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Nurture, Nature, and Caring: We Are Not Prisoners of Our Genes

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Abstract. This article develops a theory for how caring behavior fits into the makeup of humans and other mammals. Biochemical evidence for three major patterns of response to stressful or otherwise complex situations is reviewed. There is the classic fight-or-flight response; the dissociative response, involving emotional withdrawal and disengagement; and the bonding response, a variant of which Taylor *et al.* (2000) called tend-and-befriend. All three of these responses can be explained as adaptations that have been selected for in evolution and are shared between humans and other mammals. Yet each of us contains varying tendencies toward all of these responses. How does development interact with genes to influence these tendencies? How do individuals, societies, and institutions make choices between these types of responses? We review the evidence, based on behavioral, lesion, single-cell, and brain imaging studies, for cortical-subcortical interactions involved in all three of these response types, and propose partial neural network models for some of these interactions. We propose that the orbitomedial prefrontal cortex mediates this choice process. This area of prefrontal cortex performs this mediation through its connections with areas of sensory and association cortex that represent social contexts or stimuli, and with areas of the hypothalamus, limbic system, and autonomic nervous system that represent emotional states or classes of response patterns. The article concludes with implications of our theory for social interactions and institutions. We argue that despite the wide prevalence of fight-or-flight responses, the bonding, caring responses remain available. We show with historical and contemporary examples how social settings – whether in education, work places, families, politics, and informal social customs – can be designed to support and enhance the natural caring responses of the brain.

Key words: bonding, brain, caring, dissociation, evolution, fight-or-flight, orbitomedial prefrontal cortex, social influences, tend-and-befriend

Where do caring and altruism come from? Why are some people caring to their children while others are abusive? Why do people and other animals sometimes feel enough concern for others who may be genetically unrelated to them, or even of different species, to risk their own survival, comfort, or reproductive capability for the other's welfare? These questions have long posed a challenge for behavioral biologists and psychologists steeped in the theory of natural selection.

Some degree of caring is essential for mammal, and particularly human, babies to survive – so caring behaviors clearly have an evolutionary function. In mammals, and particularly humans, a capacity for caring for offspring would have been

selected for in the course of evolution. But this would not explain the great variance of parental behaviors. The emergence of altruism, of empathizing with and caring for those who are not kin, is likewise not easily explained within the framework of neo-Darwinian theories of natural selection.

Charles Darwin himself in *The Descent of Man* (Darwin, 1871/1981, p. 163) doubted that survival of the fittest could account for caring parenting or altruism. He also argued that at the human level factors other than natural selection come into play.

This insight has led evolutionary scholars to develop a variety of extensions of the Darwinian paradigm of natural selection. For example David Loye highlights Darwin's emphasis in *The Descent of Man* and other writings on love rather than pure self-interest as a factor in evolution, particularly at the human level (Loye, 1999, 2000, this issue).

Probably the most widely known theory to explain cooperative behaviors (which in many cases include some empathy and caring) has been some type of group selection, which Darwin was also first to articulate. As Patrick Bateson (2000) put it: ". . . some assemblages of individuals may, through their concerted efforts, generate an outcome that puts their group at an advantage over other groups."

We believe that group selection is enhanced by empathy and caring. This would be another reason these qualities were selected for in evolution. But group selection does not explain why caring and respectful parenting is sometimes present and sometimes absent. Nor does it explain why altruism is sometimes present and sometimes absent.

Saying that a trait is selected for in evolution does not tell us what the biological or neuropsychological mechanisms are for expressing that trait. Nor does it shed light, as Bateson himself noted, on what environmental contexts will enhance or suppress that trait. Without such contextual knowledge, it is not possible to draw conclusions about how the trait affects, and is affected by, social and cultural interactions.

In other words, we here move from questions about genes to questions about *gene expression*: to the physical and social environment that will lead to the expression or inhibition of the human capacity for caring and altruistic behaviors. We also move to questions about the biochemical and neurophysiological mechanisms of caring and uncaring behaviors. We will look at both these issues in this article.

A WORKING HYPOTHESIS

While our knowledge of the neuroscience involved in caring is far from complete, it has grown enough in the last few years to suggest a partial hypothesis, or set of hypotheses, about the expression or inhibition of caring. There appears to be in all mammals (it has been studied most extensively in rodents) a system of neurotransmitters and peptide hormones, in which the peptide oxytocin is particularly

pivotal, for affect regulation and mediation of social bonding. While this neural system has been most studied in mother-child interactions and in female-male sexual pair bonding, there is spotty evidence that the same system also operates in other bonding relationships such as non-kin friendships, as well as in relaxation responses and general stress reduction. In humans, the feedback between complex processing areas of the cerebral cortex, especially the orbital and medial prefrontal cortex, and the subcortical affect regulation system inherited from other mammals is a good candidate for mediating cultural expression, or suppression, of our caring capacities.

We believe that an examination of these interactive dynamics, as well as of how these dynamics interact with an individual's physical and social environment, can provide a better understanding of caring and uncaring behaviors. We also believe that this inquiry is particularly urgent today when the mix of high technology and uncaring and violent behaviors puts our very survival at issue.

There is a credible argument that caring both for offspring and others arose as an individual adaptation, at least in women. The social psychologist Shelley Taylor and her colleagues (Taylor *et al.*, 2000) described what they called the "tend-and-befriend" response that women and female animals often employ as a response to stress, in preference to the traditionally studied "fight-or-flight" response. This response, mediated by the oxytocin system in the brain, includes both the tending of offspring and social bonding between females (mutual grooming for nonhuman animals, friendship for humans) around mutual protection of selves and offspring. Taylor and her colleagues left open the question of whether there are analogous mechanisms in males, a matter we will return to.

But again, the issue is not just one of natural selection of particular genes for caring. For many decades by now psychologists have demonstrated the operation of many other motivations beyond survival and reproductive fitness, especially in humans but to a lesser extent at least in other primates. These motivations include the desire for pleasure or positive affect (Mellers *et al.*, 1999; Pfaffmann, 1960), intrinsic curiosity (Deci and Ryan, 1975), mastery (White, 1959), and expression of one's potential (Maslow, 1971).

One could argue that the fact that caring behavior produces positive affect or pleasurable feelings has an evolutionary function, and hence that caring behavior is rooted in natural selection. But it would not necessarily serve this function once it is established.

It is in no way a contradiction of the theory of natural selection to say that some behavior is based on other motivations *in addition to* survival and reproduction. Caring and altruism partly fit under these broader motivations. Much caring and altruistic behavior is based on a desire for the pleasure, stress reduction, and positive self-expression that arises from warm relationships with others, whether family, friends, or acquaintances. Also, people continue to be motivated by their own survival beyond reproductive years, when it is irrelevant to passing on genes. For older people, in particular, it is well documented that social support

is one of the major factors in withstanding the effects of serious illness (Knox and Uvnäs-Moberg, 1998; Ryff and Singer, 1998).

There is also the fact that the evolution of greater thinking capacity in humans allows us to widen the range of empathy and caring from what is available to other animals. In particular, the capacity for drawing analogies allows us to detect similarities between other people and ourselves, which can promote empathy towards those people. Depending on the depth of our moral development and the stresses we are under, we can notice these similarities only in those who share specific characteristics (such as family, gender, race, ethnic group, profession, et cetera) or, to varying degrees, in the entire human race. If the connections between rational and emotional processes in our brains (in which the orbitomedial prefrontal cortex is especially vital) are working at their best, analogy leads to empathy (see Barnes and Thagard, 1997; Eslinger, 1998) and cooperation and caring are much more likely.

In light of these factors, a purely genetic explanation for caring or any other behavior is inadequate. Certainly there is a genetically based capacity for caring behaviors. Yet there is ample evidence that experience influences development of the brain circuits involved in any behavior.

The cumulative evidence of much research indicates that genetics and social experiences together produce brain changes that guide the ways we express hope and fear, anger and generosity, hostility and warmth. We propose that the capacity for caring is part of our species' evolutionary heritage, but that the expression or inhibition of this genetic capacity is a function of the interaction of inherited temperament and personality with experiences. We propose that these experiences affect temperament and personality, and thus behavior, by altering brain chemistry and structure.

The purpose of this article is to explore the intricacies of the dynamic patterns for this interaction.

The Human Capacity for Caring and Uncaring Behaviors

How does caring develop – or fail to develop – as a behavioral trait in humans? What are the neural circuits and biochemical substances involved? And how is the release of these substances related to what we experience, both as children and adults?

We do not yet have systematic studies of effects of social environments on human brain biochemistry. But we know some of the neurochemical pieces involved. Other pieces we can intuitively gather from what we know of human emotional and behavioral responses. This means we can arrive at a useful description of the interacting systems involved in this process, even if our description is more like an impressionist painting than like a photograph.

Evidence from many sources, along with what we know in general about brain plasticity, suggests that positive and caring experiences should selectively

strengthen neural circuits that represent positive emotions and caring social bonding – for adults as well as children. We do not know exactly how this selective enhancement works in our brains. But we do have strong evidence about some of the biochemical substances involved.

Two such substances are dopamine, one of our most important neurotransmitters, and oxytocin, one of our commonest peptide hormones.

CARING, DOPAMINE, AND OXYTOCIN

Dopamine is the major transmitter involved in the brain's pleasure pathways, some of which run from the hypothalamus, gateway to the endocrine glands, through the emotional areas of the limbic system (in particular, the nucleus accumbens) to the planning and working memory areas of the frontal lobes (Ashby *et al.*, 1999; Brown *et al.*, 1999; Schultz *et al.*, 2000). The dopamine pathways that have been of most interest in recent studies both of pleasure and addiction come from dopamine producing neurons in different areas of the midbrain and go out both to the nucleus accumbens and parts of the prefrontal cortex. Figure 1 shows the location in the brain of these pathways and some of the others that will be of interest in this article.

The dopamine inputs are believed to be important for the proper development of frontal lobe circuits in young children. This has been proposed as the mechanism by which proper caregiving, including pleasurable emotional experiences with parents or other caregivers, contributes essentially to the growth of a child's mental capacities (Schore, 1994).

Dopamine also probably plays a role in surges of both generosity and creativity in adults brought on by good moods (Ashby *et al.*, 1999). The social psychologist Alice Isen and her colleagues have done over twenty years of experiments on people who are temporarily manipulated into having positive moods (Dovidio *et al.*, 1995; Isen, 1987, 1993, 1999), by such mild inducements as giving them candy or returning a coin after they made a paid telephone call. Isen's group found that positive moods increase people's mental flexibility on cognitive tasks, enabling them, for example, to come up with nonstandard uses for objects to solve a mechanical problem. Also, positive moods cause people to stretch favorable categories of people further than they do in neutral moods, such as including bartenders as examples of nurturers. "Positive mood" subjects were more generous than "neutral mood" subjects, contributing more, for example, to boxes set up in the room for charitable causes. Isen *et al.* hypothesized that these positive moods and the caring and creative behaviors that accompanied them involved release of dopamine to particular receptors.

Whereas dopamine is involved in a wide range of positive emotions, oxytocin is specifically important for positive emotions relating to social and family connections. This hormone, found only in mammals, was first discovered to be essential for maternal behaviors such as uterine contraction and milk ejection. But in a remarkable series of studies on rodents, Thomas Insel, James Winslow, and their

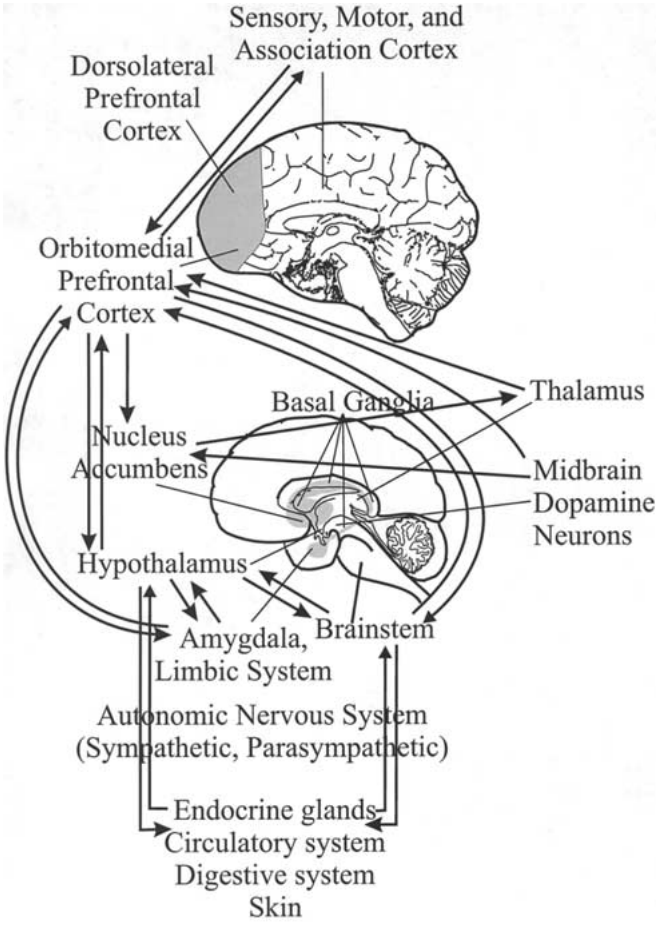

Figure 1. Approximate location in the brain of some areas that are particularly important for affective regulation. Dark lines with arrows denote neural pathways connecting those areas. The top brain diagram highlights regions of the cerebral cortex (outer layer of the brain). The bottom brain diagram highlights subcortical regions that are largely common to humans and other mammals. The pathway from nucleus accumbens to thalamus is actually indirect through other parts of the basal ganglia. Specific parts of these regions and pathways that transmit peptides (oxytocin and vasopressin) and stress related substances (cortisol and norepinephrine) are not shown here and will appear in other figures.

colleagues discovered that oxytocin has broader importance for bonding, in male as well as female animals (Insel, 1992; Insel and Winslow, 1998; Winslow *et al.*, 1993).

Insel and Winslow looked at two species of North American rodents that are closely related but have radically different social organization: the *prairie vole*, which is monogamous with strong male-female pair bonding and both parents involved in care of young, and the *montane vole*, which is promiscuous with fathers uninvolved with young. They found that oxytocin attaches to receptor molecules in

reward-related areas of the brain's limbic system in the pair-bonding prairie vole but not in the promiscuous or non-bonding montane vole. Also, in female prairie voles, pair bonding – with the first male they smell after reaching puberty – can be induced by direct injections of oxytocin, and abolished by drugs that reduce the amount of oxytocin (Insel *et al.*, 1998).

This pattern of oxytocin binding to reward sites in the brain seems to carry over to other bonding mammals, including humans and apes, although this is less well established. Insel's group has bred male mice that lack a gene for producing oxytocin and found that these animals are selectively deficient in social memory. Unlike normal mice, they cannot remember the smell of another mouse with which they have engaged in affiliative behavior (e.g., sex, play, or grooming), even though their memory for other kinds of smells is intact (Ferguson *et al.*, 2000).

There is also a variety of results suggesting that oxytocin inhibits both fight-or-flight responses and another type of common response to stress that Perry *et al.* (1995) and others have called dissociative. Dissociative responses are characterized by freezing and by withdrawal from social interactions, and like fight-or-flight responses are common in chronically stressed people such as abused children. By contrast, oxytocin promotes responding to stress by seeking positive social interactions and nonnoxious sensory stimulation. A subclass of these responses is what Taylor *et al.* (2000) termed tend-and-befriend.

OXYTOCIN AND THE CHEMISTRY OF STRESS AND CARING

Uvnäs-Moberg (1997, 1998) reviews evidence from her laboratory and others that oxytocin administration in both male and female rats counteracts many of the typical physiological and behavioral effects of stress. For example, oxytocin causes decrease in blood pressure and in the amount of cortisol, a hormone typically released in stressful situations. More generally, it reduces activity in the sympathetic part of the autonomic nervous system, which is precisely what is activated in the fight-or-flight response. Oxytocin has also been shown to delay the onset of withdrawal to heat and mechanical stimuli, and to increase the healing rate of wounds, possibly through a shift in the allocation of energy in the body.

The physiological antistress effects of oxytocin are known to occur in association with both lactation and sexual intercourse. What is less certain, but what Uvnäs-Moberg also strongly suspects, is that oxytocin is also released by other forms of pleasurable social contact, such as mutual grooming in animals and supportive friendship in humans.

If oxytocin is indeed involved in a wide range of pleasurable experiences, this points to a physiological mechanism for the health benefits of positive social experiences as well as for such therapies as massage. Indeed Turner *et al.* (1999) found that oxytocin levels in the blood of women who had never been pregnant increased in response to relaxation massage. They also found the same hormone sometimes decreased in response to sad emotions, mainly in women who were insecure in

their interpersonal relationships. Uvnäs-Moberg (1998) suggested that since the release of oxytocin can become conditioned to psychological state or imagery (for example, in female prairie voles it becomes conditioned to the first male encountered during the receptive period in adolescence), the release of oxytocin could also provide a physiological basis for the health benefits attributed to more indirect therapies such as hypnosis and meditation.

The evidence that oxytocin counteracts the dissociative response to stress comes particularly from the literature on addictive drugs. Drugs of abuse interact with the dopamine system, usually by increasing dopamine levels at the nucleus accumbens (see Figure 1) in a way that makes the maintenance of high dopamine levels dependent on the drug, thus creating a variant of the dissociative response of trying to feel good through psychological withdrawal. But administration of oxytocin to rats and mice has been found to inhibit the development of drug tolerance, that is, the tendency to progressively need larger doses, to several drugs including cocaine, morphine, heroin, and ethanol (Kovács *et al.*, 1998; Sarnyai and Kovács, 1994). The inhibition of behavioral tolerance also reduced symptoms from drug withdrawal. This is believed to be mediated by some type of interaction between oxytocin and a particular type of dopamine receptor (called the D2 receptor) in the nucleus accumbens.

We have focused on oxytocin because of such dramatic and fairly recent results (by Insel, Uvnäs-Moberg, and others) linking this hormone both with positive social bonding (not just maternal and sexual but also the type of bonding involved in friendship) and with reduction of potentially unhealthy responses to stress. Yet like all brain chemicals, oxytocin does not operate in isolation.

There are other substances that are important to the brain's caring system. These include at least two other peptide hormones, vasopressin and CCK; the class of peptides called beta endorphins; and the neurotransmitters dopamine and serotonin. The interactions among all these substances are far from worked out, but here are a few of them:

(1) Oxytocin and vasopressin (which are closely related chemically) are both essential to female-male sexual pair bonding in prairie voles. Some studies have hinted that oxytocin is more essential in female voles and vasopressin in male voles (Insel *et al.*, 1998); the latter hormone is particularly related to male aggression in defense of the mate and young, and to paternal care. Yet more recent work indicates that partner preference development in either sex requires intact brain receptors for both hormones (Cho *et al.*, 1999).

(2) Pair bonding in addition involves the D2 receptors for dopamine in the nucleus accumbens (Gingrich *et al.*, 2000; Wang *et al.*, 1999). This suggests the same dimly understood interaction between oxytocin and D2 receptors suggested by drug tolerance studies (Kovacs *et al.*, 1998).

(3) Dopamine is involved not only in the affective rewards from positive social interactions but in other types of affective rewards including those from sex, eating, and drugs. Oxytocin has been found in other studies to poten-

tiate CCK, the peptide often tied to dopamine and involved in food rewards (Uvnäs-Moberg *et al.*, 1999).

(4) Serotonin, being involved in affective stabilization, tends to inhibit sexual expression, which accounts for some of the negative sexual side effects of serotonergic antidepressant drugs. In male rats, injection of oxytocin has been found to block this blunting of sexuality (Cantor *et al.*, 1999).

(5) Aspects of the "tend-and-befriend" response in female primates are blocked by naloxone, an inhibitor of the beta endorphins, which are among the most important of the brain's natural opiates or pain-reducing substances (Taylor *et al.*, 2000).

FROM MICE AND VOLES TO HUMANS

What does all this mean? And what can we learn about human caring or noncaring from voles and other nonhuman species?

There are critical differences between humans and other species such as mice, voles, and others about which we have relevant laboratory findings. For one thing, we have much more complex brains, largely due to our vastly expanded cerebral cortex. And while the fight-or-flight, dissociative, and tend-and-befriend systems are all still present in humans, and all serve useful evolutionary purposes, how much each one is actually expressed, and how much this expression becomes part of each of our personality structure, depends in large part on how many positive or stressful life events we experience.

Through an elaborate network of brain connections, involving both our orbitomedial frontal cortices and subcortical affective regions, each of us has a different set of associations of both other persons and objects with caring or noncaring. Some of the associations each of us has, our specific likes and dislikes, are probably inborn, but probably more of them are learned in the context of family and cultural upbringing. It is these associations that determine the unique feelings and passions of each of us, and the prevailing mores and values of each society, culture, and subculture.

We have already seen that a host of substances travel through our bodies, carrying messages back and forth in response to varying external and internal stimuli. In later sections we will speculate on which particular neural connections of the prefrontal cortex might be the loci at which learning of emotional valuations take place. The network of Figure 3, to be discussed in a later section, suggests a hypothesis for how oxytocin and vasopressin may be involved in conditioning an organism (vole or primate) to bond with a specific partner.

But, particularly in humans, this conditioning occurs at still another level. Persistent stress seems to decrease the activity of the oxytocin system itself – and therefore the ability to bond with anybody. This process is described by Henry and Wang (1998):

> With only minor challenges in the early stages of arousal, oxytocin and ... attachment behavior ... can be maintained at a high level. But with strong activation and the development of helplessness, the oxytocin system becomes less active ... When extremely stressful situations have activated these hormonal systems and lead to post-traumatic stress disorder (PTSD), there is a long-lasting activation of the sympathetic system evidenced by sustained elevations in urinary norepinephrine and epinephrine ... The victims are vigilant, readily angered and display a dysphoria with a lack of interest in daily activities. Sleep is disrupted, emotional responses are blunted and feelings of meaninglessness emerge. (p. 867)

We know that long-term negative experiences have lasting effects on brain chemistry that make future fight-or-flight and dissociative responses more likely. We also know that in humans, particularly during the crucial first years of human development, many of the brain's neurochemical pathways are laid in response to different experiences.

In the sections that follow we will look at the interplay of genetics and environment in the neural basis of personality traits. We will begin with studies showing that experience should not be ignored, whether in human or nonhuman species.

Experience and Brain Development

In discussing human personality and behavior, the generic question of "Is it based on nature or nurture?" is not a useful one to ask. A more productive question is "What forms of nurture bring out what aspects of human nature?" This is true in particular of prosocial (caring and altruistic) behavior as well as antisocial (uncaring and hurtful, even criminal) behavior.

Genetics supplies what Taylor *et al.* (2000) called central tendencies. But interactions during development can either enhance or suppress these genetic tendencies.

Our brain has accurately been called a "work in progress" (Shore, 1997). Babies do not have fully developed brains when they are born. If they did, they would not be able to fit through the birth canal. So the human brain must instead continue to develop outside the mother's womb after the baby is born, particularly during the first year, but also for many years after.

Experimental results in areas ranging from visual pattern development in cats (Blakemore and Cooper, 1970) to childhood abuse in humans (Perry *et al.*, 1995) make it clear that our early experiences literally provide the organizing framework for our brains (Perry *et al.*, 1995, p. 276). This organizational framework and the traits and behaviors that flow from it – including whether a child grows up to be unresponsive and violent or responsive and nonviolent – are largely shaped by whether the interactions she or he experiences are with adults who are unresponsive and violent or responsive and nonviolent.

Neuroscientists now generally agree, based on the observed plasticity of single neurons in both invertebrates and vertebrates (Bliss and Lømo, 1973; Byrne, 1987; Kandel and Tauc, 1965), that day-to-day events can cause changes in the chemistry of neural transmitters at many synapses. These studies do not specifically deal with the effects of different kinds of stimuli on the brain. But they indicate that if there is a pattern of stimulation, such as a pattern of caring or abusive treatment of a child, there will be lasting synaptic effects. And this is precisely what studies of the brain development of chronically abused children show.

CHILDREN'S BIOCHEMICAL/NEURAL DEVELOPMENT

Receiving and giving caring are pleasurable experiences for all life forms. Sharing with others is among the most empowering and pleasurable experiences for humans. It enables us to remain open to seize opportunity, express creativity, and draw the best from others and ourselves. By contrast uncaring, violent, or abusive experiences are stressful for all life forms. For humans, powerlessness, poverty, events such as the loss of a job or a significant relationship, and other experiences that cause pain are also stress-inducing.

As we saw earlier, three responses to stress have been identified: the "flight or fight" response, the dissociative response, and the tend-and-befriend response, which involves caring and caregiving rather than aggressive or escapist behaviors.

The response to stress that has been most studied is fight or flight. This response involves various parts of the brain as well as the endocrine glands, the immune system, and the cardiovascular system, which coordinate to produce characteristic biochemical changes in response to unpleasant or potentially threatening environmental events. This interconnected system serves useful functions in evolution: its hyperarousal prepares the body for either fighting the stressful event or withdrawing from it.

The hyperarousal response involves an increase in activity of the brain's system for distribution of the neurotransmitter norepinephrine. Norepinephrine, also sometimes called noradrenalin, is the transmitter that is most involved with fight and flight responses: with "pumping up" the brain's connections to the cardiovascular and endocrine systems involved in active responses to stressful situations. In children with typical hyperarousal patterns from early traumas, these receptors for norepinephrine have been shown to exhibit an altered pattern (Perry, 1988; Perry *et al.*, 1995).

Under normal circumstances, when the stressful events have ceased, the stress-based profile disappears and the body recovers its pre-stress biochemical configuration. When the stresses are too severe or persistent, however, as with children who are physically or sexually abused repeatedly, the recovery cannot take place fast enough to keep up with the new stresses that occur. In this case, the biochemical configuration often changes permanently. The child may survive into adulthood, but the changes in the brain remain, with damaging effects.

Recent studies of chronically abused children such as the studies of Bruce Perry show what some of these effects are (Perry *et al.*, 1995; see also Perry, this issue). The fight-or-flight response to stress is described as a *hyperarousal* response. This is characterized by sensitization of the pathways in the nervous system and other bodily organs (including the heart and endocrine glands) responsible for fight-or-flight responses to danger. After this sensitization takes place, the person becomes more likely to have an arousal response even to stimuli somewhat milder than the initial traumatic event. This helps account, for example, for the propensity of some traumatized individuals to violence even in the face of what to someone else would seem a mild insult, or no insult at all.

The dissociative response to stress is opposite to hyperarousal in that it involves freezing rather than fighting or fleeing. Dissociation is often accompanied by depression or a tendency to withdraw into fantasy or daydreaming. It helps account for the withdrawal of some traumatized individuals into addiction to alcohol or drugs.

The long-term physiological changes in children exhibiting a dissociative pattern have not yet been extensively studied. However, it is known that the key neural transmitter for the expression of that pattern is dopamine (Perry *et al.*, 1995), the transmitter that is mainly involved with the rewarding effects of desirable stimuli (not only natural positive reinforcers but also addictive drugs), and with positive affect in general. Rather than mobilizing the organism toward a fighting or other coping response, the dissociative response mobilizes the organism to withdraw emotionally from the current aversive situation and try to "feel good." In contrast to the tendency of hyperaroused children to show a resting rapid heart rate (brought on by the nervous system connections), dissociated children tend toward hyperactivity of the counteracting vagus nerve, which slows down the heart.

In the Perry studies, neither hyperarousal nor dissociative responses were uniformly found in all abused children. Each was more likely to occur in children who had a family history of particular types of disorders. This could signal inherited genetic predispositions, or it could signal patterns of emotional and physical response passed on from generation to generation through both conscious and unconscious learning.

As Perry points out, both professionals and lay people have often conveniently accepted the myth that "children are resilient" and can therefore get over whatever abuse they have suffered. The fact, he continues, is that the brain is malleable all through life, but much more so in the early years. Neural transmitter changes that influence learning in adult life actually impinge on neuron and nerve pathway growth in the young child. And what happens, again in his words, is that "states become traits" (Perry *et al.*, 1995).

Perry reports that the regions of the cortex and limbic system responsible for emotions, including attachment, are in the brains of severely abused children 20 to 30 percent smaller than in normal children. In adults who were abused as children the memory-making hippocampus is smaller than in nonabused adults (see also

Markowitch *et al.*, 1998, and for related rat data, Brunson *et al.*, 2001). A high level of the hormone cortisol, typically produced by the endocrine system in response to trauma, during the vulnerable years of zero to three also increases activity in the brain structures involved in vigilance and arousal.

Another neurotransmitter affected by stress is serotonin. Low levels of serotonin are characteristically found in people who are suicidal or impulsively violent (Bligh-Glover *et al.*, 2000; Courtet *et al.*, 2001). So serotonin's major function seems to be to stabilize emotional responses. Research by Rosenblum *et al.* (1994) suggests that lower levels of this neurotransmitter are due to the fact that stress and lack of good caregiving thwart the development in children of the pathways that circulate serotonin in the brain. This is the finding behind the wide use of antidepressants such as Prozac, which release serotonin from being captured by cells, freeing more of it to flow as needed to reduce stress.

EXPERIMENTS ON MONKEYS AND CATS

Studies of brain development showing that the kind of care a child receives affects the neural and biochemical architecture of his or her brain were prefigured by the pioneering studies in the late 1950s by Harry and Margaret Harlow on infant rhesus monkeys. While those studies did not specifically deal with the neurochemistry of brain development, they suggested that the monkey (and human) brain is strongly affected by what is present or absent in early social experience, both with parents and with peers.

In one study (Harlow, 1958), infant monkeys were taken away from their mothers and placed in a cage with two types of surrogate mothers. One was a terrycloth mother, that is, a soft figure in the shape of a mother monkey. The other was a wire mesh mother that could provide heat and structural support but not comfortable contact.

One group of infant monkeys was provided with milk by the cloth mother, the other group by the wire mother. These baby monkeys became very attached to the cloth mothers, clinging to them for hours. And they did so whether these surrogate mothers provided them with milk or not. When faced with a novel stimulus, like a teddy bear that played a drum, they found comfort and security in the presence of the cloth mother, which emboldened them to investigate the teddy bear with confidence. Wire mesh mothers, on the other hand, did not provide this kind of comfort and confidence. In fact, when given a choice, the little monkeys would always go to the terrycloth mother. Even when the wire mesh figure had the milk, they would simply stay with it long enough to satisfy their hunger and go back to the terrycloth one.

However, neither a terrycloth nor a wire mother was a good substitute for a real mother in providing eventual adjustment to adult life. But another study showed that surrogate mothers could be adequate if the infant monkeys also had opportunities for play with other infants (Harlow and Harlow, 1962). The monkeys

that played with each other for several hours a day grew up to be normal in their relationships with other monkeys, including initiating sex and later giving maternal care to their own infants. On the other hand, the monkeys raised with only their mothers, when later brought together with other monkeys their age, did not know how to have any social or sexual relations with them.

The monkeys raised in complete isolation from both mothers and peers developed the kinds of extreme pathologies sometimes seen in neglected and abused human children. They would stare fixedly into space, hug themselves or rock themselves interminably, and react to the approach of people by biting or scratching bleeding holes into their own skin.

When they were later put together with other monkeys, these monkeys were not able to have sex and would indiscriminately hit and bite, in apparent terror. When females from this group were artificially inseminated, they were unable give their babies any attention, much less affection. They carelessly stepped on them, shoved them away, and sometimes even deliberately injured them.

In short, these monkeys' capacity for caring had been almost totally inhibited because of experiences they had been subjected to in their childhoods. Specifically, like some of the children in the Perry studies, severe stress had led to a state where fight or flight and/or dissociative behaviors had become habitual.

Other animal experiments further support the conclusion that early experiences have lasting effects on the brain. One of the most striking of these was an experiment where cats were raised in an isolated chamber where the walls were covered either with horizontal or vertical stripes (Blakemore and Cooper, 1970). These cats as adults bumped into walls that were covered with stripes of the opposite orientation. They were unable to see vertical stripes if they grew up seeing only horizontal ones, or vice versa.

In other words, when particular visual patterns were lacking in the kittens' early environment, their brains did not develop the ability to detect those specific patterns in the way that a normal cat's brain does because the electrical responses of each neuron in the visual cortex to different line orientations is shaped by what orientations the animal sees. So when the visual patterning of the brain has been shaped by experiences that do not include a full range of orientations, the organism lacks the neural capacity to see the excluded possibilities. The implications of this finding for the perceptions and behaviors of individuals whose early environment has been chronically uncaring rather than caring are borne out by Perry's findings on chronically abused children.

CARING, GENES, AND DEVELOPMENT

Although there is strong evidence that experience has a profound effect on the development of caring or uncaring behaviors, there are studies that also link uncaring behaviors with genetic factors. For example, a study by Raine *et al.* (2000)

showed that men diagnosed with antisocial personality disorder have an average of 11 percent less gray matter in their frontal lobes than normal men.

It is, however, not clear from this study whether the lack of gray matter was primarily due to inheritance (genes) or experience (environment). Certainly, like every other mental or emotional capacity, caring and uncaring are based in neurochemical interactions whose actual or potential strengths vary widely between individuals. But the question of how experience affects these capacities still remains.

Another Raine study sheds interesting light on this issue. This study focused on the relationship between traumas around the time of birth and violent crime in males around the age of 18 (Raine *et al.*, 1994). It was done in Denmark, the country that keeps perhaps the most comprehensive and accurate records both of criminal behavior and of early hospitalizations. It showed that violent crimes were more likely to be committed by those young men who had suffered *both* complications in the birth process and early maternal rejection. Maternal rejection was defined as an attempt to abort the fetus followed by placing the child in an institution in his first year. Neither maternal rejection nor birth complication alone predisposed the child to violence. And none of these factors predicted later nonviolent crime.

What this study indicates is that no simple explanation can completely predict patterns of behavior – be they caring or uncaring. It indicates what we are here also suggesting: that we have to look at an individual's experiences, and that even there we can't just look at one experience but rather at the interaction of a number of variables.

The role of everyday experience has proved surprisingly powerful in producing prosocial change. This means that finding a biochemical basis for sociopathic behavior does *not* mean "once a sociopath, always a sociopath."

A dramatic case in point was Larry Trapp, a Grand Dragon of the Ku Klux Klan in Nebraska who converted to a speaker for racial tolerance and respect for human rights as a result of a life-changing friendship with Michael and Julie Weisser, a Jewish cantor and his wife who moved into Trapp's neighborhood (*Dallas Morning News*, September 9, 1992). Trapp was stunned when the Weissers returned his harassing hate phone calls with kindness and neighborly offers to help him out (he was going blind and had to have help getting groceries). Trapp later even converted to Judaism, and when he died, his Jewish friends were at his side.

Some behavioral therapies have had varying degrees of success in bringing this sort of positive experience into the clinic. For example, behavioral therapy has been quite successful in reducing aggressive behavior in children with oppositional-defiant disorder who seem to have some genetic tendency toward violence (Altepeter and Korger, 1999; Kazdin, 1987; Lochman, 1992).

In other words, caring or uncaring behaviors and emotional traits – and the neural and biochemical patterns that go with them – are not fixed. Indeed, for those conversant with modern neuroscience, and therefore with studies of neural

plasticity in all ages of animals, it should not come as a surprise that the prevalence of any behavior based on complex neurochemistry should be influenced strongly by experience.

An animal study that dramatically showed the impact of experience on the brain, and with this on behavior, was conducted by the neurophysiologist William Greenough and his colleagues. These experimenters looked at both sensory and motor areas of the brains of rats placed in what they called an "enriched condition" environment (Greenough *et al.*, 1993; Jones *et al.*, 1997; Kleim *et al.*, 1998a; Kleim *et al.*, 1998b) and found significant effects on brain development.

The typical laboratory rat, even if well treated, lives in a cage that is much more boring, monotonous, and lacking in stimulation than the natural world of an animal. By contrast, Greenough and his collaborators describe the "enriched condition" (EC) laboratory environment in which they raised some of their rats as follows:

> EC rats were housed together for 60 days in a large wire mesh cage filled with a daily-changing set of toys and other objects. Once a day, animals were placed in an open field arranged with a new set of objects for 30 to 45 min. (Jones *et al.*, 1997)

As these researchers emphasized, the EC was still not as stimulating or complex as the natural environment of a wild animal, but even that degree of stimulation had a positive effect on the growth of synapses in the rat brain. The rats reared in the enriched cages had more of a certain type of connection on each neuron in the visual part of their cerebral cortex than did rats reared in standard laboratory cages. Specifically, the types of connections that were increased in number in the brains of rats in the enriched environment were formations of multiple synapses that connect with more than one part of the dendrites of other neurons.

These multiple synapses are thought to be important in learning due to some role they play in the synchronization of neural responses. This would mean that these types of neural structures could be important for coherent responses to complex and confusing arrangements of stimuli, which is certainly a large part of intelligence.

Greenough and his colleagues also found a similar enhancement of multiple synapses in the cerebellum, a part of the brain strongly involved in motor control, when the rats had been taught complex motor skills. They found that this synaptic enhancement was not simply an effect of motor *activity* but of motor *skill learning*. That is, rats who repeatedly ran a treadmill but did not acquire any new motor capability did not show such an enhancement in synapses.

These experiments on rats who were encouraged to learn motor skills also suggest the importance of encouraging children to learn by doing and not just by observing. Indeed, while these experiments specifically dealt with motor skills, the same thing could probably be said about cognitive skills such as language – and about emotional skills such as empathy and caring.

Other animal experiments show that blood levels of neurotransmitters such as serotonin also change in response to different experiences. For example, a series of

studies on male vervet monkeys by Michael Raleigh, Michael McGuire, and their colleagues show that amount of serotonin in the blood is related to a monkey's social status within a dominance hierarchy, being about twice as high in dominant as in subordinate animals. But this is a two-way relationship in which experience plays a decisive role. It is not a matter of high-serotonin monkeys being genetically dominant. Changes in the status of a particular monkey dramatically change its serotonin level. When the experimenters temporarily removed the currently dominant monkey from the colony so that another became dominant, serotonin levels changed accordingly (Brammer *et al.*, 1994; McGuire and Raleigh, 1986; Raleigh *et al.*, 1984).

The Neural Dynamics Mediating Selective Gene Expression

The specifics of how experience influences humans to be more or less caring (particularly as children but even as adults, as in the Trapp case) are not yet well understood. But we can hypothesize that, except for abnormal or severely injured brains and nervous systems, the capacity for caring is a human characteristic. We can further hypothesize that this capacity is related to neural circuits and biochemicals that are either activated or not activated by experience.

As we have seen, there is a large body of data on the neural and biochemical patterns involved in the development of uncaring and violent behaviors. Severe abuse or deprivation of caring have extremely negative effects on the brain. They inhibit caring behaviors, can lead to sexual dysfunction, and even to behaviors destructive to self or others.

The neural and biochemical patterns involved in the development of empathic and caring behaviors, which are a particular interest of this article, have been far less studied. Scientists have tended to focus on failure and discouragement in laboratory situations. They have focused their chemical and electrical measurement tools on the study of afflicted animals. Similarly, the focus of early psychotherapy on maladjustment led to studies of disturbed people.

However, as we have also seen, we have findings showing that bonding between individuals is influenced by various neurotransmitters, such as dopamine and serotonin, and peptide hormones, such as oxytocin and vasopressin. Preliminary findings as those of Uvnäs-Moberg (1998) suggest that persistent positive social bonding or attachment experiences can increase levels of oxytocin and the parasympathetic nervous system pathways this hormone enhances, which tend to counterbalance activities of the sympathetic stress system Henry and Wang discuss.

These findings would help explain why caring children are produced by societies, such as the Papago Indians of Arizona, in which parents tend to be lovingly attached to their children and not to use physical punishment (Eisenberg, 1992). They could explain how the Klan Grand Dragon Larry Trapp converted to a much more caring and less prejudiced person after a positive encounter with a Jewish

couple. They could also explain how mice *genetically bred* to be violent can become less violent in a different social setting.

Gariépy *et al.* (1998) and Gariépy *et al.* (1996) (see also Gariépy and Rodriguiz, this issue) bred mice to be either more or less aggressive and then reared them in isolation, which tends to reinforce aggressive tendencies, up to reaching puberty (about 45 days old). But when the high-aggression mice were brought out of isolation and placed in groups between 45 and 69 days, many of them became less aggressive and more cooperative.

This experiment is especially relevant to the persistent claim that genes determine behavior. It supports our hypothesis that what needs to be looked at is not genes per se, but the conditions that determine gene inhibition or expression.

The results of Gariépy's group are a particularly strong argument for the plasticity of whatever brain systems mediate aggressive or cooperative behavior. Just bringing the mice more consistently into social groups made them more cooperative than their genes would lead us to predict.

Extrapolating from mice to humans is difficult because human social interactions are more complex, and the criteria for a supportive environment may be different for humans than for mice. Yet the Gariépy group's finding on plasticity of behavior in mice supports the hypothesis of at least as much behavioral plasticity in humans – and probably much more, given the much greater role of learning in human behavior. It supports the conclusion that while people may differ genetically in their capacities for caring behavior, even those at the low end of this capacity scale can engage in caring behavior if their social contexts are structured in a way that encourages rather than inhibits such behavior.

THE ROLE OF THE ORBITOMEDIAL PREFRONTAL CORTEX

If we begin with the premise that caring behaviors are genetically available to normal humans, three questions arise. First, what are the neural dynamics mediating selective gene expression? Second, what biochemical and neural structures and connections are involved? And third, what are the experiences and social conditions that will lead to the expression or inhibition of these behaviors? We will address all three in the rest of this paper, starting with the first two.

It is now generally accepted that in the process of the brain's evolution from reptiles to non-primate mammals to humans and other primates, most of the structural and functional systems found in earlier species were preserved to some extent at the same time that additional mental capacities developed due to massive growth of the cerebral cortex (MacLean, 1990; Pribram, 1981). Specifically, in humans the subcortical system of socially based affective regulation shared with rodents now interacts, by extensive feedback connections, with networks in the cortex, particularly the prefrontal cortex, not found in rodents that process complex social stimuli, rewards, rules, and customs.

The conclusion that the prefrontal cortex is involved in this process is reinforced by the fact that patients with orbitomedial prefrontal damage show a deficit in learning to gauge their behavior appropriately to the current social context (Damasio, 1994). Indeed, it has been suggested that effective parents of young children supply their children with a "substitute prefrontal cortex" until the child's prefrontal cortex develops enough to function on its own (Schore, 1994).

The prefrontal cortex has often been called the brain's executive (Luria and Pribram, 1973). Whether or not the phrase "executive system" adequately takes into account the complex interaction between the brain, the immune system, and other bodily organs and cells (see Pert, 1997), the orbital and medial parts of the prefrontal cortex have long been recognized as the part of the human brain that uniquely mediates complex emotional responses including social responses. This has been suspected ever since the famous 19th century patient Phineas Gage lost the ability to make plans and respond appropriately to social situations after a railroad accident in which an iron rod went through his cheek and out the top of his head. The contemporary neuroscientist Antonio Damasio and his colleagues (Damasio, 1994) reconstructed Gage's case in a mechanical model, based on reports from that patient's attending physician about where the rod had gone, and discovered it was indeed in the orbitomedial prefrontal cortex where Gage had been most damaged. This region is unique in the extent of its connections both to high-order sensory and association areas of the cortex and to emotion-related areas below the cortex (hypothalamus, limbic system, and basal ganglia; see Figure 1) with extensive autonomic and visceral projections.

Neuroscientists have reached a consensus, from varied clinical and lesion studies, that the orbitomedial prefrontal cortex forms and sustains mental linkages between specific sensory events in the environment – for example, particular people or family and social structures – and particular positive or negative emotional states. This type of mental linkage is accomplished through the neural connections of the prefrontal cortex with sensory areas of the cerebral cortex, on the one hand, and with the hypothalamus and autonomic nervous system, on the other hand. It is widely believed that, through a process that is still little understood, the prefrontal cortex sustains connections between neural activity patterns in the sensory cortex that somehow reflect the influence of past sensory events, and other neural activity patterns in autonomic regions that reflect innate or learned expressions of emotional states. Aspects of this set of orbitomedial prefrontal functions have been given various names, among them interoceptive censorship of plans (Nauta, 1971), formation of somatic markers (Damasio, 1994), and sensory-visceromotor linkage (Öngür and Price, 2000).

It seems a plausible speculation that the area of the brain mediating the emotional and visceral significance a person attaches to objects and classes of objects (see also Elliott *et al.*, 2000; Rolls, 2000) also mediates the prevalence of large classes of responses such as fight-or-flight, dissociation, and tend-and-befriend. How might this occur?

The orbitomedial prefrontal cortex is likely to operate via reciprocal connections with several subcortical brain areas that play major roles in emotional regulation. One of them is a part of the hypothalamus (see Figure 1) called the *paraventricular nucleus (PVN)* which is of fundamental importance for controlling endocrine secretion. Different parts of the PVN contain, among other hormones, oxytocin, vasopressin, and corticotrophin releasing factor, the precursor of the stress hormone cortisol. The prefrontal cortex does not synapse directly on PVN, but synapses on other parts of the hypothalamus that in turn connect to PVN. In particular there are prefrontal connections to an area called the *dorsomedial hypothalamus* that sends inhibitory neurons to the PVN, as shown in Figure 2. These connections within the hypothalamus (from dorsomedial to PVN) are mediated by GABA, the brain's commonest inhibitory transmitter.

BEHAVIORAL INHIBITION AND DISINHIBITION

A related question is how an organism's nervous system goes about selecting responses to both external stimuli and internal states. One generally recognized method is inhibition. That is, the brain chooses between two sets of activity patterns or responses by inhibiting the response not chosen.

One of the meta-functions that clinicians and behavioral neuroscientists have often ascribed to the prefrontal cortex is *behavioral inhibition* (e.g., Davidson and Rickman, 1997). This ascription is based on the observation that prefrontal damage often leads to emotional impulsiveness, particularly uncaring and violent behaviors.

However, this emphasis on inhibition of emotions carries an implicit bias left over from Cartesian and Enlightenment rationalism, the assumption that the highest possible human functioning takes place when emotions are inhibited. This assumption is not congruent with what we know from psychology about damage to the brain's emotional pathways stunting effective (even rational) decision making (Damasio, 1994), and about positive emotions enhancing creativity (Isen, 1999).

We believe that the term "behavioral inhibition" does not do justice to the richness of prefrontal influences on human behavior. While prefrontal regulation can selectively decrease the probability of (that is, inhibit) some behaviors generated by subcortical areas, this same prefrontal regulation can selectively increase the probability of (that is, disinhibit) other behaviors (see Van Eden and Buijs, 2000, for more discussion of this point).

The orbitomedial prefrontal cortex has evolved in humans to enable us to make behavioral choices in an increasingly complex social environment (Damasio, 1994). We can infer this from evidence that patients with damage to this area are more likely to act in ways that are inappropriate for the social context in which they find themselves.[1]

[1] Of course there is sometimes a virtue in acting inappropriately for social contexts that are themselves pathological. Milne and Grafman (2001) discovered that male patients with orbitofrontal

Specifically, we hypothesize that for a person in a supportive environment, undergoing supportive therapy, or even making a conscious choice to engage in more caring behavior, the orbitomedial prefrontal cortex is involved in releasing or disinhibiting her or his caring capacities, as well as in preventing their inhibition by emotionally stressful stimuli and beliefs. This is a process whose mechanisms we plan to explore in much more detail through our neural network modeling, which we hope can point the way to future experimental tests of this hypothesis (see the discussion in the next section).

Based on the simplified schema in Figure 2, we can conjecture that at any given time the prefrontal cortex sends different strengths of inhibitory signals to the different parts of PVN that contain oxytocin or the cortisol precursor, and that this can be a means of influencing the relative likelihood of oxytocin-mediated (tend-and-befriend) versus cortisol-mediated (fight-or-flight or dissociative) responses. As we will develop in the next section, since the orbitomedial prefrontal cortex seems to store in some fashion the emotional or visceral significance of social memories, the relative strengths of these pathways could be influenced by the amount of stress in the organism's early experiences. As we will also develop, the types of behavior that prefrontal regulation would tend to disinhibit are likely to be those that are encouraged by the society, family, and other people that a person interacts with.

A second set of prefrontal pathways for response selection is probably the loops between cortex, thalamus, and basal ganglia (see Figure 1 for locations of these areas). These loops are a basis for several neural network models of reward-based behavioral regulation (e.g., Bullock *et al.*, 1999; Monchi and Taylor, 1999). These same pathways are also believed to be repetitively and compulsively activated as part of the disrupted regulation caused by drug addiction (Koob and LeMoal, 2001). In particular, we believe the strong connections between the prefrontal cortex and the nucleus accumbens (a primary area for both natural and drug-related dopamine rewards) are likely to be important for both tend-and-befriend and dissociative responses.

Finally, this part of prefrontal cortex has strong reciprocal connections with areas of the limbic system (see Figure 1) involved in emotional evaluation of stimuli. These include two parts of the amygdala (central and basolateral) that are also part of a positive feedback loop that mediates stress-related responses (Koob, 1999). This is a third set of pathways by which the orbitomedial prefrontal cortex might influence what type of response is chosen.

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lesions showed less tendency than normal males to attach gender stereotypical qualities (such as strength or weakness) to names that sounded male or female! Many forms of creativity could be akin to some forms of mental illness or brain damage in that they involve an ability to think outside the "box" of the prevailing set of social customs in which the person lives. What areas of the brain are involved in this kind of creativity is unknown: one of us (Levine, 1995) has speculated that it may involve another part of the prefrontal cortex (dorsolateral) and the hippocampus.

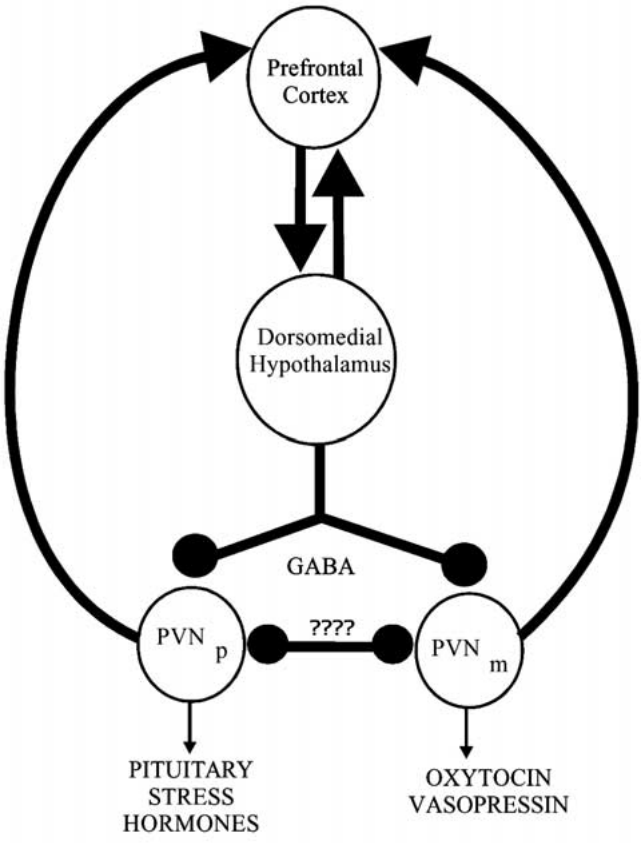

Figure 2. Part of the stress-regulating interactions between the prefrontal cortex and hypothalamus, as discussed by Buijs and Van Eden (2000). Arrows denote excitatory synapses, circles inhibitory ones. PVNp = parvocellular part of paraventricular nucleus, PVNm = magnocellular part. Different parts of PVN are known to have neural connections with one another, but it is not known whether there is direct inhibition between these two parts or whether the inhibition between oxytocin and stress hormone systems operates through effects of these hormones on other areas such as the limbic system.

But how does the context mediate *what* influence the prefrontal cortex exerts on behavioral responses? This region's reciprocal connections mean it is influenced by neural signals from many of the same brain areas to which it sends signals. Specifically, the orbitomedial area is roughly divided into two parts: an orbital part that receives inputs from sensory association areas of the cortex that reflect effects of experiences, and a medial part that receives inputs from areas of the hypothalamus that reflect effects of emotional states (Price, 1999). If we can understand how these two sets of inputs interact, our insights can be applied to describing effects of learning, and of moods and emotions during learning, on whether a person reacts to a given situation caringly or uncaringly.

We can conjecture that connections to this prefrontal region from other parts of the cortex and limbic system, representing social stimuli, are strengthened or weakened with experience, including the severity of previous stresses and the person's previous responses. This in turn influences the tendency toward any of three types of behaviors – fight-or-flight, dissociative, or tend-and-befriend – in a given social context.

Recall that each person's orbitomedial prefrontal cortex stores memories of associations between particular sensory stimuli and particular states of the viscera (e.g., Öngür and Price, 2001). These memories are dynamically changing over time with experience. Yet all through life, they are also heavily influenced by early social conditioning, which comes from both the family and the culture as a whole. These stored associations in turn have strong influence on how people respond to future stimuli, at the level of body responses as well as behavior.

Other types of conditioning that have been studied neurally require modifiable (plastic) synapses that can become strengthened or weakened with experience. Are there any modifiable synapses in the main connections of orbitomedial prefrontal cortex? This has not been established, but we can speculate that the synapses between prefrontal cortex and either dorsomedial hypothalamus (see Figure 2), nucleus accumbens, amygdala, or any combination of these would be good candidates. But whatever the locus at which such conditioning operates, interoceptive inhibition (what Nauta, 1971, called interoceptive censorship) can be biased in the direction of whatever sets of behaviors are favored by parents and/or society at large, including influential institutions such as education, media, politics, economics, and religion. Similarly, disinhibition would be biased by early influences in the absence of new experiences or learning opportunities.

Neural Network Theory-Building and Modeling

We have seen that understanding the complex dynamics involved in regulation of fight-or-flight, dissociative, and tend-and-befriend responses requires integrating very disparate kinds of data. Animal lesion studies, human brain imaging studies, and clinical observations of abused children, for example, all involve different measurement techniques. As the wealth of scientific tools grows, so does the complexity of relating one result to another and one theory to another (Grafman and Warden, 2000) and the need for a common theoretical language. Increasingly, researchers in all areas of behavioral neuroscience have turned to neural network modeling, and drawn on the expertise of established schools of computational modelers, to provide just such a common language.

This type of modeling involves building theories of the behaviorally significant dynamic interactions between a number of interconnected brain regions, and then, when these interactions have been specified to some level of precision, simulating them on a computer. As neural network models have become increasingly sophisticated in recent years, the mathematical dynamics of network variables have come

closer to reproducing effects involved in human or animal performance of cognitive tasks, including the influence of emotional states on task performance (see Levine, 2000, Chapter 7, for review).

We believe these methods can be applied to help us better understand the selective expression of genes for caring or uncaring behaviors, and even more specifically, the neural dynamics of context-dependent selection among tend-and-befriend, fight-or-flight, and dissociative responses.

The first step in developing a plausible neural network theory of any complex cognitive/emotional or behavioral process is to break it down into sub-processes that can be modeled by networks. Since these smaller networks typically involve dynamically interacting, and often overlapping, parts of the brain, the next step is to synthesize these smaller network models and their interconnections into a larger network model.

Our eventual aim is to develop as accurate and predictive as possible a theory of how, and in what contexts, prefrontal-subcortical pathways influence selective expression among genetically derived neural patterns representing caring and bonding responses, fight-or-flight responses, and dissociative responses. Such a theory requires a more detailed understanding than we have given so far of the brain regions involved in each of these types of responses separately. Hence we now sketch some hypotheses for the neural pathways that may be involved in each type of response, starting with caring and bonding.

NEURAL PATHWAYS FOR CARING AND BONDING

Caring or bonding responses across different species of mammals are diverse, ranging from pair bonding in prairie voles (Insel *et al.*, 1998) to mutual grooming (or friendship) and shared rearing of offspring in female animals and women (Taylor *et al.*, 2000). Yet some of the same biochemical substances (e.g., oxytocin and dopamine) appear to be involved in most of these responses. So as a starting point toward building a later, more complete, theory, we assume that there at least some brain mechanisms common to these different bonding patterns.

Hence, we have developed a first approximation to a neural network theory of human bonding responses based on the simpler brains of voles and their involvement in male-female pair bonding. Our starting point is the results of Insel *et al.* (1998) showing that oxytocin and vasopressin, the two peptide hormones most important for pair bonding in these animals, both have different binding patterns in the brain of the pair-bonding prairie vole than in the brain of the promiscuous or non-bonding montane vole. Also our theory builds on results of Cho *et al.* (1999) on gender differences in prairie voles. These researchers showed that even though oxytocin is more associated with maternal behavior and vasopressin with paternal behavior, pair bonding could be abolished in either male or female voles by drugs that blocked brain receptors for either of the two peptides. This suggests that both peptides are required for pair bonding in both sexes.

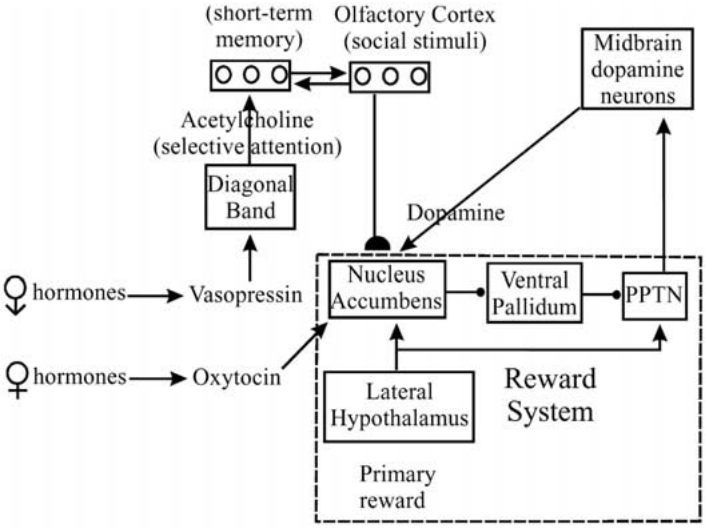

Figure 3. Proposed network related to subcortical bonding effects of oxytocin and vasopressin. PPTN is the pedunculopontine tegmental nucleus, a part of the midbrain. Ventral pallidum is a part of the basal ganglia. Both of these areas, along with the lateral part of the hypothalamus and the nucleus accumbens (see Figure 1 for locations of large brain regions) are known to be part of the neural circuit for processing rewards. Arrows between boxes represent excitatory (glutamatergic?) connections; filled circles represent inhibitory (GABAergic?) connections; semicircles represent modifiable connections.

Our theory of bonding (Figure 3) is based on the assumption that if we identify those brain regions that oxytocin and vasopressin bind more to in the prairie vole than in the montane vole, we will have identified regions that in both voles and humans play a role in bonding (tend-and-befriend) behavior. Insel *et al.* (1998) review data suggesting that the key area for oxytocin binding seems to be the nucleus accumbens (see Figure 1 for its location), well known to be a key part of the dopamine-modulated stimulus-response system (see, e.g., Brown *et al.*, 1999). The key area for vasopressin bonding seems to be an area called the *diagonal band* that produces the neurotransmitter acetylcholine, which is believed to be involved in selective attention (Everitt and Robbins, 1997). The acetylcholine signal connects, among other areas, to the hippocampus, the key area for consolidating short-term memories. These data suggest complementary roles for the two peptides in bonding, with oxytocin more related to the part of the process that drives behavior via reward, and vasopressin more related to the part of the process that focuses attention on relevant stimuli – in this case, focuses attention on the opposite-sex voles with which the particular animal is forming a pair bond.

The other parts of the network of Figure 3 (particular regions of the hypothalamus, midbrain, and basal ganglia; see Figure 1) are inspired by the previous neural network model by Brown *et al.* (1999) of how behaviors can become conditioned due to the effects of unexpected rewards. While these researchers looked

at different behaviors than we are interested in, we borrow part of their network because it illustrates some of the major brain pathways likely to be involved in any type of conditioned response. After all, partner preference is a *conditioned* association, whereby the smell – for prairie voles – or visual appearance – for primates – of a particular fellow member of one's species becomes linked to social and/or sexual rewards.

As our modeling proceeds from voles to humans, the kind of conditioning that takes place will of course be far more complex. It will also be more susceptible to change through new experiences and learning. However, the mechanisms that operate in animals can be built upon to include factors particular to humans. Starting from the network of Figure 3 as a base, we can say that the greater complexity of human as compared to vole behavior enhances the social conditionability of responses connected with oxytocin that has been noted by several authors (e.g., Uvnäs-Moberg, 1998).

But there is a still more fundamental difference between humans and species such as voles. Humans (and other primates) undergo conditioning not just, as voles do, about whom to bond with, but about how strong is the tendency to bond with anybody, as opposed to engaging in fight-or-flight or dissociative behavior. Moreover, for humans a major factor to be considered is the effect of social and cultural conditioning (e.g., cultural pressures to bond with some groups of people and not bond with others).

NEURAL PATHWAYS FOR FIGHT-OR-FLIGHT AND DISSOCIATION

As for fight-or-flight and dissociative responses, both involve activity of pathways connecting the hypothalamus (see Figure 1) with two important endocrine glands, the pituitary and adrenal glands. These pathways, known as the *hypothalamic-pituitary-adrenocortical (HPA) axis*, are involved in production of the hormone cortisol, which is typically released during stress. These systems are active in normal individuals during acute stress situations and, as Perry *et al.* (1995), Henry and Wang (1998), and others have noted, changes in receptor properties make them chronically active in individuals who have been abused or otherwise undergone trauma.

As we saw earlier, another substance that is typically released during fight-or-flight responses is the neurotransmitter associated with arousal, norepinephrine. An extensive system has been mapped out of interactions in the brain between these two major "fight-or-flight" substances, cortisol and norepinephrine (see, e.g., Ferry *et al.*, 1999; Herman and Cullinan, 1997; Koob, 1999).

In addition to the HPA axis, this stress system, common to all mammals, includes parts of the amygdala and other loci in the limbic system, which process the degree of fearfulness associated with stimuli in the environment, and parts of the hypothalamus, especially an area of hypothalamus called the *paraventricular*

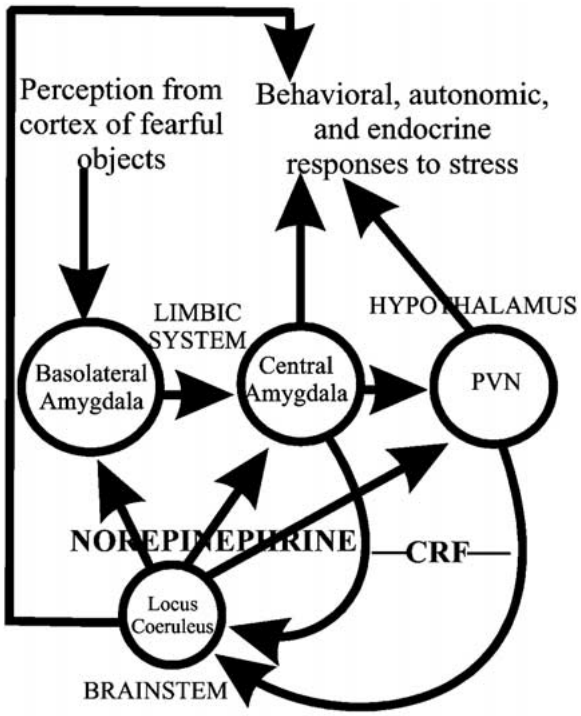

Figure 4. Part of the interactive feedback system between CRF (the precursor to cortisol) and norepinephrine stress-related systems in the brain. The basal and lateral nuclei of the amygdala receive inputs from the cortex and particularly respond to fear-inducing stimuli. These areas project to the central nucleus of the amygdala which projects to the hypothalamus and autonomic regions of the brain stem, including the locus coeruleus. Other parts of the limbic system which may be involved in these interactions (such as the bed nucleus of the stria terminalis) are not shown here for simplicity. See Figure 1 for locations of these areas in the brain.

nucleus (PVN), which is of fundamental importance for controlling endocrine secretion. This stress system also includes loci in the brainstem that connect to the autonomic nervous system, especially the nucleus (called the *locus coeruleus*), which is the source of most of the norepinephrine synapses going to other parts of the brain.

Figure 4 shows a very simplified picture of these interactions. The precursor to cortisol, known as corticotrophin releasing factor (CRF), in addition to being produced by the adrenal cortex, is actually utilized as a neural transmitter in parts of the limbic system and hypothalamus, as discussed by Koob (1999). There is pharmacological evidence that cortisol signals reach the norepinephrine-producing locus coeruleus, and that this nucleus in turn sends norepinephrine signals to the amygdala and hypothalamus. All those areas in turn generate behavioral responses to stress (fighting or fleeing) as well as responses of both the HPA axis (endocrine)

and the sympathetic autonomic nervous system (which affects the viscera). Thus a positive feedback loop tends to enhance and perpetuate the stress response once it gets going, unless the external environment becomes substantially less stressful. In the case of chronic stress – such as childhood abuse – we expect that the system shown in Figure 4 becomes more excitable so that even mildly unpleasant events can generate activity in this positive feedback loop.

These chronic states of hyperarousal would typically get in the way of positive social interactions, making the individual less receptive, more suspicious, more prone to uncaring and even violent behaviors. This in turn would mean that caring from others would be discouraged, making the biochemical and neural responses associated with receiving caring less likely in a self-perpetuating cycle of chronic hyperexcitablility. Nestler *et al.* (1999) have largely confirmed this hypothesis by studying a complex set of molecular events, whereby chronic stress increases the excitability of neurons of the locus coeruleus, the norepinephrine-producing locus shown in Figure 4.

One more part of the puzzle that we discussed earlier is the role of serotonin in emotional stabilization, and conversely, of chronic childhood stress (or stress of social domination) in reducing serotonin levels. Serotonin is not a transmitter in the autonomic nervous system, but could exert some inhibitory influence on the stress-related positive feedback between cortisol and norepinephrine shown in Figure 4, and in turn could be reduced by activity in this stress feedback loop. Some antidepressants that increase circulating serotonin levels have been found to decrease activity of this loop (Nestler *et al.*, 1999) or depress the activity of the sympathetic nervous system involved in fight-or-flight responses (Shores *et al.*, 2001). Yet there is such a multiplicity of different types of serotonin receptors (see, e.g., Tecott, 1996) that a general theory of how this important neurotransmitter operates will require much further research.

The brain interactions involved in dissociative responses are less well worked out than those in fight-or-flight responses. Based on the work summarized by Perry *et al.* (1995) and Henry and Wang (1998), we would expect some of the same brain areas to be involved as in fight-or-flight responses (Figure 4), but with differences in the biochemical activation patterns. For example, there should be substantially less norepinephrine activity in dissociated individuals. Dissociation is similar to fight-or-flight, though, in that cortisol levels are generally high and oxytocin levels low. The decrease in oxytocin means that chronically active dissociative pathways, like chronically active fight-or-flight pathways, severely reduce the likelihood of caring behavior. The exact mechanism by which elevated cortisol depresses oxytocin is not known: this interaction might occur at the PVN, the brainstem, or in the autonomic nervous system.

Dissociative responses, as we said earlier, involve dopamine, more specifically, dysfunctions of the reward system in which dopamine is the most important neurotransmitter. Dissociation then will also typically mean that the enduring rewards of positive social interactions are less available.

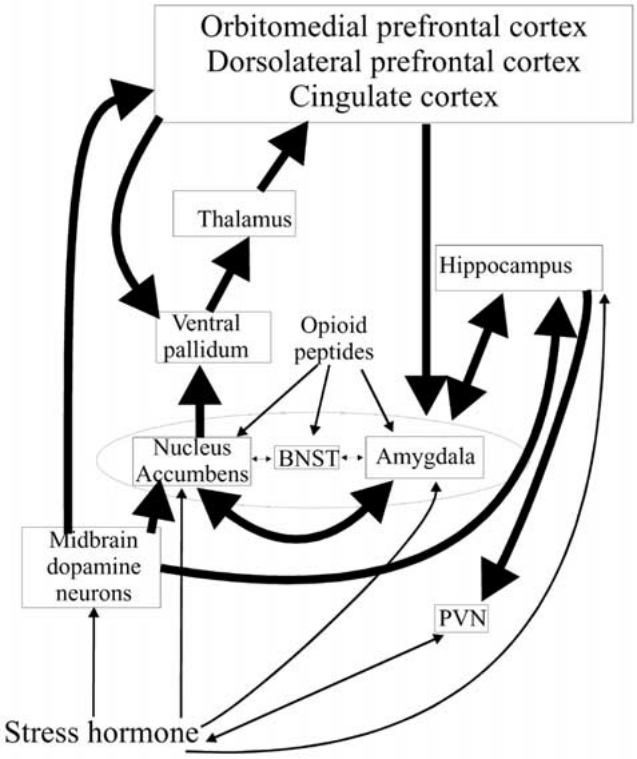

Figure 5. Circuit diagram of the reward system. Parts of the nucleus accumbens, bed nucleus of the stria terminalis (BNST), and central nucleus of the amygdala have been hypothesized to from a key component of the brain reward circuit. Opioid peptides and midbrain dopamine neurons perform critical modulatory functions on this circuit. Stress hormones fuel dysregulation of the reward circuit, which is expressed as compulsive behavior of the cortico-thalamic-pallidal loop. PVN = paraventricular nucleus. See Figure 1 for locations of some of these areas in the brain. (Adapted from *Neuropsycho-pharmacology*, *24*, Koob, G. F., & LeMoal, M., Drug addiction, dysregulation of reward, and allostasis, *Neuropsycho-pharmacology*, 97–129, Copyright 2001, with permission from Elsevier Science.)

The literature on the neurobiology of addiction offers clues to more general dissociative responses. Although most of the studies have been about the action of a particular drug such as cocaine or heroin, Koob and LeMoal (2001) reviewed some common themes in the study of all drugs of abuse. They note particularly that these drugs tend to interact with the brain's reward system in such a way that once a drug has become associated with reward, progressively more of the drug is needed to achieve the same state of reward. Koob and LeMoal described the reward system on which this operates, which includes the prefrontal cortex, in Figure 5.

Koob and LeMoal reviewed evidence (also see Volkow and Fowler, 2000) that excess cortisol disrupts the proper functioning of the brain's reward system by generating compulsive activity in a circuit that includes the prefrontal cortex and

parts of the thalamus and basal ganglia (see Figure 1 for locations of those areas). As a consequence of this compulsive neural activity, behavior that once led to pleasure is compulsively repeated even after it leads to much less pleasure. Figure 5 is an illustration of the neural pathways likely to be involved in such responses.

NEURAL NETWORK MODELING OF EMOTIONAL FUNCTIONING

Our neural network models (Levine and Leven, 2001) are currently at the stage of theory building that comes before computer simulation can occur. We start with a model of the tend-and-befriend or bonding response, the basic structure of which is shown in Figure 3. We plan to later extend this modeling to include the brain systems involved in hyperarousal and dissociation, along the lines of Figures 4 and 5. Finally, we will extend this model to humans, based on the assumption that similar biochemical patterns occur in humans as in other mammals, but with the addition of a vastly expanded cerebral cortex.

Ultimately we plan to combine all these pathways, and the prefrontal disinhibitory pathways of Figure 2, into a neural network model of selective gene expression among these different response classes. This will be a model that can accommodate the influences of human social contexts on such selective expressions.

However, we want to emphasize that the conclusion that social and cultural interactions, and not just genetics, play an important part in promoting caring or uncaring behavior does not depend on the exact biochemical mechanisms we are discussing. Rather, it is based on widely recognized findings from psychology and sociology, as well as findings from neuroscience showing that experience alters the strengths of connections in many parts of the brain, and specifically in those networks that promote different types of behavioral responses.

The influence of the cortex on the subsystems involved in each of the responses is exerted partly through the disinhibitory pathways of Figure 2 but also through a variety of prefrontal connections to other cortical and subcortical areas (see, e.g., Price, 1999) that we have discussed broadly but we have yet to map out. It is through these other connections that we will model the selective effects of experience – especially the effects of a repeated pattern of experience, such as a family that is either caring or abusive, or social policies and societal customs that either enhance or suppress caring interactions.

How Does Society Interact with Our Brains?

Without fully mapping out a set of brain mechanisms, we will now discuss in more detail how family and social influence are likely to operate on our biology.

Once we have some understanding of the brain systems that tend to encourage or discourage caring behavior, we can start to embed these brain systems in networks of social interaction. This can help suggest mechanisms for how different types

of social arrangements interacting with the brains of the individuals in them can enhance or suppress caring behavior.

If prairie voles can pair bond to the first opposite-sex vole they encounter at the right time, then humans are all the more conditionable, at least as children, to love or hate just about anybody or any group of people. Furthermore they can be raised to bias their overall orientations toward love or hate, depending on the kind of social system they are born into.

One of us (Eisler, 1987, 1995) argues that throughout human history there has been a conflict between those who would inhibit uncaring behavior and promote mutually respectful and caring relations, and those who would inhibit caring behavior in order to protect social hierarchies. Rigid hierarchies – whether man over woman, man over man, race over race, religion over religion, or nation over nation – require the inhibition of caring and empathy. In earlier times, these rankings were considered normal. And even today, beliefs, institutions, and behaviors required to maintain hierarchies of control are often seen as normal – from violence in childrearing and male-female relations to socially and environmentally unsound business practices and the idealization, and even religious incitement, of violence in intranational and international relations.

In the neuroscience framework of this article, such beliefs, institutions, and behaviors are not viewed as normal. Rather, they are seen as the results of interactions among large numbers of people whose prefrontal-subcortical loops have been disrupted by the chronic stresses inherent in establishing and maintaining hierarchies of domination that are ultimately backed up by fear and force. This is a type of hierarchy that is very different from a hierarchy of actualization (Eisler, 1987, 1995, 2000), where power is used not to control and disempower others but to inspire and nurture others' capacities and talents, as in the contemporary movement to redefine the manager from cop and controller to facilitator and mentor (Bloch, 1987; Eisler, 1987, 2002).

Drug addiction provides a model for understanding these dynamics. Recall from the prior sections that drug addiction – a dissociative response to stress – often leads to repetitive activity in a loop including the prefrontal cortex, basal ganglia, and thalamus, which in turn drives the compulsion to engage in certain behaviors even though they have adverse consequences. We conjecture that similar dynamics may be occurring for a host of other "addictive" noncaring behavior patterns, ranging from domestic violence, terrorism, and other criminal behaviors to compulsive buying to running corporations without regard for human welfare or environmental sustainability.

So again, when we engage in uncaring behavior, it is not necessarily, or even most of the time, the case that we *want* to be uncaring. We may simply be trapped in a compulsive pattern, or not know we have an alternative. This means we are not prisoners of our genes: the availability of an alternative, or sufficiently strong negative consequences of the current pattern, can lead to a prefrontally regulated readjustment of the set points for reward that the uncaring behavior disrupted. What

this suggests is that uncaring behavior is reversible when there is sufficient social support.

BIOLOGY AND SOCIETY

Conditioning, even conditioning from early childhood, is not impossible to overcome, only difficult. This is seen for example in the results mentioned earlier of Gariépy *et al.* (1996, 1998), showing that even mice genetically bred to be aggressive can often become less aggressive and more cooperative when brought out of isolation at a critical time during their puberty.

But *how much* of our genetic makeup can be overcome? The standard argument of some sociobiologists is that essential parts of our makeup vary little if at all across cultures, since they arose as evolutionary adaptations (see, e.g., Pinker, 1997). Unequal social hierarchies of power, concentrations of wealth, control and domination, so the argument goes, are due to evolution. Double standards for women and men, both in sexual and in interpersonal behavior, these sociobiologists also say, arose out of the separate evolutionary adaptations of the "selfish genes" of males who have less investment in each offspring because they can produce hundreds in their lifetime, and females who have more investment in each offspring because they can produce much fewer. Attempts to transform society, they further claim, fly in the face of human nature – so the best we can do is try to be as humane and cooperative as possible within these severe, cross-cultural genetic limitations on how caring we can be for each other and the planet.

While we believe that evolutionary studies are an important contribution to a better understanding of both human limitations and human possibilities, we disagree with these positions. We argue that they are rooted not in scientifically verifiable data but in deeply embedded cultural assumptions about human nature – as in the assertion of Hobbes that humans are selfish, nasty, and brutish.

Human social potential is far less limited than much of sociobiological theory would have us believe. Challenges over the last 300 years to entrenched traditions of domination – from the rule of "divinely ordained" kings to men's control of women and children in the "castles" of their homes – have brought once unimaginable changes in beliefs and behaviors. The intellectual superiority of white over darker-skinned races and of men over women, termed "natural" by 19th century Social Darwinism, has been discredited, and the social arrangements that have supported these false beliefs have been and continue to be challenged.

Nations such as Norway, Sweden, and Finland exemplify the movement toward what one of us (Eisler) calls the partnership rather than domination model of structuring human relations. These are nations where there is much greater economic and political democracy – where there are not such huge gaps between haves and have-nots, where women comprise approximately 35–40 of the elected officials, and where caring for children, the elderly, and our natural environment have been integrated into social policy through economic inventions such as government

funding for child care, elder care, and paid parental leave (Eisler, 1987, 1995, 2002).

These developments support a much less limited view of "human nature." They indicate that many unpleasant aspects of society all over the globe that we often take for granted are not human universals, but are the product of historical factors and can be changed. These include, for example, fear-based dominance hierarchies, male oppression of women, eroticization of violence, repression of sexual pleasure, overpopulation due to restrictions on contraception, religious glorification of self-induced pain, and cultural/religious glorification of terrorism and war.

In investigating the roots of the dominator based mores of most contemporary societies, Eisler (1987, 1995) found that there was a cataclysmic change in most societies in Europe and Asia, spurred in Europe between about 4300 and 2800 B.C.E. by invasions from warlike nomads based in the harsh Asian steppes and variously called Kurgan or Indo-European. This moved earlier societies away from a partnership toward a dominator orientation, bringing a fundamental shift in many common categorizations and beliefs. Eisler also found that over the last 300 years there has been strong movement toward the partnership model – albeit countered by fierce resistance and periodic regressions, for example, Nazi Germany, Stalin's Soviet Union, Khomeini's Iran, and the Taliban of Afghanistan.

How can we understand such cultural developments from the perspective of behavioral neuroscience?

Again the conditionability of the dopamine system for positive affect, and the oxytocin system for the specifically social and interpersonal aspects of positive affect, allows our brain to learn a range of associations. For example, these neurochemical systems allow us to learn the associations many cultures have developed between love and domination, between war and heroism, or between sexuality and violence (Eisler, 1995). But these neurochemical systems also allow us to learn opposite associations such as a valuing of pleasure-based partnership and reciprocity, cultural glorification of peace, and a positive view of sexuality based not on domination and submission but on the mutual giving and receiving of pleasure.

GENDER DIFFERENCES IN CARING?

Eisler's historical and cross-cultural analysis shows that a key element in whether social arrangements enhance or suppress caring behavior is the degree to which the socially prescribed childrearing relies on empathy and nonviolence (the partnership model) or suppression of empathy and the use of violence (the domination model). A second key element is the nature of the socially prescribed roles and relationship of the two main divisions of humanity – women and men. Where we see the rigid ranking of the male half of humanity over the female half, as in the Muslim fundamentalist Taliban of Afghanistan, we can predict rigid hierarchies of domination in all relations and a high degree of socially and/or religiously condoned violence to maintain these rankings Conversely, the more we move toward a more equal part-

nership between the female and male halves of humanity, as in the Scandinavian world, we can predict a more politically and economically democratic society with policies that fund caring and nonviolence, as in the Scandinavians' pioneering of health and elderly care, paid parental leave, and peace rather than war academies.

Based on the knowledge we now have about the social construction of gender roles and relations, as well as about some of the more important hormones for bonding and female and male sex hormones (see Figure 3), we will take a brief look at what our neuroscience perspective has to say about gender roles and the potentialities of both sexes for caring.

Nowhere is there more passionate debate about nature and nurture than in the area of gender traits, roles, and relations. Again, we are told by some sociobiologists that the traits, roles, and relations of women and men are the result of evolutionary forces, and thus built into our genes.

But then how do we account for the enormous changes in the traits, roles, and relations of women and men we can see with our own eyes? How do we account for the fact that as girls and boys are less rigidly confined by gendered socialization, they are no longer so stereotypically "feminine" and "masculine" in their behaviors? How can we explain that women today are doing very well in higher education, even though according to 19th century evolutionary theory they were considered incapable of such intellectual achievements? How do we account for the fact that many men are changing the role of fathering to be much more like that stereotypically defined as mothering, giving babies and children tender loving care? If all this were genetically fixed, surely neither women nor men could make such radical changes in their behavior. Nor if male dominance were evolutionarily fixed could couples today have the pleasure of relations of much greater equality – relations conforming more to the partnership rather than domination model.

This is not to say that there are no biological changes involved in these changes in gender traits, roles, and relations. As we have seen, experience alters the biochemicals that send emotional messages to us. But the point is that these changes are possible: that gender roles and relations are not genetically fixed.

There is a mammalian history where, in most species, females have taken the major caregiving role, and this has biochemical implications. For example, in the prairie voles, oxytocin is more prominent in females and vasopressin in males (Insel *et al.*, 1998). While oxytocin is released by orgasm in both sexes, it is particularly stimulated by estrogens and vasopressin by androgens, as noted in the neural network of Figure 3. Much of this difference probably persists in primates, including humans. So females may in the course of evolution have developed biochemical patterns that favor caregiving behaviors. But these behaviors are not imprinted – as shown by females who are poor caregivers, and sometimes not only neglect but even intentionally harm their babies and children.

To say that only females can naturally be caring is a gross oversimplification that is used to reinforce pernicious social customs and policies. While oxytocin is involved in maternal functions such as lactation and its level is enhanced by female

hormones, it is present in both sexes and provides the same anxiety reducing and socially rewarding benefits to both (Cho *et al.*, 1999; Uvnäs-Moberg, 1998).

Taylor *et al.* (2000) note that some of the key studies of gender differences have not been done yet. While the fight-or-flight idea was based disproportionately on studies of male animals and men, the more recent ideas about affiliative responses to stress have been based disproportionately on studies of female animals and women. Hence the literature on gender differences remains somewhat confusing. Yet the results suggest that these differences are not exclusively genetic nor exclusively cultural. Genetic ranges on caring and prosocial behavior might differ (on the average, if not in every individual) between the sexes. But cultural institutions can selectively enhance or inhibit the expression of the caring capacity in *both* women and men.

Even if the capacity for caring social bonding were *statistically* greater in females (which has not been proved), it is sufficiently present in both genders to flourish when encouraged by social arrangements, and sufficiently vulnerable in both genders to disruption by childhood abuse or by major adult stresses. Given social roles imposed on women and men in societies that orient closely to the domination model, these disruptions will manifest themselves in different ways in males and females. But there seems little question that childhood abuse inhibits caring in both mothering and fathering and disinhibits cruelty and violence. And when this abuse is built into the cultural fabric, as in many contemporary fundamentalist societies where girls and women are terrorized into submission and boys are brought up to believe that violence against out-groups (other nations, religions, and even sects) is holy, the adverse consequences extend beyond the groups directly involved. In our high technology age, when nations and even individual terrorists can wreak mass destruction across the globe, there are adverse consequences for us all.

Moreover, if men continue to be socialized to suppress their caring capacity, this deprives men of the mutual emotional support that aids in solving complex problems in both work and interpersonal settings. The resulting prevalence of fight-or-flight behaviors also has much to do with the high incidence of violent deaths and other injuries males have historically suffered at each other's hands, both in war and in street crime.

Again, we call for a reinterpretation of traditional ideas about evolutionary adaptation. We do not dispute the argument that a fight-or-flight response has often served an adaptive purpose in enhancing survival in the face of predators or other dangers. Yet in modern technological society, where external predators are not a factor, this response is much less adaptive. It can shorten individual life spans due to cardiovascular and other degenerative diseases, and given the nature of modern nuclear and biological weaponry, threatens the survival of our species.

Men have often been discouraged by their peers from feeling empathy and from forming deep, caring bonds, which are considered "too emotional" or "womanly." These male peer groups have also often involved conditions of war or other phys-

ical danger, and encouraged men to seek out these dangerous conditions in order to get the camaraderie and emotional networking they want. Often, this is a type of camaraderie that relies on being a part of an in-group that is in opposition to an out-group, as in sports or wars, and so discourages empathy toward those in the out-group. And it often creates bonding only on a superficial level, such as talking about football games but not about the real problems men face in jobs or relationships. So while there are of course male social networks in dominator societies, these are often based on power over others – women, less aggressive men, "inferior" races or religions, or "dangerous enemies."

HEALTHY AND UNHEALTHY SOCIETIES: A NEUROSCIENCE PERSPECTIVE

There are no good or evil brain chemicals. The fight-or-flight, dissociative, and tend-and-befriend systems developed during evolution for different purposes. Yet there is a balance between the activities of these systems, reflected, for example, in the balance between the parasympathetic and sympathetic autonomic nervous systems.

We argue that the biochemical balance we have learned to accept in "normal" society is in fact not the level of balance that promotes the best physical and mental health. In other words, we need to readjust the levels we consider normal. And the most efficient way of making that readjustment is changing the level of caring or noncaring behavior by both men and women that is supported by the social institutions of a society. Since supportive social attachments (in and out of families) tend to increase oxytocin levels and decrease levels of stress hormones such as cortisol, there is every reason to suspect the same biochemical effects from increasing the level of interpersonal support on a societal scale through institutions and policies that disinhibit rather than inhibit caring.

The chronic stress inherent in social arrangements ultimately based on fear and force to maintain rankings of domination leads to a vast array of unhealthy phenomena. These range from denial and escape from pain through compulsivity and addiction to the unconscious deflection of fear and anger against those on top to those perceived as less powerful and/or dangerous through scapegoating, child-beating, wife-beating, terrorism, and aggressive wars (Eisler, 1995, 2002). While there are historical and contemporary data supporting this hypothesis, it is difficult to test empirically without longitudinal studies in which social mores are manipulated over a period of generations.

However, some testing can come from computer models that combine neural and social systems. In such models, brain-like neural networks, each with intricate cognitive-emotional interactions, are integrated into social systems that include cultural beliefs that feed back on individual behavior.

Leven and Elsberry (1990), for example, developed a neural network model of the negotiation process between two individuals. Each of their two "negotiators" includes a part that simply follows unvarying patterns, such as traditional social

rules; a part that responds to emotion; and a part that selects among alternatives by rational choice. The rule-following, emotional, and rational elements of each individual are not necessarily in conflict: at best they are working in harmony with one another as parts of an interdependent behavioral system. This is a very preliminary version of the type of future computational modeling that is likely to yield answers to questions about interactions, healthy or addictive, between societies and individual brains.

At this stage of knowledge, any conclusions have to be speculative. Yet we can conjecture that an understanding of the mechanisms of drug addiction might yield some clues about the dynamics of many unhealthy behaviors. The neurophysiologist Jerome Lettvin has said that addiction can serve as a prototype for all forms of neurosis (personal communication to author Levine, January, 1974). Can hierarchies of domination, which are stressful in different ways for the people "on top" and "on the bottom," and their attendant social neuroses, be perpetuated by a mechanism analogous to drug addiction on a societal level, as well as tending to promote different types of addictive (or fetishistic) behavior in individuals?

Many of the commonest drugs of abuse operate by causing massive releases of dopamine in the area around the nucleus accumbens, and then making later replenishment of dopamine dependent on further ingestion of the drug (Koob and LeMoal, 2001; Kovács *et al.*, 1998). Could some of our social pathologies operate in an analogous manner? For example, the glorifying and eroticizing of violence could mean that in many people the much sought after activation of the dopamine reward system, and the oxytocin social reward system, have both become conditioned to watching or engaging in violence.

Another example of how a society that relies heavily on dominance hierarchies has difficulty meeting people's genuine needs for emotional fulfillment is the susceptibility of many people to the superficial appeals of anything that promises to meet those needs, such as commercial products ranging from perfume to designer clothes to beer. Two contemporary videos (*The Ad and the Ego* and *Advertising and the End of the World*) vividly portray the social and environmental costs of this increasing commercialization (with advertising even bombarding elementary schools). The narrator of these videos (Dr. Sut Jhally of the University of Massachusetts) notes what psychologists have found – that happiness comes from personal relationships, not from commodities. Yet advertisers since the 1920s have increasingly conditioned people to link the satisfaction of the human need for friendship, family life, and sexual expression with buying more and more commodities – which then inevitably results in disappointment, and buying even more, in vain efforts to satisfy unmet needs for pleasurable, caring bonds.

Similarly, psychoactive drugs, while needed to treat people with certain conditions (see Embry, this issue), cannot compensate for social and economic binds. Noninvasive therapies such as meditation can have beneficial effects for people stressed out by society, but if not accompanied by social change they amount to privatizing problems that are societal in nature. Such privatized therapies are

only palliatives that alleviate symptoms of the real social problems of insufficient bonding, trust, caring, cooperation, and intimacy, and cannot of themselves lead to long-term solutions of those problems.

Conclusion

From the perspective we have briefly developed, the yearning by both men and women for caring connections, for peace rather than war, for equality rather than inequality, for freedom rather than oppression, can be seen as part of the human genetic equipment. The degree to which this yearning can be realized is not a matter of changing our genes, but of building social structures and systems of belief that support rather than inhibit the human capacity for caring.

Again we want to emphasize that our thesis that social structures matter, and that caring or uncaring behavior is not purely genetically determined, does not hinge on the specific biochemical and physiological mechanisms we have suggested in Figures 2–5. This thesis is rooted in the fact that the brain's plasticity, and its dependence on experience, has been demonstrated in a wide variety of settings. Moreover, there have been many demonstrations, as other authors in this issue will attest, that persistent stresses tend to bias the brain's pathways in the direction of hyperaroused or dissociative responses, and caring relationships tend to bias the brain's pathways in the direction of tend-and-befriend responses. The exact mechanisms for these effects are likely to vary immensely between species and between individuals within a species, and Figures 2–5 merely suggest one possible set of mechanisms.

With this caveat, we strongly believe that science has an important role in helping us develop a clearer understanding of the neural and biochemical dynamics involved in caring and uncaring behaviors, as well as how these dynamics are affected by experience. We also believe that this understanding is urgently needed to pave the way for scientifically-grounded criteria for not only individual health but also social health.

This article is not the best place for detailed description of changes in society that would promote healthy functioning of our brains. Good descriptions are found elsewhere (Calhoun, 1974; Eisler, 1987, 1995, 2000, 2002). Suffice it to say here that they range from more compassionate social policies, education for empathic and nonviolent parenting, and changes in the acceptable level of teasing in schools, which might prevent tragedies such as the Columbine massacre (Aronson, 2000; Eisler, 2000), to a global politics supporting gender equity and an economics of caring rather than a system based on short-term financial profits and top-down control (Eisler, 2002). (Cory, this issue, develops some economic implications of brain systems related to caring behavior).

We believe that the theoretical framework and network modeling we are developing can have applications for both social and individual mental health. This network modeling would encompass both prosocial and antisocial "personality

profiles" based on different amounts of activation in different loci within the orbitomedial prefrontal cortex that have different prevailing effects on the autonomic system. For example, there are PET results from Jordan Grafman's laboratory at the National Institutes of Health (Pietrini *et al.*, 2000) showing that blood flow in orbitomedial cortex decreased in subjects who were imagining reacting violently to a situation. Dr. Grafman (personal communication with author Levine, March, 2001) confirmed that there have been few if any published studies of cerebral blood flow patterns in the course of people imagining *loving* or *generous* reactions but added that he and Pietro Pietrini from the University of Pisa have been funded to do brain imaging studies of people engaged in acts of forgiveness. We will closely monitor the progress of this forgiveness study and hope to extend our network model to incorporate its results. In general, we advocate following the call of Maslow (1971) to study mental processes (and the brain) by studying positive caring and self-actualizing behavior and not just pathological behavior.

We also believe that to focus only on genes diverts science from the essential inquiry into how gene expression is inhibited or disinhibited by experience. It has become increasingly fashionable to despair of the possibility of social change because of what we think is true of the brain and human nature. But we believe that the brain's very complexity refutes such cynicism.

Genetic factors are important: differences between individuals or groups in the capacity for caring, like any other mental capacity, are real. Yet the effects of conditioning, context, and social expectation, a few of which we have shown here, have a profound influence on which parts of our genetic repertoire are enhanced or suppressed, particularly in early development but all during life. So while other authors have invoked brain mechanisms to argue for the futility of social change, we invoke brain mechanisms to argue that social change makes a tremendous difference in human behavior.

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