21

Affiliative Responses to Stress

A SOCIAL NEUROSCIENCE MODEL

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When scientists choose a metaphor to characterize stress, they usually pick "fight or flight." This characterization of stress response seems incomplete when one realizes that humans have few of the physical resources necessary to fight or flee. Humans do not have sharp teeth, claws, or thick skin. We are slow of foot and unable to fly or hide under water. One advantage humans do have is the impulse to affiliate with others, and we propose that this is a core aspect of human responses to stress. Human survival has depended on group living, and manifold evidence shows that under conditions of threat, human beings come together to protect one another (Caporeal, 1997). On the one hand, this observation is so obvious that it scarcely needs documentation. Despite this fact, until recently little attention has been devoted to understanding why humans affiliate under stress and the biological underpinnings of that affiliation.

We begin this chapter by characterizing existing models of stress responses, focusing on the fight-or-flight response. We then describe a biobehavioral model of affiliative responses to stress that our laboratory has been developing over the past few years. From animal studies and our own data, we infer that there is an affiliative system that signals the need for affiliation, especially in response to stress, in some animal species and in humans. We suggest that elevations in the neuropeptide oxytocin (OT) may act as a biological marker, indicating that social affiliations have fallen below an adequate level to meet current challenges. This might occur, for

example, if there were chronic gaps in one's social network, such as separation or a loss of companionship, or it might occur in response to externally imposed demands from the environment, such as those resulting from stress or threats. Once signaled, the need for social contacts is met through purposeful social behavior, such as affiliation. Supportive affiliative contacts reduce biological and psychological stress responses, but contact with hostile or nonsupportive others in times of stress can augment these stress responses. The vital importance of quality of social ties in stressful circumstances points to a need to understand the mechanisms that prompt affiliation under stress.

We hypothesize that OT may act, roughly, as a social thermostat that is responsive to adequacy of social resources, which prompts affiliative behavior when social resources fall below an adequate level and which reduces biological and psychological stress responses once positive social contacts are (re)established. Although some of the links in the model are currently speculative, the bones of a model that may characterize affiliative processes, especially in response to stress, appear to be in place.

RESPONSES TO STRESS: FIGHT OR FLIGHT

The dominant conception of human and animal biobehavioral responses to stress has been the fight-or-flight response (Cannon, 1932). Fight or flight has two aspects—a behavioral component and a biological component. The behavioral component of fight or flight is obvious: In response to a threat, one can become aggressive and mount an antagonistic response to the threatening circumstances or one can flee, either literally or metaphorically. Among the responses that contemporary stress researchers interpret as flight behavior are coping strategies such as social withdrawal and patterns of substance use, especially drug and alcohol abuse.

The biological component of fight or flight depends on two interacting stress systems, the sympathetic nervous system and the hypothalamic–pituitary–adrenocortical (HPA) axis. The actions of the sympathetic–adrenomedullary (SAM) system are mediated primarily by the catecholamines norepinephine and epinephrine, which exert effects on adrenergic receptors in target tissues to produce, among other changes, increases in heart rate and blood pressure, dilation of the airways, and enhanced availability of glucose and fatty acids for energy. These coordinated responses facilitate short-term mobilization of an organism's resources for rapid, intense physical activity. Threatening stressors also engage the HPA axis. Corticotropin-releasing hormone (CRH), produced in the paraventricular nuclei (PVN) of the hypothalamus, stimulates the secretion of adrenocorticotropic hormone (ACTH) by the anterior pituitary, resulting in the release of glucocorticoids, such as cortisol. Glucocorticoids serve an important function at low basal levels by permitting or restoring processes that

prime homeostatic defense mechanisms. This integrated pattern of HPA-axis activation modulates a wide range of functions, including energy release and immune activity.

These two systems are important because they account for both the protective effects of stress responses and their long-term costs. Together these systems shunt reserves of energy for fight or flight, and the subjective experience is arousal and often fear or anxiety. As such, these responses have short-term benefits under stressful circumstances because they mobilize the body to meet the demands of pressing situations and then prime homeostatic mechanisms that restore the body to its previous functioning. With repeated or recurrent stress, however, biological stress responses can have long-term costs that have implications for health (McEwen, 1998). For example, excessive or repeated discharge of epinephrine or norepinephrine can lead to the suppression of cellular immune function, produce hemodynamic changes such as chronic increases in blood pressure, and provoke abnormal heart rhythms. Glucocorticoids have immunosuppressive effects, and stress-related increases in cortisol have been tied to an increased susceptibility to infectious disorders (Cohen et al., 2002). More long-lasting elevations in glucocorticoids, such as occur in chronically or recurrently stressful environments, are prognostic for the development of hypertension, cardiovascular disease, and insulin resistance, enhancing risk for diabetes, among other disorders (McEwen & Lasley, 2002).

Research on human responses to stress has focused on fight or flight, both because it was one of the earliest responses to stress identified by research and because the scientific study of stress is based heavily on animal studies, which provide ample evidence for fight or flight. When stress researchers began to study stress in human beings, they borrowed from the animal paradigm in ways conducive to identifying fight-or-flight responses in humans as well (see Taylor et al., 2000, for a review). Although fighting and fleeing are unquestionably in the repertoire of human responses to threats and stress, there are at least two reasons to suspect that they are unlikely to be the only responses, and perhaps not even the dominant responses. First, fighting could leave vulnerable offspring at risk for predation. Fleeing, likewise, may have been impractical because abandoning a young infant would almost always be fatal to the offspring, and fleeing with an infant or young toddler might slow the caregiver down enough to be at enhanced risk for attack. Human beings would not have survived as a species had they not developed stress responses that protected their offspring in times of danger.

Moreover, fighting or fleeing may not be humans' best defense against predators. Humans evolved in small hunter–gatherer groups. Coming together as a group, instead of fleeing or fighting on one's own, would provide more hands for defense and perhaps confuse or intimidate a predator. These groups would have provided advantages in the face of other stressors as well, such as information about resource location. In short, there are

good reasons to think humans have evolved to use social relationships as a primary resource to deal with stressful circumstances.

TEND AND BEFRIEND

To address social responses to stress, our laboratory has been working with the metaphor "tend and befriend" (Taylor, 2002; Taylor et al., 2000). Our position is that under conditions of stress, tending to offspring and affiliating with others (what we call befriending) are at least as common responses to stress in humans as fight or flight.

From animal studies and our own data, we infer that there is an affiliative neurocircuitry that prompts affiliation, especially in response to stress, in many animal species, and especially in humans. We suggest that this system regulates social-approach behavior and does so in much the same way as occurs for other appetitive needs. That is, just as people have basic needs, such as hunger, thirst, sexual drives, and other appetites, they also need to maintain an adequate level of protective and rewarding social relationships.

Just as occurs for these other appetites, we suggest that there is a biological signaling system that comes into play if one's affiliations fall below an adequate level. Once signaled, the appetitive need is met through purposeful social behavior, such as affiliation. If social contacts are hostile or unsupportive, then psychological and biological stress responses are heightened. If social contacts are supportive and comforting, stress responses decline. Positive contacts then lead to a decline in need and, in the context of stress, a decline in stress responses. The fact that affiliation may look very much like other appetitive needs is not coincidental. Because biological neurocircuitries tend to be efficient, the dopamine and opioid systems that are recruited for other reward-based systems are likely to be recruited for the satisfaction of affiliative needs, as well (see Depue & Morrone-Strupinksy, 2005).

In building our model, we have focused heavily on OT and the opioid system (see Figure 21.1). We maintain that OT and opioids are released in response to (at least some) stressors, especially those that may trigger affiliative needs; OT prompts affiliative behavior in response to stress, in conjunction with dopaminergic and opioid systems; and OT, in conjunction with positive social contacts, attenuates biological stress responses (SNS, HPA axis) that can arise in response to social threats. This OT–opioid–dopaminergic system is an appetitive system that regulates social approach behavior and recruits the neurocircuitry for reward in its enactment. Finally, we suggest that some of the health benefits associated with social support and social integration may be mediated by this appetitive social-approach system via attenuation of threat responses. We address each of these links.

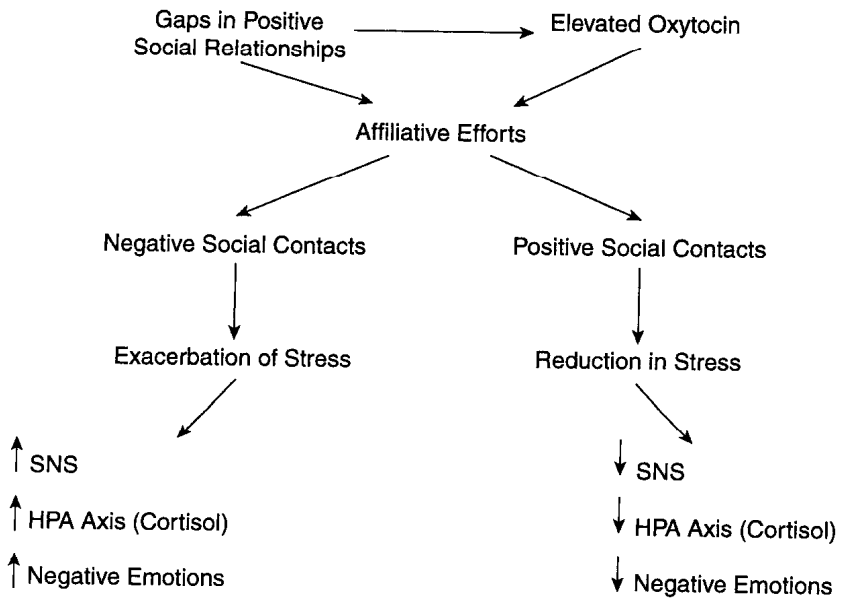


FIGURE 21.1. A model of affiliative responses to stress.

SEPARATION DISTRESS AND OPIOID FUNCTIONING

Affiliation is vital to the survival of human beings. Accordingly, there are likely to be biobehavioral mechanisms that are sensitive to social threats or loss of social contact, resulting in social distress and consequent efforts to remedy the situation. A paradigm for such a system is separation distress, which has been studied primarily in young animals and human infants. When the young are separated from the mother, separation distress in offspring can result, especially during particular developmental periods. The experience of separation leads to distress vocalizations (e.g., crying in human infants or active searching for the caregiver in toddlers) that may prompt the return of the caregiver.

This system appears to depend, in part, on brain opioids. Evidence consistent with this pathway includes the fact that brain opioids reduce separation distress and that drugs such as morphine reduce distress vocalizations in animals (Panksepp, 1998). In experimental animal studies, opioid consumption can be increased by depriving animals of companionship (Alexander, Coambs, & Hadaway, 1978). Mice that lack the μ-opioid receptor gene emit fewer distress vocalizations when separated from their mothers, further suggesting that endogenous opioid binding is a significant basis of infant attachment behavior (Moles, Kieffer, & D'Amato, 2004). From data such as these, researchers have inferred that the neurocircuitry for social pain draws on the neurocircuitry for physical pain, a hypothesis

that has recently been lent additional credibility by neuroimaging studies in humans (Eisenberger, Lieberman, & Williams, 2003). Opioids also appear to be involved in the experience of positive social interaction (Panksepp, 1998). OT may underlie some of these processes as well, as we next suggest.

OXYTOCIN AND SOCIAL DISTRESS

OT is a hypothalamic neuropeptide that is implicated in human and animal stress responses (Miaskowski, Ong, Lukic, & Haldar, 1988). Although its exact role in stress processes has not been fully identified, its potential role in modulating psychological and biological stress responses has garnered particular scientific interest (Taylor et al., 2000).

Researchers have theorized that OT is implicated in infant bonding and in processes involving separation and reunification (Panksepp, 1998). For example, Nelson and Panksepp (1996) separated rat pups from their mothers for several hours and then reunited them for half an hour. Before each reunion, the mothers' ventral surface was sprayed with a distinctive odor; control animals were reunited with a cotton pad permeated with the same order. Following 3 days of this testing, the pups were tested for attraction to the conditioned odor. Only pups that had been reunited with the mothers showed selective approach and attraction to the odor. The attraction was blocked in animals that had received an OT antagonist, suggesting that OT is implicated in this pattern. Thus there appears to be a role for OT in the neurocircuitry that underlies separation and reunification.

Our research has focused on the role of OT in social distress in adults. Adults, as well as infants and young children, experience gaps in their social relationships and may experience an analog of separation distress, which may implicate the same biological systems as in the young. OT is known to be released in response to some stressors (Sapolsky, 1992), but, in humans, the kinds of stress that may be associated with OT have, until recently, been largely unknown. Drawing on the literature relating OT to separation distress, we hypothesized that elevated OT may be a marker of the need for positive social contact (Taylor et al., 2006).

To examine these processes, we assessed the stress responses of older women who either were or were not on hormone therapy (Taylor et al., 2006). Levels of OT are strongly augmented by estrogen, and so animal studies that have examined the effects of OT often use estrogen-treated females (McCarthy, 1995). Postmenopausal women are a human analog for this paradigm, because postmenopausal women produce little or no estrogen, whereas women who are on hormone therapy receive a dose of estrogen every day. Accordingly, a sample that has substantial variability in estrogen levels is likely to also produce substantial variability in OT, as was

true in our work. As such, one may see what OT's role may be with respect to stress (Taylor et al., 2006).

To test our hypothesis that OT is a marker for social distress, we gave women measures of psychological and social functioning and related their responses to levels of OT. The questionnaires included assessments of gaps in relationships (that is, whether the women had experienced any decline in their contacts with significant others) and assessments of how positive and how negative their relationships with significant others were. For comparative purposes, the women filled out a detailed assessment of psychological distress, the Symptom Checklist–90 (SCL-90; Derogatis & Spencer, 1982), as well as a self-esteem scale (Rosenberg, 1965).

Women who were experiencing gaps in their social relationships had elevated levels of OT, as we had predicted. In particular, women with higher levels of OT were more likely to report reduced contact with their mothers, with their best friends, with a pet, and with the social groups of which they were a part. OT levels were sensitive to the absence of positive relations with the partner, as well. Women who reported that their husbands were not supportive were more likely to have high levels of OT. Specifically, women with high levels of OT reported that their husbands were less likely to understand the way they felt about things and less likely to care for them and that they could not open up to their husbands if they needed to share their concerns. Poor quality of the marital relationship and infrequent display of affection by one's partner were also associated with higher levels of OT. These findings suggest that OT may be sensitive to the absence of positive aspects of significant social relationships.

Similar results were found by Turner and her colleagues (Turner, Altemus, Enos, Cooper, & McGuinness, 1999), who looked at the relation of OT to social relationships in a sample of young women. They found that elevated OT was associated with anxiety over relationships, with perceived coldness or intrusiveness of relationships, and with not being in a primary romantic relationship. Taken together, these two studies (Taylor et al., 2005; Turner et al., 1999) are consistent with the inference that OT may signal gaps or problems in social support.

However, to make this case requires several additional steps. First, one would have to rule out the possibility that OT is simply related to any kind of distress. We found that OT was not related to self-esteem or to general psychological distress, only to gaps in or problems with positive relationships. This evidence for discriminant validity suggests that the distress that OT signals may be distinctively social in nature. A second step for establishing discriminant validity would be to show that OT is related to social distress and that other stress hormones are not. As a comparison, we examined the relation of cortisol to the social indicators that were associated with OT. None of the correlations was significant.

Because we did not manipulate levels of OT, there is a possibility that causality goes in the other direction. Although the alternative direction of

causality cannot be entirely ruled out, some data are inconsistent with it. The women with high levels of OT were more likely to have recently lost their mothers or their pets to death, or in the case of their mothers, to mental and physical deterioration. It is unlikely that women high in OT would be more likely than other women to experience the deaths or deterioration of their mothers or their pets. Consequently, it is more likely that elevated OT is a marker of gaps in positive relationships.

Our portrayal of OT as a stress hormone that is naturally elevated in response to social distress conflicts sharply with the characterization of OT that has appeared in some of the scientific literature and much of the popular literature. A substantial amount of research has documented the anxiolytic effects of OT (McCarthy, 1995), tying OT to a relaxed, calm psychological state. This view of the "emotional" underpinnings of OT has also found its way into the popular literature, in which OT has, for example, been characterized as a "feel-good" or "cuddling" hormone (e.g., *CBS Evening News*, May 19, 2000), among similar characterizations.

There are at least two possible reconciliations of these seemingly opposing views. One possibility is that basal OT reflects social distress but that OT pulsatility is associated with calm and companionable feelings (Turner et al., 1999). OT pulsatility, as induced exogenously and in conjunction with affiliation, may produce the anxiolytic effects of OT that have been so widely documented in the experimental animal literature (McCarthy, 1995). A second possibility stems from the fact that past research has not consistently disentangled the effects of OT from the effects of affiliative contact. The pleasurable feelings credited to OT may be due instead to its positive affiliative consequences and/or to OT's impact on other aspects of the affiliative neurocircuitry, for example, modulation of pathways that implicate reward, such as the mesolimbic dopamine and opioid systems (Depue & Morrone-Strupinsky, 2005; Young, Lim, Gingrich, & Insel, 2001). That is, returning to our model (Figure 21.1), it may be the case that OT initially signals distress and subsequently induces affiliative efforts, which result in affiliative contact. If those contacts are supportive, then affiliation should produce accompanying positive feelings, perhaps underpinned by dopamine and opioid involvement.

RELATION OF OT AND OPIOIDS TO AFFILIATION

If OT is related to social distress, as we suggest, then as an affiliative hormone, OT may provide an impetus for social contact to ameliorate stress. Taylor et al. (2000) raised this possibility in their tend-and-befriend account of female responses to stress. Specifically, we hypothesized that the seeking of social support in response to stress may be mediated, in part, by the release of OT in response to stress.

Manifold evidence, most of which has come from animal studies, relates OT to affiliation. In a typical study, a rat, monkey, or sheep is injected with OT, and the impact on behavior is observed. Exogenous administration of OT has been found to increase maternal behavior in several species (see Carter, Lederhendler, & Kirkpatrick, 1999; Fahrbach, Morrell, & Pfaff, 1985; Kendrick, Keverne, & Baldwin, 1987). Opioid mechanisms are also implicated in these processes. Administration of opioid antagonists, for example, such as naloxone or naltrexone, results in less caregiving and protective behavior toward infants in rhesus monkeys (Martel, Nevison, Rayment, Simpson, & Keverne, 1993), inhibits maternal behavior in sheep (Kendrick & Keverne, 1989), and diminishes the attractive qualities of conditioned maternal cues in rats (Panksepp, Nelson, & Bekkedal, 1999). The facts that OT is elevated in response to at least some stressors and that it provides an impetus for maternal behavior represent important links for the "tending" aspect of the tend-and-befriend model (Taylor, 2002; Taylor et al., 2000). Specifically, it suggests that OT may function both as a stress indicator and as an impetus for protection of offspring.

Animals demonstrate a preference for other animals in whose presence they have previously experienced high brain OT and opioid activity, suggesting that companionship has some of the same biological underpinnings as maternal–infant bonding (Panksepp, 1998). Social contact is enhanced and aggression is diminished following OT treatment in estrogen-treated female prairie voles (Witt, Carter, & Walton, 1990), and the exogenous administration of OT in rats causes an increase in social contact and in grooming (Carter, De Vries, & Getz, 1995; Drago, Pederson, Caldwell, and Prange, 1986; Witt, Winslow, & Insel, 1992).

With reference to humans, Carter (1998) suggested that OT may be at the core of many affiliative contacts, including mother–infant attachments, adult pair bonds, and friendships. However, in humans, the relation of OT to affiliative behavior is somewhat more conjectural, in part because it is hard to get at OT's central nervous system activity in humans. As a result, researchers have related OT to behaviors observed in people with naturally high levels of OT, especially nursing mothers (e.g., Light et al., 2000), or have administered OT exogenously. Despite the complexities of tests in humans, OT is thought to underlie social bonding, including initial formation of adult pair bonds (Panksepp, 1998).

Opioid involvement is implicated in affiliative activity as well. Jalowiec, Calcagnetti, and Fanselow (1989), for example, found that administration of an opioid antagonist suppressed juvenile social behavior. Opioid-blocking agents also lead to reduced social activity and grooming in animals. For example, Martel et al. (1993) administered naltrexone to female rhesus monkeys and observed a decline in social grooming. Opioid mechanisms appear to be implicated in human affiliative responses as well. Jamner, Alberts, Leigh, and Klein (1998) administered naltrexone to col-

lege students and found that, in women only, it increased the amount of time that women spent alone, reduced the amount of time they spent with friends, reduced the likelihood that they would contact their friends, and reduced the pleasantness of their interactions with friends. It thus appears that a fairly broad array of affiliative behaviors may be subserved by OT and opioid mechanisms.

OT and opioids, then, are implicated in affiliative behaviors, a fact that takes on particular significance in the context of stress. McCarthy (1995) has suggested that, for animals to exhibit social responses to stress, arousal must be sufficiently controlled to avoid the aggression or flight behavior that might otherwise ensue. Similarly, Taylor (Taylor, 2002; Taylor et al., 2000) has suggested that at least partial inhibition of the fight-or-flight response may be required for tending-and-befriending activities to be initiated. Thus one would expect to see evidence that, over time, OT in conjunction with opioids leads to affiliative contact, which, when positive, leads to reduced stress responses.

RELATION OF OT AND OPIOID FUNCTIONING TO STRESS RESPONSES

OT has been related to reduced autonomic activity and HPA-axis responses to stress. In species as varied as rats, sheep, and prairie voles, exogenous administration of OT or stimulation of OT secretion via stroking has been found to decrease sympathetic reactivity (Uvnäs-Moberg, Ahlenius, Hillegaart, & Alster, 1994), blood pressure (Petersson, Alster, Lundeberg, & Uvnäs-Moberg, 1996), pain sensitivity, and corticosterone levels, among other findings suggestive of a reduced stress response (Carter, 1998; Insel, 1997; Uvnäs-Moberg, 1997; Uvnäs-Moberg et al., 1994).

As noted earlier, a substantial amount of research has also documented the anxiolytic effects of OT (McCarthy, 1995). For example, experimental evidence from animal studies suggests that exogenous administration of OT enhances sedation and relaxation (Uvnäs-Moberg, et al., 1994). OT has also been tied to behavioral signs of reduced fearfulness (such as less freezing and more exploration) among female rodents in open field tests (Mantella, Vollmer, Li, & Amico, 2003; McCarthy, 1995).

Although the stress-reducing properties of OT are less well documented in humans, the existing research is consistent with the evidence from animal studies. High levels of OT or exogenous administration of OT in humans produces decreases in sympathetic activity (e.g. Light et al., 2000; Uvnäs-Moberg, 1997) and inhibits the secretion of adrenocorticotropic hormone (ACTH) and cortisol (Altemus, Deuster, Gallivan, Carter, & Gold, 1995; Chiodera & Legros, 1981). For example, Heinrichs, Baumgartner, Kirschbaum, and Ehlert (2003) administered or did not administer OT to 37 men via nasal spray and found reduced anxiety and

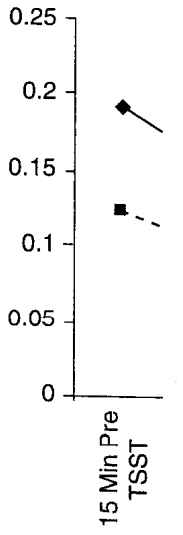
lower cortisol levels during the course of a laboratory stress challenge (the Trier Social Stress Task; TSST) among those who had received OT; the reduced cortisol response was especially pronounced in those men who also experienced social support from a friend. Studies comparing breast-feeding mothers (in whom OT levels are high) with bottle-feeding mothers have found lower anxiety among the breast-feeding mothers (Virden, 1988) and lower anxiety, depression, stress, and guilt following breast feeding (which prompts OT release) as compared with bottle feeding (Modahl & Newton, 1979).

The inhibitory action of OT on cortisol secretion may be due to hypophysial inhibition of ACTH release, as well as to effects at the adrenal gland level (Legros, Chiodera, & Geenen, 1988). OT also increases the sensitivity of brain opioid systems. If OT injection is accompanied by naloxone, cortisol levels do not change, but OT administration alone leads to significant reduction in cortisol secretion (Coiro et al., 1985). These findings suggest that some of the antistress properties of OT may be mediated by an opioid pathway.

Thus the evidence that OT attenuates stress responses is strong in animal studies and highly suggestive in human studies. However, as noted earlier, many of the studies that document the stress-reducing qualities of OT have not disentangled the effects of OT from affiliation. We hypothesize that the stress-reducing qualities of OT may depend on rewarding social contact, but that hostile or unsupportive social contacts during stressful times will exacerbate psychological and biological stress responses.

We examined this issue in our recent research (Taylor et al., 2005). We recruited postmenopausal women who were or were not on hormone therapy who completed a laboratory challenge task, specifically the TSST. The TSST involves the preparation and delivery of a speech to an unresponsive audience and performing difficult mental arithmetic under harassing conditions. It reliably increases heart rate, blood pressure, and cortisol responses to challenge (Kirschbaum, Pirke, & Hellhammer, 1995). Blood draws were taken from an indwelling intravenous catheter at three time points to assess oxytocin levels at baseline, postchallenge, and recovery. Eight saliva samples were taken across the stress challenge to assess cortisol, and blood pressure was also taken at these times.

We found that women low in oxytocin showed the expected increase in cortisol in response to stress tasks, followed by a decrease in cortisol during recovery. By contrast, women with high OT levels had significantly higher cortisol levels initially, which decreased early on in the laboratory procedures but which became elevated again following the stress tasks (see Figure 21.2). Cortisol levels then decreased during recovery. Although not definitive, this pattern suggests that elevated OT, in conjunction with relationship distress, is associated with greater, not less, HPA activity. The next section integrates these observations into an overall perspective on affiliation under stress.



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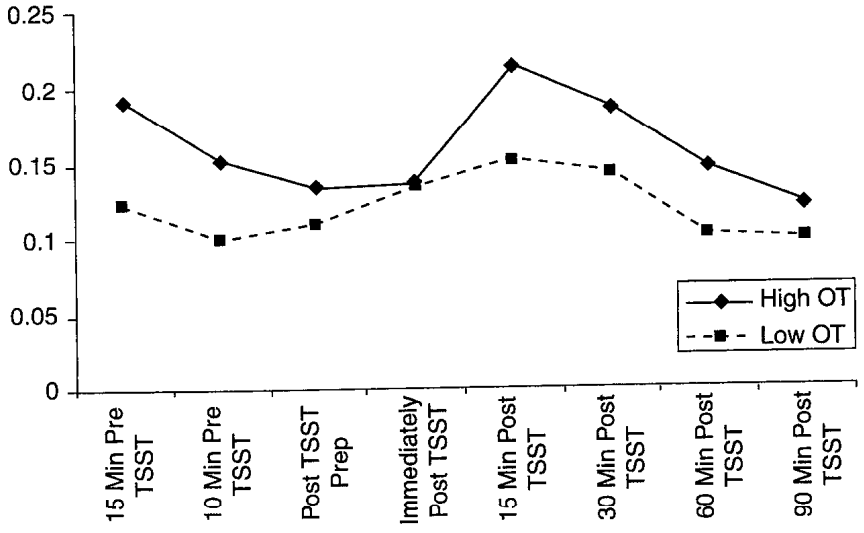

FIGURE 21.2. Cortisol levels across stress task for women with high and low levels of oxytocin.

A MODEL OF AFFILIATION UNDER STRESS

Humans and animals need positive social relationships. Relationships are essential to survival, because others provide the protection needed to maintain both one's own safety and that of offspring. We suggest that humans have evolved a warning system that alerts them to gaps in their relationships that may signal a threat to safety. OT, as well as opioids, is implicated in this process. In our research, OT is distinctively associated with gaps in positive relationships and with an absence of rewarding emotional contact with a partner.

Additional evidence that affiliation engages a biobehavioral social-approach regulatory system that draws on OT, opioids, and the dopamine neurocircuitry is provided in a recent review by Depue and Morrone-Strupinsky (2004). Although their goal was to characterize the trait of affiliation, they suggested, as we have, that affiliation is a reward-based system that has appetitive and consummatory phases, as other reward-based systems have. They suggest that the appetitive phase of affiliation especially implicates dopamine and that opioids are implicated in the consummatory phase of affiliation. Our analysis, although at a different level than that of Depue and Morrone-Strupinsky's (2005), is largely consistent with their model. However, our model departs from theirs in a few respects. First, we believe that the research evidence implicates opioids at both the appetitive and consummatory phases of affiliation. The fact that opioids are involved in separation distress and in seeking affiliative contacts supports this con-

clusion. Second, we suggest that the physical quiescence often associated with affiliative contact not only is due to opioid involvement at the consummatory phase of affiliation, as Depue and Morrone-Strupinsky (2005) maintain, but also results from attenuation of HPA-axis and sympathetic activity via oxytocinergic and opioid pathways, at least under stressful circumstances and in conjunction with positive social contacts.

Third, we suggest that OT and, as discussed shortly, vasopressin (AVP) have a greater role in affiliation than the relatively modest role accorded them in the Depue and Morrone-Strupinksy (2005) model. Depue and Morrone-Strupinsky suggest that OT and AVP may be implicated primarily in the perception and recognition of and memory for affiliative partners. They point out that affiliation relies on the underlying capacity to experience the rewards elicited by affiliative stimuli and that much social affiliation depends on the establishment of conditioned preferences for specific individuals, which is dependent on their reward capacity. As noted, our model suggests a more central role of OT and, to be discussed shortly, AVP, extending beyond memory for affiliative stimuli and the ability to recognize familiar conspecifics to include the signaling of affiliative needs, the initiation of affiliative activity, and concomitant impact on psychological and biological stress responses. Although one would hardly disagree with the conclusion that some individuals are more rewarding than others, we suggest that the affiliative neurocircuitry is only somewhat dependent on the establishment of conditioned preferences for specific individuals. Indeed, what is notable about human affiliative behavior, especially under stress, is that it occurs not only with familiar others but often with complete strangers. Despite these differences, the model of Depue and Morrone-Strupinsky (2005) and our own model have substantial points of commonality, especially in their overall characterization of affiliative processes as an appetitive system.

BENEFITS OF AFFILIATION UNDER STRESS

What would be the benefits of a biobehavioral system that is sensitive to relationship quality, that prompts affiliation, and that modulates stress responses? Looking at the affiliative system from the standpoint of evolutionary theory suggests clear survival benefits of a biobehavioral mechanism that signals gaps in social support and prompts affiliation for communal responses to stress. Individual safety, as well as the safety of offspring, would be ensured by such a system. What is intriguing, though, is that such a system continues to have such powerful effects on health and survival into the present day. Few of us encounter predators on a daily basis that provide threats to our own safety or to our children. Yet this biobehavioral system, nonetheless, has a major effect on health through social support and social integration.

Research consistently shows that social support reduces psychological distress, such as depression or anxiety (e.g. Fleming, Baum, Gisriel, & Gatchel, 1982; Lin, Ye, & Ensel, 1999), and promotes psychological adjustment to a broad array of stressful conditions (see Taylor, 2007, for a review). Because anxiety and depression are significant predictors of the progression of several chronic diseases, the amelioration of distress via affiliation may represent one pathway by which OT and opioid mechanisms exert effects on health.

In both animal and human studies, social isolation is tied to a significantly enhanced risk of mortality (House, Landis & Umberson, 1988) and a heightened risk of both chronic and acute health disorders (Taylor, 2007). Although not all the mechanisms that explain these strong relationships are known, one key pathway is via stress responses (Cacioppo & Hawkley, 2003). When humans are socially isolated, their sympathetic nervous system and HPA-axis responses to stress may continue unabated, leading to a state of immunological vulnerability. People without social support systems, for example, are more vulnerable to infectious disorders (Cohen, Doyle, Skoner, Rabin, & Gwaltney, 1997). Correspondingly, the positive impact of social ties on health outcomes is as powerful as or more powerful than established (negative) risk factors for diseases, including lipid levels and smoking.

Whether the attenuation of stress responses by OT and opioids is sufficient to produce these clinical effects of social support is, at present, unclear. However, recent animal research on wound healing has suggested that this is a promising avenue for research (Detillion, Craft, Glasper, Prendergast, & DeVries, 2004). Specifically, in this study, Siberian hamsters received cutaneous wounds and were then exposed to immobilization stress. The stressor increased cortisol concentrations and impaired wound healing, but only in socially isolated, not in socially housed, animals. Thus social housing acted as a stress buffer. Removing cortisol via adrenalectomy eliminated the impact of the stressor on wound healing, thereby implicating the HPA axis in the wound-healing process. Of particular relevance to the current arguments, treating the isolated hamsters with OT eliminated the stress-induced increases in cortisol and facilitated wound healing; treating socially housed hamsters with an OT antagonist delayed wound healing. These data strongly imply that social contacts protect against the adverse effects of stress through a mechanism that implicates OT-induced suppression of the HPA axis. Thus there appear to be discernible clinical consequences (wound healing) of OT suppression of the HPA axis.

But social contacts during stressful times are not always positive. Indeed, social stress is one of the most taxing threats that humans experience, significantly engaging the HPA axis (Dickerson & Kemeny, 2004). During stressful times, potentially supportive companions may also be under stress, compromising their ability to be sources of comfort or help.

When this occurs, stress responses may not only not be attenuated by OT, but also may actually be exacerbated. Thus quality of social contacts would appear to be an important factor influencing the relation of OT to stress responses.

POTENTIAL SEX DIFFERENCES IN AFFILIATION UNDER STRESS

Does the model described in this chapter primarily characterize female responses to stress (Taylor et al., 2000), or might it characterize males' responses as well? The fact that OT's effects are strongly influenced by estrogen makes this an important question. Much of the animal evidence on the stress-reducing effects of OT has been conducted with females, especially estrogen-treated females, and much of the data from humans comes from women, as well.

As noted, Heinrichs et al. (2003) administered oxytocin via nasal spray to men and then put them through a laboratory stress challenge (i.e., TSST). They found the same antianxiety effects and reduction in HPA-axis activity in his men as has been found in animal studies. Clearly OT can have stress-reducing effects in men (see also Chiodera & Legros, 1981). However, because Heinrichs et al.'s paradigm used exogenous administration of OT, it showed that OT *can* have these effects in men but not that it necessarily *does*. Because OT secretion is strongly enhanced by estrogen (McCarthy, 1995) and antagonized by androgen in at least some species (Jezova, Jurankova, Mosnarova, Kiriska, & Skultetyova, 1996), OT levels may not typically be high enough in men for their stress-reducing effects to be significant (see Taylor et al., 2000, for a discussion).

Women's consistently stronger affiliative responses to stress, compared with those of men (Tamres, Janicki, & Helgeson, 2002; Taylor, 2002), is also potentially consistent with a greater role for OT in women's than men's stress responses in that OT is consistently tied to affiliative activity. Although the sex difference in affiliation under stress is moderate, it is extremely robust. In addition, the stress literature indicates that men's and women's responses to stress may assume somewhat different forms, with women disproportionately involved in reducing the stress of offspring. At the time when human stress responses evolved, work was largely segregated by sex, with men responsible for hunting and women responsible for food gathering and for child care. This segregation suggests that the selection pressures on females for stress responses that benefit both themselves and their offspring may have been greater than was true for males (Taylor, 2002).

Taking these points together, the biological underpinnings of men's social behavior under stress will likely be somewhat different than those of women. The hormone vasopressin (AVP) has a molecular structure that is

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very similar to that of OT. Unlike OT, AVP's effects appear to be enhanced in the presence of androgens, and so it has been thought to play a more important role in men's behavior than in women's (Panksepp, 1998). AVP is important to stress responses because it is involved in the maintenance of plasma volume and blood pressure during shock, among other functions. AVP may also be implicated in the modulation of neuroendocrine responses to stress. Exogenous administration of AVP appears to enhance HPA-axis responsivity to stress. In a review of 30 studies, Fehm-Woldsdorf and Born (1991) found that exogenous administration of AVP increased central nervous system arousal and increased anxiety, as well. AVP has also been tied to prosocial responses to stress in male prairie voles—for example, guarding and patrolling of territory, defense of mate, and defense of offspring against intruders (see Carter, 1998; Carter, et al., 1995, for a review). The AVP receptor gene is associated with pair bonding and monogamous behavior in voles (Lim et al., 2004). It is unknown whether AVP underlies men's affiliative responses to stress, and virtually nothing is known about the behavioral implications of vasopressin in humans. Thus a biobehavioral model of men's affiliative behavior under stress remains a work in progress, but a possible role for AVP in these processes would be a logical place to begin.

CONCLUSIONS

The affiliative neurocircuitry is increasingly understood, at least at the molecular level. Social neuroscientists are now beginning to integrate that neurocircuitry with its psychological and behavioral components. The evidence to date suggests that this will be a worthwhile endeavor. A picture of the emerging regulatory role of affiliation in response to stress and its biological underpinnings is coming into view.

OT and opioids appear to be biomarkers of social distress that accompany gaps in or problems with social relationships and that may provide an impetus for affiliation. OT and opioids are implicated in the seeking of affiliative contact, especially in animal studies. This reasoning is consistent with previous arguments that the human tendency to seek social support in response to stress may be mediated, in part, by OT and opioids, as well (Taylor, 2002; Taylor et al., 2000). Linking the signaling function of OT directly to affiliative behavior in humans is an important next step. OT, in conjunction with opioids, also modulates stress responses. In conjunction with positive affiliative contacts, OT attenuates psychological and biological stress responses, but in conjunction with hostile and unsupportive contacts, OT appears to exacerbate psychological and biological stress responses.

Finally, our research underscores the enduring importance of investigating the interplay of social and biological responses to stress. Recently,

great strides have been made in mapping the neurobiological underpinnings of affiliative behavior (Carter et al., 1999; Depue & Morrone-Strupinsky, 2005; Panksepp, 1998). With each effort, the affiliative neurocircuitry and its engagement in response to stress come closer to being understood.

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