is dose and timing of Atosiban. Prior research utilizing Atosiban has utilized primarily i.p. and s.c. injections of 1 mg/kg s.c. 30-45 min prior to data collection (e.g., Björkstrand, Eriksson, & Uvnäs-Moberg, 1992; Petersson, Lundeberg, & Uvnäs-Moberg, 1999; Uvnäs-Moberg et al., 1993). However, this dosage and timing as well as these methods of injection have not consistently yielded expected antagonism (e.g., Petersson, Alster, Lundeberg, & Uvnäs-Moberg, 1996). In addition, a great deal of variability exists, including s.c. injection of 1 mg/kg Atosiban 60 min (Björkstrand, Ahlénius, Smedh, & Uvnäs-Moberg, 1996) and 120 min before data collection (Björkstrand, Hulting, & Uvnäs-Moberg, 1997). In the current study, s.c. injections were chosen as the least stressful method of drug administration; 2 mg/kg was chosen as a slightly higher injection than previously used based on the report that only 1-2% of the drug reaches the CNS (Jones & Robinson, 1982). Injections were given 60 min prior to testing to give the drug time to be absorbed and based on

the methodology of Björkstrand and colleagues (1996). Further, Kurosawa, Lundeberg, Ågren, Lund, & Uvnäs-Moberg (1995) found that Atosiban was an effective oxytocin antagonist for up to 75 min when blood pressure was measured. Unfortunately, the majority of available research is not based on behavior, making comparisons of dosage, timing, and route of injection difficult. Perhaps differences on any of these dimensions would enhance antagonism of oxytocin in a social setting.

A second possible explanation for no difference between Atosiban- and saline-treated animals is based on testing these two groups of animals together. It could be argued that saline controls did not receive optimum social buffering from Atosiban animals. However, research strongly indicates that touching affects prolactin, at least in the open field, with touch decreasing prolactin (Wilson, 2001). Therefore, it was imperative that pairs of animals experience identical duration and latency of touch. This could only be ensured by testing each pair together.

Several mechanisms for the control of prolactin have been reviewed by Freeman and colleagues (2000). One possible mechanism involves the tuberoinfundibular (TIDA) region of the hypothalamus. TIDA neurons release dopamine (DA), the primary prolactin inhibiting factor (PIF), to the external layer of the median eminence, which outputs to the anterior pituitary through the long portal veins, thereby inhibiting prolactin secretion by lactotrophs found in the anterior lobe. With stimulation from oxytocin, TIDA neurons should secrete more DA and inhibit prolactin release from the anterior pituitary. Indeed, activation of TIDA neurons by oxytocin has been shown to decrease prolactin and stress (Mormede, Vincent, & Kerdelhue, 1986; Muir & Pfister, 1987). In the current study, Atosiban blocked social buffering, perhaps through CNS inhibition of oxytocin. In turn, dopamine, the primary prolactin-inhibiting factor, may have been less available to attenuate prolactin.

Although the TIDA system seems a likely candidate for the control of prolactin responses during stress, the eventual role of prolactin during stress is not yet clear. Prolactin does not seem to be necessary for immune-system function in healthy, nonstressed animals (Foster et al., 2000), but it stimulates immune function during stress (Freeman et al., 2000). Lower levels of prolactin appear to fuel immune function such that the immune system is enhanced, perhaps through counteracting the negative effects of glucocorticoids (Dorshkind & Horseman, 2000). However, higher levels of prolactin tend to compromise the immune system based at least in part on data concerning the involvement of prolactin in autoimmune diseases (Dorshkind & Horseman, 2000). Social buffering during stress could serve to lower prolactin to levels associated with positive immune function, and oxytocin may facilitate this benefit.

Thus, the interplay among prolactin, oxytocin, and social interaction may provide insight into at least one mechanism responsible for functioning in a stressful environment. Given the paucity of experimental research in the area of social buffering, additional research would help to provide a foundation for the protective influences of social interactions during stress. For example, injections of Atosiban (or similar substances) directly into the CNS would more directly assess the role of central oxytocin systems in social buffering. The ability for oxytocin to facilitate social buffering may eventually allow clinical applications such as providing medications to stimulate oxytocin systems in patients who have limited social contacts (e.g., elderly patients with restricted mobility).

## **Conclusions**

The results of this study extend the available literature in three ways. First, female rats respond to the CER chamber in the same manner as male animals, with higher levels of prolactin than controls. Second, social buffering occurs in adult rats exposed to the CER stressor. Third, oxytocin systems may be involved in social buffering. In particular, Atosiban blocks social buffering as measured by prolactin levels.

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## Literature Cited

- Abel, E. L. (1993). Physiological correlates of the forced swim test in rats. *Physiology & Behavior*, *54*, 309-317.
- Armario, A., Lopez-Calderon, A., Jolin, T., & Balasch, J. (1986a). Response of anterior pituitary hormones to chronic stress: The specificity of adaptation. *Neuroscience & Biobehavioral Reviews*, *10*, 245-250.
- Armario, A., Lopez-Calderon, A., Jolin, T., & Castellanos, J. M. (1986b). Sensitivity of anterior pituitary hormones to graded levels of psychological stress. *Life Sciences*, *39*, 471-475.
- Amario, A., Marti, O., Molina, T., de Pablo, J., & Valdes, M. (1996). Acute stress markers in humans: Response of plasma glucose, cortisol and prolactin to two examinations differing in the anxiety they provoke. *Psychoneuroendocrinology*, *21*, 17-24.
- Biondi, M., & Picardi, A. (1999). Psychological stress and neuroendocrine function in humans: The last two decades of research. *Psychotherapy & Psychosomatics*, *68*, 114-150.
- Biondi, M., Pancheri, P., Falaschi, D., Teodori, A., Paga, G., Delle Chiaie, R., DiCasare, G., & Proietti, A. (1986). Social support as a moderator of the psychobiological stress response. *New Trends Experimental and Clinical Psychiatry*, *2*, 173-183.
- Björkstrand, E., Ahlénus, S., Smedh, U., & Uvnäs-Moberg, K. (1996). The oxytocin receptor antagonist 1-deamino-2-D-Tyr-(OEt)-4-Thr-8-Orn-oxytocin inhibits effects of the 5-HT<sub>1A</sub> receptor agonist 8-OH-DPAT on plasma levels of insulin, cholecystokinin and somatostatin. *Regulatory Peptides*, *63*, 47-52.
- Björkstrand, E., Eriksson, M., & Uvnäs-Moberg, K. (1992). Plasma levels of oxytocin after food deprivation and hypoglycaemia, and effects of 1-deamino-2-D-Tyr-(OEt)-4-Thr-8-Orn-oxytocin on blood glucose in rats. *Acta Physiologica Scandinavica*, *144*, 355-359.
- Björkstrand, E., Hulting, A., & Uvnäs-Moberg, K. (1997). Evidence for a dual function of oxytocin in the control of growth hormone secretion in rats. *Regulatory Peptides*, *69*, 1-5.
- Carter, C. S., & Altemus, M. (1997). Integrative functions of lactational hormones in social behavior and stress management. *Annals of the New York Academy of Sciences*, *807*, 164-174.
- Castro, W. L. R., & Matt, K. S. (1997). The importance of social condition in the hormonal and behavioral responses to an acute social stressor in the male Siberian dwarf hamster (*Phodopus sungorus*). *Hormones & Behavior*, *32*, 209-216.
- Courvoisier, H., Moisan, M., Sarrieau, A., Hendley, E. D., & Mormède, P. (1996). Behavioral and neuroendocrine reactivity to stress in the WKHA/WKY inbred rat strains: A multifactorial and genetic analysis. *Brain Research*, *743*, 77-85.
- Dijkstra, H., Tilders, F. J., Hiehle, M. A., & Smelik, P. G. (1992). Hormonal reactions to fighting in rat colonies: Prolactin rises during defense, nor during offense. *Physiology & Behavior*, *51*, 961-968.
- Dorshkind, K., & Horseman, N. D. (2000). The roles of prolactin, growth hormone, insulin-like growth factor-I, and thyroid hormones in lymphocyte development and function: Insights from genetic models of hormone and hormone receptor deficiency. *Endocrine Reviews*, *21*, 292-312.
- Foster, M. P., Jensen, E. R., Montecino-Rodriguez, E., Leathers, H., Horseman, N., & Dorshkind, K. (2000). Humoral and cell-mediated immunity in mice with genetic deficiencies of prolactin, growth hormone, insulin-like growth factor-I, and thyroid hormone. *Clinical Immunology*, *96*, 140-149.
- Freeman, M. E., Kanyicska, B., Lerant, A., & Nagy, G. (2000). Prolactin: Structure, function, and regulation of secretion. *Physiological Reviews*, *80*, 1523-1631.

- Gala, R. R. (1990). The physiology and mechanisms of the stress-induced changes in prolactin secretion in the rat. *Life Sciences*, *46*, 1407-1420.
- Gerritsen, W., Heijnen, C. J., Weigant, V. M., Bermond, B., & Frijda, N. H. (1996). Experimental social fear: Immunological, hormonal, and autonomic concomitants. *Psychosomatic Medicine*, *58*, 273-286.
- Hennessey, M. B. (1986). Effects of social partners on pituitary-adrenal activity during novelty exposure in adult female squirrel monkeys. *Physiology & Behavior*, *38*, 803-807.
- Jones, P. M., & Robinson, I. C. A. F. (1982). Differential clearance of neurophysin and neurohypophysial peptides from the cerebrospinal fluid of conscious guinea pigs. *Neuroendocrinology*, *34*, 297-302.
- Kant, G. J., Meyerhoff, J. L., Bunnell, B. N., & Lenox, R. H. (1982). Cyclic AMP and cyclic GMP response to stress in brain and pituitary: Stress elevates pituitary cyclic AMP. *Pharmacology, Biochemistry, & Behavior*, *17*, 1067-1072.
- Kikusui, T., Winslow, J. T., & Mori, Y. (2006). Social buffering: Relief from stress and anxiety. *Philosophical Transactions of the Royal Society of London, Series B, Biological Sciences*, *361*, 2215-2228.
- Kirschbaum, C., Klauer, T., Filipp, S. H., & Hellhammer, D. H. (1995). Sex-specific effects of social support on cortisol and subjective responses to acute psychological stress. *Psychosomatic Medicine*, *57*, 23-31.
- Kiyokawa, Y., Kikusui, T., Takeuchi, Y., & Mori, Y. (2004). Partner's stress status influences social buffering effects in rats. *Behavioral Neuroscience*, *118*, 798-804.
- Kurosawa, M., Lundeberg, T., Ågren, G., Lund, I., & Uvnäs-Moberg, K. (1995). Massage-like stroking of the abdomen lowers blood pressure in anesthetized rats: Influence of oxytocin. *Journal of the Autonomic Nervous System*, *56*, 26-30.
- Levine, S. (1993). The influence of social factors on the response to stress. *Psychotherapy and Psychosomatics*, *60*, 33-38.
- Lorens, S. A., Hata, N., Handa, R. J., Van de Kar, L. D., Guschwan, M., Goral, J., Lee, J. M., Hamilton, M. E., Bethea, C. L., & Clancy, J. (1990). Neurochemical, endocrine and immunological responses to stress in young and old Fischer 344 male rats. *Neurobiology of Aging*, *11*, 139-150.
- Mast, M., Blanchard, R. J., & Blanchard, D. C. (1982). The relationship of freezing and response suppression in a CER situation. *Psychological Record*, *32*, 151-167.
- Mormede, P., Vincent, J. D., & Kerdelhue, B. (1986). Vasopressin and oxytocin reduce plasma prolactin levels of conscious rats in basal and stress conditions. Study of the characteristics of the receptor involved. *Life Sciences*, *39*, 1737-1743.
- Muir, J. L., & Pfister, H. P. (1987). Time course of the corticosterone and prolactin response following predictable and unpredictable novelty stress in *Rattus norvegicus*. *Physiology & Behavior*, *40*, 103-107.
- Orr, T. E., Meyerhoff, J. L., Mougey, E. H., & Bunnell, B. N. (1990). Hyperresponsiveness of the rat neuroendocrine system due to repeated exposure to stress. *Psychoneuroendocrinology*, *15*, 317-328.
- Panksepp, J., Nelson, E., & Bekkedal, M. (1997). Brain systems for the mediation of social separation-distress and social-reward. *Annals of the New York Academy of Sciences*, *807*, 78-100.

- Paris, J. M., Lorens, S. A., Van de Kar, L. D., Urban, J. H., Richardson-Morton, K. D., & Bethea, C. L., 1987. A comparison of acute stress paradigms: Hormonal responses and hypothalamus serotonin. *Physiology & Behavior*, 39, 33-43.
- Petersson, M., Alster, P., Lundeberg, T., & Uvnäs-Moberg, K. (1996). Oxytocin increases nociceptive thresholds in a long-term perspective in female and male rats. *Neuroscience Letters*, 212, 87-90.
- Petersson, M., Lundeberg, T., & Uvnäs-Moberg, K. (1999). Short-term increase and long-term decrease in blood pressure in response to oxytocin-potentiating effect of female steroid hormones. *Journal of Cardiovascular Pharmacology*, 33, 102-108.
- Seggie, J. (1983). Corticomedial amygdale lesions, behavior, corticosterone, and prolactin: Unexpected separation of effects. *Journal of Psychiatry Research*, 10, 139-150.
- Stanton, M. E., Patterson, J. M., & Levine, S. (1985). Social influences on conditioned cortisol secretion in the squirrel monkey. *Psychoneuroendocrinology*, 10, 125-134.
- Telner, J. I., Merali, S., & Singhal, R. L. (1982). Time-dependent changes in plasma prolactin level and stress controllability in rats. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, 6, 459-462.
- Thorsteinsson, E. B., James, J. E., & Gregg, M. E. (1998). Effects of video-relayed social support on hemodynamic reactivity and salivary cortisol during laboratory-based behavioral challenge. *Health Psychology*, 17, 436-444.
- Uvnäs-Moberg, K. (1998). Oxytocin may mediate the benefits of positive social interaction and emotions. *Psychoneuroendocrinology*, 23, 819-835.
- Uvnäs-Moberg, K., Bruzelius, G., Alster, P., & Lundeberg, T. (1993). The antinociceptive effect of non-noxious sensory stimulation is mediated partly through oxytocinergic mechanisms. *Acta Physiologica Scandinavica*, 149, 199-204.
- Van de Kar, L. D., Lorens, S. A., Urban, J. H., Richardson, K. D., Paris, J., & Bethea, C. L. (1985). Pharmacological studies on stress-induced renin and prolactin secretion: Effects of benzodiazepines, naloxone, propranolol and diisopropyl fluorophosphate. *Brain Research*, 345, 257-263.
- Wilson, J. H. (2000). A conspecific attenuates prolactin responses to open-field exposure in rats. *Hormones & Behavior*, 38, 39-43.
- Wilson, J. H. (2001). Prolactin in rats is attenuated by conspecific touch in a novel environment. *Cognitive, Affective, & Behavioral Neuroscience*, 1, 199-205.
- Wilson, J. H., McKinley, S. A., & Young, B. L. (2000). Prolactin levels in juvenile and adult rats following acute restraint and the open field. *Physiology & Behavior*, 68, 383-387.
- Windle, R. J., Wood, S., Shanks, N., Perks, P., Conde, G. L., & da Costa, A. P. C. (1997). Endocrine and behavioural responses to noise stress: Comparison of virgin and lactating rats during non-disrupted maternal activity. *Journal of Neuroendocrinology*, 9, 407-414.
- Yelvington, D. B., Weiss, G. K., & Ratner, A. (1984). Effect of corticosterone on the prolactin response to psychological and physical stress in rats. *Life Sciences*, 35, 1705-1711.