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10 Lust, Romance, Attachment: Do the Side Effects of Serotonin-Enhancing Antidepressants Jeopardize Romantic Love, Marriage, and Fertility?

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Today, millions of people of reproductive age take selective serotonin-reuptake inhibitors (SSRIs) and other serotonin-enhancing antidepressants. Approximately 80% of these drugs are prescribed by nonpsychiatric physicians, including internists, general practitioners, pediatricians, and gynecologists, who disseminate them to a wide array of men and women. In the first five months of 2004, American doctors wrote 46 million prescriptions for antidepressants, largely for these drugs. In the United States alone, antidepressants account for $14 billion a year in wholesale revenues (Morais, 2004).

These medications effectively treat a wide range of serious conditions, including major depression, posttraumatic stress disorder, generalized anxiety disorders, panic disorders, obsessive-compulsive disorder, social phobias, eating disorders, Asperger's syndrome, irritable bowel syndrome, and chronic pain syndromes. But they also produce various side effects. In both men and women, these antidepressants can cause emotional blunting, weight gain, and several types of sexual dysfunction, interfering with sexual desire, sexual arousal, genital sensation, lubrication, erection, ejaculation, and orgasm (Montejo, Lorca, Izquierdo, & Rico-Vallademoros, 2001; Rosen, Lane, & Menza, 1999). The number of men and women affected by these forms of sexual dysfunction vary; some studies report that as many as 73% of patients taking serotonin-enhancing antidepressants experience one or more of these sexual side effects (Montejo et al., 2001).

We propose that serotonin-enhancing antidepressants can have far more serious psychological, social, and genetic consequences through their effects on several other neural mechanisms that evolved to enable mate assessment, mate choice, mate pursuit, feelings of romantic love, and expressions of attachment to a long-term partner.

This chapter discusses the neural correlates of the three primary brain systems for courtship, mating, pair formation, and reproduction: the sex drive, romantic love, and male-female attachment (companionate love). It explores the neurochemical relationships between these three neural systems to show how serotonin-enhancing antidepressants can potentially jeopardize the ability to fall in love and maintain a stable, long-term partnership. It discusses the potential effects of the long-term use of serotonin-enhancing medications on other brain-body mechanisms that evolved to foster courtship and pair-bond stability, including penile erection and female orgasm. Finally, the discussion considers how serotonin-enhancing antidepressants can adversely affect fertility and one's genetic future.

Three Neural Systems for Mating and Reproduction

Neuroscientists currently believe that the basic human emotions and motivations arise from distinct systems of neural activity, that these brain systems derive from mammalian precursors, and that these brain mechanisms evolved to enable survival and reproduction (Davidson, 1994; Panksepp, 1998). Among these primary neural systems are three discrete, interrelated motivation/emotional systems for mating, reproduction, and parenting: the sex drive, romantic love, and male-female attachment. Each of these motivation/emotional systems is associated with a different behavioral repertoire, each is associated with a different and dynamic constellation of neural correlates, and each evolved to direct a different aspect of reproduction (Fisher, 1998).

The sex drive is characterized by the craving for sexual gratification. In nonprimate mammalian species, it is associated primarily with the estrogens and androgens. In humans and other higher primates, the estrogens have little direct influence on sexual desire (Meston & Frolich, 2000); instead, the androgens, particularly testosterone, are crucial to sexual desire in both sexes (Edwards & Booth, 1994; Sherwin, 1994; Van Goozen, Wiegant, Endert, Helmont, & Van de Poll, 1997). The sex drive evolved principally to motivate individuals to seek sexual union with a *range* of reproductive partners.

Romantic love (also known as obsessive love, passionate love, or being in love) is characterized by intense energy, focused courtship attention, ecstasy, mood swings, sexual possessiveness, emotional dependency, obsessive thinking about the beloved, craving for emotional union with the beloved, and intense motivation to win this *preferred* mating partner

(Fisher, 1998; Gonzaga, Keltner, Londahl, & Smith, 2001; Harris, 1995; Hatfield, 1988; Hatfield & Sprecher, 1986; Shaver, Schwartz, Kirson, & O'Connor, 1987; Tennov, 1979). Evidence suggests that romantic love is primarily associated with elevated activity in dopaminergic pathways of the reward system of the brain (Aron et al., 2005; Bartels & Zeki, 2000, 2004), and data suggest that other mammals share central biological and behavioral aspects of this brain system (Fabre-Nys et al., 1997; Gingrich, Liu, Cascio, Wang, & Insel, 2000; Liu & Wang, 2003; Wang et al., 1999). The neural system associated with romantic love evolved to motivate individuals to prefer a *specific* mating partner, thereby conserving courtship time and energy.

Partner attachment in humans is associated with feelings of calm, security, social comfort, and emotional union with a long-term mating partner, as well as with some of the traits of mammalian attachment, including mutual territory defense and nest (home) building, mutual feeding and grooming, maintenance of close proximity, separation anxiety, shared parental chores, and affiliative gestures (Carter et al., 1997; Lim, Murphy, & Young, 2004; Lim & Young, 2004; Young, Wang, & Insel, 1998). Animal studies suggest that this brain system is associated primarily with the neuropeptides oxytocin and vasopressin (Carter, 1992; Lim, Murphy et al., 2004; Lim & Young, 2004; Winslow, Hastings, Carter, Harbaugh, & Insel, 1993). Adult male-female partner attachment evolved primarily to motivate individuals to sustain an affiliative connection with a reproductive partner at least long enough to complete species-specific parental duties (Fisher, 1992).

We propose that when individuals use serotonin-enhancing antidepressants, they can potentially jeopardize not only their sex drive but also these related neural mechanisms for romantic love and partner attachment.

The Sex Drive

The androgens, particularly testosterone, are central to sexual desire in both men and women (Edwards & Booth, 1994; Sherman, 1994; Van Goozen, Wiegant, Endert, Helmond, & Van de Poll, 1997). Individuals with higher circulating levels of testosterone tend to engage in more sexual activity (Edwards & Booth, 1994; Sherman, 1994). Male athletes who use testosterone and other anabolic steroids to increase their strength and stamina have more sexual thoughts, more morning erections, more sexual encounters, and more orgasms. Middle-aged women

who inject or apply testosterone cream to the skin boost their sexual desire. The male libido peaks in the early twenties, when the activity of testosterone is highest. Many women feel more sexual desire around ovulation, when testosterone increases (Van Goozen et al., 1997). Both sexes also have fewer sexual fantasies, masturbate less regularly, and engage in less frequent intercourse as they age and testosterone levels decline (Edwards & Booth, 1994). People vary in their degree and frequency of sexual desire, in part because levels of testosterone are inherited (Meikle, Stringham, Bishop, & West, 1988). Moreover, the balance between testosterone, estrogen, and other bodily systems, as well as social circumstances, childhood experiences, and a host of other factors, play a role in determining when, where, and how often one feels lust (Nyborg, 1994). Nevertheless, testosterone is central to the sex drive.

The sex drive is also associated with a specific range of neural correlates. Using functional magnetic resonance imaging (fMRI), Arnow and colleagues reported that when young male heterosexual subjects viewed erotic video material while wearing a custom-built pneumatic pressure cuff around the penis, they showed strong activations in the right subinsular region, including the claustrum, the left caudate and putamen, the right middle occipital/middle temporal gyri, the bilateral cingulate gyrus and right sensorimotor and premotor regions, and the right hypothalamus (Arnow et al., 2002). Beauregard, Levesque, and Bourgouin (2001) measured brain activation (using fMRI) in men as the subjects viewed erotic film excerpts. Activations occurred in limbic and paralimbic structures, including the right amygdala, right anterior temporal pole, and hypothalamus.

Using fMRI, Karama and colleagues (2002) also recorded brain activity while men and women viewed erotic film excerpts. Activity increased in the anterior cingulate, medial prefrontal cortex, orbitofrontal cortex, insula, and occipitotemporal cortices, as well as in the amygdala and the ventral striatum. Men showed activation in the thalamus and significantly greater activation than women in the hypothalamus, specifically in a sexually dimorphic area associated with sexual arousal and behavior. In another experiment, researchers measured brain activity among eight men as these subjects experienced orgasm. Blood flow decreased in all regions of the cortex except one region of the prefrontal cortex, where it increased (Tiihonen et al., 1994). Animal studies also indicate that several brain structures are associated with the sex drive and sexual expression, including the medial amygdala, medial preoptic area, paraventricular nucleus, and periaqueductal gray (Heaton,

2000), and the septum and ventromedial hypothalamus (Dixson, 1998).

These data indicate that the constellation of neural correlates associated with the sex drive are dynamic yet specific. Moreover, data on the neural correlates associated with romantic love indicate that the sex drive and romantic love are overlapping yet distinct neural systems.

The Neural Correlates of Romantic Love

Intense courtship attraction, commonly known as romantic love, is recorded in all human societies for which data are available (Jankowiak & Fischer, 1992), and despite the varied ways that this phenomenon is expressed cross-culturally, this multipartite experience is associated with a specific constellation of motivations and emotions (Fisher, 1998; Gonzaga et al., 2001; Harris, 1995; Hatfield, 1988; Hatfield & Sprecher, 1986; Shaver et al., 1987; Tennov, 1979).

Romantic love begins as a person starts to regard another as special, unique. The lover focuses his or her attention on the beloved, doting on the beloved's worthy traits and overlooking or minimizing that person's flaws. The lover expresses increased energy, ecstasy when the love affair is going well, and mood swings into despair during times of adversity. Barriers heighten romantic passion, in what has been referred to as "frustration attraction" (Fisher, 2004). The lover suffers separation anxiety when apart from the beloved and often a host of sympathetic nervous system reactions when with the beloved, including sweating and a pounding heart. Lovers are emotionally dependent; they tend to change their priorities and daily habits to remain in contact with or to impress the beloved. They exhibit empathy for the beloved; many are willing to sacrifice, even die for this special other. The lover expresses sexual desire for the beloved, as well as intense sexual possessiveness. Yet their craving for emotional union supersedes their craving for sexual union. Most characteristic, the lover thinks obsessively about the beloved. Rejected lovers generally protest and try to win the beloved back, as well as express "abandonment rage" and despair. Romantic passion is also involuntary, difficult to control, and generally impermanent.

To investigate the neural correlates of romantic love, Fisher, Brown, Aron, and colleagues used fMRI to study the neural activity of 10 women and 7 men who reported being "madly in love" (Aron et al., 2005). The participants' age range was 18–26 years (mean, 20.6; median,

21), and subjects reported being in love an average of 7.4 months (median, 7; range, 1–17 months).

A preliminary investigation had identified a photograph of the beloved as an effective stimulus for eliciting feelings of intense romantic love (Mashek et al., 2000), so the protocol employed photographs and consisted of four tasks presented in an alternating block design. For 30 seconds each participant viewed a photo of the beloved (positive stimulus); for the following 40 seconds each performed a countback distraction task; for the following 30 seconds each viewed a photograph of an emotionally neutral acquaintance (neutral stimulus); and for the following 20 seconds each performed a similar countback task. The countback task involved viewing a large number, such as 8,421, and mentally counting backward (beginning with this number) in increments of seven. The countback task was included to decrease the carryover effect after the participant viewed the positive stimulus because it is difficult to quell intense feelings of romantic love. This four-part sequence (or a counterbalanced version beginning with the neutral stimulus) was repeated six times; the total stimulus protocol was 12 minutes.

Group activation specific to the beloved occurred in the right ventral tegmental area (VTA), localized in the region of A10 dopamine cells, and the right medial and posterodorsal body of the caudate nucleus (Aron et al., 2005). The VTA is rich in cells that produce and distribute dopamine to many brain regions, including the caudate nucleus. The VTA is also a central part of the brain's "reward system" (Breiter, Aharon, Kahneman, Dale, & Shizgal, 2001; Fiorillo, Tabler, & Schultz, 2003; Martin-Soelch et al., 2001; Schultz, 2000; Schultz, Dayan, & Read Montague, 1997; Wise, 1989), the neural network associated with sensations of pleasure, general arousal, focused attention, and motivation to pursue and acquire rewards (Delgado, Nystrom, Fissel, Noll, & Fiez, 2000; Elliot, Newman, Longe, & Deakin, 2003; Gold, 2003; Schultz, 2000). The caudate nucleus is also associated with reward, motivation, and goal-oriented behaviors. It plays a role in reward detection and expectation, the representation of goals, and the integration of sensory inputs to prepare for the appropriate actions to win rewards (Lauwereyns et al., 2002; Martin-Soelch et al., 2001; O'Doherty et al., 2004; Schultz, 2000). Some 80% of receptor sites for dopamine reside in the caudate nucleus.

Using fMRI, Bartels and Zeki also investigated brain activity in 6 men and 11 women who reported being "truly, deeply, and madly in love" (Bartels & Zeki, 2000). Participants looked at a photograph of the

beloved, as well as photographs of three friends of similar age, sex, and length of friendship. Individuals reported being in love an average of 28.8 months, longer than the love relationships studied by Aron et al. (2005), who were in love an average of 7.4 months. Those in the Bartels and Zeki study also were less intensely in love. In spite of these differences, Bartels and Zeki (2000, 2004) found that romantic love also activated regions of the caudate nucleus and the VTA, as well as several different brain areas. These combined data support the hypothesis that dopaminergic pathways in the reward system of the brain play a central role in the focused attention and motivation associated with romantic love (Fisher, 1998).

Elevated activity of central dopamine is also associated with ecstasy, intense energy, hyperactivity, sleeplessness, mood swings, emotional dependence, and craving (Abbott, 2002; Colle & Wise, 1988; Kiyatkin, 1995; Post, Weiss, & Pert, 1988; Robbins & Everitt, 1996; Salamone, 1996; Schultz et al., 1997; Wise, 1988, 1996), more central traits of romantic love. The addictive behaviors associated with romantic love are most likely related to dopamine activity as well (Fisher, 2004), because acute cocaine injection has been shown to activate the VTA in fMRI studies of humans (Breiter et al., 1997); animal studies of cocaine addiction also implicate mesolimbic dopamine pathways (David, Segu, Buhot, Ichaye, & Cazala, 2004; Kalivas & Duffy, 1998; McBride, Murphy, & Ikemoto, 1999; Wise & Hoffman, 1992).

Norepinephrine also may be associated with human romantic love (Fisher, 1998), although this has not yet been recorded by neuroimaging. Increased activity of norepinephrine generally produces alertness, energy, sleeplessness, loss of appetite (Coull, 1998; Robbins et al., 1998), and increased attention (Marracco & Davidson, 1996; Posner & Petersen, 1990), some of the basic characteristics of romantic love (Fisher, 2004; Hatfield & Sprecher, 1986; Tennov, 1979). Elevated activity of central norepinephrine also increases memory for new stimuli (Griffin & Taylor, 1995), so this neurotransmitter may also contribute to the lover's ability to remember the smallest details of the beloved's actions and cherished moments spent together. Because norepinephrine is also associated with sympathetic nervous system responses, including increased heart rate and blood pressure, and these responses often occur in early stage, intense romantic love, norepinephrine may contribute to these aspects of romantic love as well.

Low activity of central serotonin also may be involved in feelings of intense romantic love (Fisher, 1998; Marazziti, Akiskal, Rossi, &

Cassano, 1999). This is hypothesized because a striking sympton of romantic love is incessant, obsessive thinking about the beloved (Fisher, 1998, 2004; Hatfield & Sprecher, 1986; Tennov, 1979), and low activity of central serotonin is associated with obsessive-compulsive disorder (OCD) (Insel, Mueller et al., 1985; Insel, Zohar et al., 1990). In fact, most forms of OCD are treated with antidepressants that elevate the activity of central serotonin (Flament, Rapoport, & Berg, 1985; Hollander et al., 1988; Thoren, Asberg, & Bertilsson, 1980).

A recent study supports the hypothesis that romantic love is associated with low levels of central serotonin. In this experiment, 20 men and women who had fallen in love in the previous 6 months, 20 patients with unmedicated OCD, and 20 normal (control) individuals who were not in love were all tested for plasma levels of serotonin (Marazziti et al., 1999). Both the in-love participants and those with OCD showed significantly lower concentrations of the platelet serotonin transporter (Marazziti et al., 1999). Although bodily activities of serotonin do not necessarily correlate with serotonin activities in the brain (Kendrick, Keverne, Baldwin, & Sharman, 1986), decreased activity of central serotonin may contribute to the lover's obsessive thinking. Because impulsivity is also associated with low activity of central serotonin (Tiihonen et al., 1997), decreased activity of this neurotransmitter may also produce the impulsivity associated with romantic love.

These data suggest that the constellation of neural correlates associated with romantic love are largely distinct from those of the sex drive. Moreover, both neural systems are fundamental human drives (Fisher, 2004).

The Drive to Love

Psychologists distinguish between emotions, affective states of feeling, and motivations, brain systems oriented around the planning and pursuit of a specific want or need; and Aron has proposed that romantic love is not primarily an emotion but a motivation system designed to enable suitors to build and maintain an intimate relationship with a preferred mating partner (Aron & Aron, 1991; Aron, Paris, & Aron, 1995). Because the experiments described in the previous section indicate that romantic love is associated with activity in the VTA and caudate nucleus, Aron's hypothesis is supported: motivation and goal-oriented behaviors are central to the experience of intense, early-stage romantic love. These

data suggest that romantic love is a *primary* motivation system, a fundamental human mating drive (Fisher, 2004).

Pfaff defines a drive as a neural state that energizes and directs behavior to acquire a particular biological need to survive or reproduce (Pfaff, 1999). Like drives, romantic love is tenacious; emotions come and go. Like drives, romantic love is focused on a specific reward, in this case the beloved; emotions, such as fear, are associated with a wider range of objects and ideas. Like drives, romantic love is not associated with any particular facial expression; all of the primary emotions have stereotypic facial poses. Like drives, romantic love is difficult to control; it is harder to curb thirst, for example, than to control anger. Finally, like all of the basic drives (Pfaff, 1999), romantic love is associated with elevated activity in the dopaminergic reward system in the brain.

Drives lie along a continuum (Fisher, 2004). Some, like thirst and the need for warmth, cannot be extinguished until satisfied. The sex drive, hunger, the craving for salt, and the maternal instinct can often be redirected, even quelled. Falling in love is evidently stronger than the sex drive because when one's sexual advances are rejected, people do not kill themselves or someone else, whereas rejected lovers sometimes commit suicide or homicide (Meloy & Fisher, in press).

Mammalian Courtship Attraction

Not only are romantic love and the sex drive distinct neural systems, but evidence suggests that they may have been distinct since the proliferation of mammalian species some 70 million years ago. All mammals have mate preferences; none will copulate with *any* conspecific (Fisher, Aron, Masher, Strong et al., 2002). The drive to pursue a *preferred* mating partner is so common that the ethological literature regularly uses several terms to describe it, including "mate choice," "female choice," "individual preference," "favoritism," "sexual choice," and "selective proceptivity" (Andersson, 1994).

This mate preference in mammals, referred to as *courtship attraction*, is associated with many of the same characteristics as human romantic love, including heightened energy, focused attention, obsessive following, sleeplessness, loss of appetite, possessive "mate guarding," affiliative gestures, goal-oriented courtship behaviors, and intense motivation to win a specific mating partner (Fisher, 2004). Moreover, animal studies indicate that elevated activities of dopaminergic reward pathways play a primary role in mammalian mate preference, data that correlate

with the previously presented evidence for the role of dopaminergic pathways in human romantic love.

For example, when a female laboratory-maintained prairie vole (*Microtus ochrogaster*) is mated with a male, she forms a distinct preference for him, associated with a 50% increase of dopamine in the nucleus accumbens (Gingrich, Liu, Cascio, & Insel, 2000). When a dopamine antagonist is injected into the accumbens, the female no longer prefers this partner; and when a female is injected with a dopamine agonist, she begins to prefer the conspecific who is present at the time of infusion, even if she has not mated with this male (Gingrich et al., 2000; Liu & Wang, 2003; Wang et al., 1999). An increase in central dopamine is associated with courtship attraction in female sheep (Fabre-Nys et al., 1998). In male rats, increased striatal dopamine release has also been shown in response to the presence of a receptive female rat (Montague et al., 2004; Robinson, Heien, & Wightman, 2002).

In most species, this excitatory state is brief (Fisher, 2004); among humans, romantic love can last 12 months or more (Marazziti, 1999). Nevertheless, mammalian courtship attraction and human romantic love have much in common, including behavior patterns and neural mechanisms. It is parsimonious to hypothesize that the neural correlates of courtship attraction developed into those for human romantic love some time during hominid evolution, perhaps along with the development of the hominid brain some 2 million years ago (Fisher, 2004). Moreover, it is likely that this neural mechanism serves the same purpose in all mammalian species: to enable individuals to discriminate between the courtship displays of an array of suitors, prefer those that advertise superior genes, better resources, or more parental investment, and motivate males and females to focus their courtship attention on these preferred individuals, thereby conserving mating time and energy (Fisher, 2004; Fisher, Aron, Mashek, Strong et al., 2002).

Despite the biological distinctions between romantic love and the sex drive, and despite what is likely their long evolutionary history, the brain systems for the sex drive and romantic love interact in many ways, suggesting that serotonin-enhancing antidepressants can potentially suppress feelings of romantic love.

Interactions Between the Sex Drive and Romantic Love

Men and women in Western societies do not confuse the ecstasy, focused attention, and obsessive thinking associated with romantic love with the

mere appetite for sexual release (Hatfield & Rapson, 1996; Tennov, 1979). Men and women in an array of traditional societies also make this distinction (Jankowiak, 1995). On the Polynesian island of Mangaia, "real love" is called *inangaro kino*, a state of romantic passion distinct from one's sexual desires (Harris, 1995). The Taita of Kenya call lust *ashiki*, whereas they refer to love as *pendo* (Bell, 1995). In Caruaru, northeastern Brazil, locals say, "*Amor* is when you feel a desire to always be with her, you breathe her, eat her, drink her, you are always thinking of her, you don't manage to live without her" (Rebhun, 1995, p. 253). *Paixao*, on the other hand, is "horniness," and *tesao* is "a very strong sexual attraction for a person" (Rebhun, 1995, p. 254).

Despite people's ability to distinguish between feelings of passionate romantic love and feelings of sexual desire, those who fall in love regularly begin to find their beloved enormously sexually attractive; sexual desire is a central trait of human romantic love. This positive association between romantic love and the sex drive may be due in part to the biological link between these two brain systems. Dopamine can stimulate a cascade of reactions, including the release of testosterone and estrogen (Hull, Du, Lorrain, & Matuszewich, 1995, 1997; Kawashima & Takagi, 1994; Szezypka, Zhou, & Palmiter, 1998; Wenkstern, Pfaus, & Fibiger, 1993; Wersinger & Rissman, 2000), and the increasing activity of testosterone and estrogen can promote dopamine release (Appararundaram, Huller, Lakhlani, & Jennes, 2002; Auger, Meredith, Snyder, & Blaustein, 2001; Becker, Rudnick et al., 2001; Creutz & Kritzer, 2002; Hull et al., 1999; Pfaff, 2005).

Animal studies confirm this positive correlation between the sex drive and the dopaminergic arousal system. When a male laboratory rat is placed in an adjacent cage where he can see or smell an estrous female, his levels of central dopamine increase and elevate sexual arousal and pursuit of the female (Hull et al., 1995, 1997; Hull, Meisel, & Sachs, 2002; Wenkstern et al., 1993; West, Clancy, & Michael, 1992). When the barrier is removed and the male is allowed to copulate, levels of dopamine continue to rise (Hull et al., 1995). When dopamine is injected into specific regions of the brain in male rats, the infusion stimulates copulatory behavior (Ferrari & Giuliani, 1995). Conversely, blocking the activities of central dopamine in rats diminishes several proceptive sexual behaviors, including hopping and darting (Herbert, 1996).

Pfaff (2005) reports that in male rats, dopamine increases male sexual behavior through at least three functional roles. It increases sexual

arousal and courtship behavior, it potentiates the motor acts of mounting, and it faciliates genital responses to stimulation.

This positive correlation between central dopamine, the sex steroids, and sexual arousal and performance is not only common in animals (Herbert, 1996; Liu, Sachs, & Salamone, 1998; Pfaff, 2005); it also occurs in humans (Clayton, McGarvey, Warnock, et al., 2000; Heaton, 2000; Walker, Cole, Gardner, et al., 1993). When individuals who suffer from hypoactive sexual desire disorder are treated with dopamine-enhancing medications, their libido improves (Segraves, Goft, Kavoossi, et al., 2001). When patients with depression take drugs that elevate the activity of dopamine, their sex drive often improves as well (Ascher et al., 1995; Coleman et al., 1999; Walker et al., 1993). In fact, some patients who currently take serotonin-enhancing antidepressants supplement their therapy with medications that elevate the activity of dopamine (and norepinephrine) solely to maintain or elevate sexual arousal (Ascher et al., 1995; Coleman et al., 1999; Rosen et al., 1999; Walker et al., 1993).

Norepineprhine is also positively linked with sexual motivation and sexual arousal (Clayton et al., 2002; Etgen & Morales, 2002; Fraley, 2002; Pfaff, 2005; Van Bockstaele, Pieribone, & Aston-Jones, 1989). When a female prairie vole is exposed to a drop of male urine on the upper lip, norepinephrine is released in parts of the olfactory bulb, contributing to the release of estrogen and concomitant proceptive behavior (Dluzen, Ramirez, Carter, & Getz, 1981), and in rats, estradiol and progesterone result in the release of norepinephrine in the hypothalamus to produce lordosis (Etgen et al., 1999). Last, when ovariectomized, sexually receptive female rats receive injections of estrogen and are then permitted to mate, copulation results in the release of norepinephrine in the lateral ventromedial hypothalamus (Etgen & Morales, 2002).

This positive relationship between norepinephrine and the sex drive may be due in part to its interaction with the androgens. Norepinephrine, like dopamine, stimulates the production of testosterone (Cardinali, Nagle, Gomez, & Rosner, 1975; Fernandez, Vidal, & Dominguez, 1975; Mayerhofer, Steger, Gow, & Bartke, 1992), and increasing levels of testosterone can elevate the activity of norepinephrine (Jones, Dunphy, Milsted, & Ely, 1998) and dopamine (Becker, 2001; Hull et al., 1999; Pfaff, 2005). Drug users attest to this positive chemical connection between norepinephrine and the sex drive. In the right oral dose, amphet-

amines (norepinephrine agonists) enhance sexual desire (Buffum, Moser, & Smith, 1988).

These data indicate that romantic love is associated with elevated activity of dopamine (and most likely also norepinephrine) in general arousal systems in the brain. Moreover, these catecholamines are positively correlated with sexual motivation and sexual arousal. Most important to this discussion, elevated serotonin activity can directly suppress all pathways for dopamine (Meston & Frohlic, 2000; Stahl, 2000) and norepinephrine (Done & Sharp, 1992), as well as suppress testosterone activity (Gonzalez, Farabollini, Albonetti, & Wilson, 1994; Netter, Hennig, Meier, & Rohrmann, 1998; Sundblad & Eriksson, 1997). Hence, serotonin-enhancing antidepressants that negatively affect the sex drive and sexual arousal are also likely to adversely affect feelings of romantic love.

Case study: A 20-year-old, single, white, female undergraduate patient with an eating disorder, recurrent depressions, and attention-deficit disorder was administered an SSRI at relatively high doses for her eating disorder. When asked about side effects, she said she had none. When asked specifically about sexual side effects, she wasn't certain and asked that they be explained. Once they were explained, she acknowledged that she did have sexual side effects but that she had attributed them to problems in her relationship. "I have not been as much in love with my boyfriend," she reported. "I am not as interested in intimate time with him. I find myself wanting more space." At the time she reported this, the dose of the SSRI had just been increased.

Emotional Blunting and Romantic Love

Serotonin-enhancing medications can also jeopardize feelings of romantic love indirectly, by affecting the emotions. A striking characteristic of romantic love is obsessive thinking about a beloved. As discussed above, this intrusive thinking is most likely associated with a low activity of central serotonin. Hence, individuals taking serotonin-enhancing antidepressants are likely to suppress the obsessive thinking characteristic of romantic love. Elation is another primary feature of romantic love, and individuals who take serotonin-enhancing antidepressants are likely to suppress this ecstasy as well.

Serotonin-enhancing medications are well known to blunt the emotions. An unsolicited letter to *The New York Times* in response to our ideas (Fisher & Thomson, 2004; O'Connor, 2004) illustrates the impact that an SSRI had on Dr. Jerry Frankel, of Plano, Texas:

> After two bouts of depression in 10 years, my therapist recommended I stay on serotonin-enhancing antidepressants indefinitely. As appreciative as I was to have regained my health, I found that my usual enthusiasm for life was replaced with blandness. My romantic feelings for my wife declined drastically. With the approval of my therapist, I gradually discontinued my medication. My enthusiasm returned and our romance is now as strong as ever. I am prepared to deal with another bout of depression if need be, but in my case the long-term side effects of antidepressants render them off limits. (Frankel, 2004)

The Drive to Attach

Love changes over time. The ecstasy, energy, focused attention, obsessive thinking, yearning, and intense motivation to win the beloved gradually diminish, often transforming into feelings of comfort, calm, and emotional union with one's partner. This male-female partner attachment system is characterized in birds and mammals by mutual territory defense and nest building, mutual feeding and grooming, the maintenance of close proximity, separation anxiety, shared parental chores, and other affiliative behaviors. In humans, partner attachment is also characterized by feelings of calm, security, social comfort, and emotional union with a partner. Hatfield refers to this feeling of attachment as "companionate love," defining it as "a feeling of happy togetherness with someone whose life has become deeply entwined with yours" (Hatfield, 1988, p. 191).

Just as men and women distinguish between feelings of romantic love and the sex drive, people distinguish between feelings of romance and those of attachment to a long-term partner. Nisa, a !Kung Bushman woman of the Kalahari Desert, Botswana, explained the feeling of man-woman attachment this way: "When two people are first together, their hearts are on fire and their passion is very great. After a while, the fire cools and that's how it stays. They continue to love each other, but it's in a different way—warm and dependable" (Shostak, 1981, p. 268). The Taita of Kenya report that love comes in two forms, an irresistible longing, a "kind of sickness," and a deep, enduring affection for another (Bell, 1995, p. 158). Brazilians have a poetic proverb that distinguishes between these feelings: "Love is born in a glance and matures in a smile"

(Rebhun, 1995, p. 252). For Koreans, *sarang* is a word close to the Western concept of romantic love, while *chong* is more like feelings of long-term attachment. Abigail Adams described these feelings, writing to John Adams in 1793, "Years subdue the ardor of passion, but in lieu thereof friendship and affection deep-rooted subsists, which defies the ravages of time, and whilst the vital flame exists" (McCullough, 2001).

Bowlby (1969, 1973) and Ainsworth, Blehar, Waters, and Wall (1978) proposed that, to promote survival of the young, primates have evolved an innate attachment system designed to motivate infants to seek comfort and safety from their primary caregiver, generally their mother. More recently, researchers have emphasized that this attachment system remains active throughout life and serves as a foundation for attachment between spouses as they raise children (Hazan & Diamond, 2000; Hazan & Shaver, 1987).

This parental attachment system has been associated with the activity of two neuropeptides, oxytocin in the nucleus accumbens and arginine vasopressin in the ventral pallidum (Carter, 1992; Lim, Murphy, et al., 2004; Lim & Young, 2004; Wang, Ferris, & De Vries, 1994; Winslow et al., 1993; Young et al., 1998), although the brain's opioid system (Moles, Kieffer, & D'Amato, 2004) and other neural systems are most likely also involved (Kendrick, 2000). When vasopressin was injected intracerebroventricularly into virgin, laboratory-raised male prairie voles, they began to defend the space around them from other males, an aspect of pair formation among prairie voles. When each was introduced to a female, he became instantly possessive of her as well (Wang et al., 1994; Winslow et al., 1993). Moreover, arginine vasopressin antagonists infused into the ventral pallidum prevented partner preference formation among male prairie voles, suggesting that V1a receptor activation in this region is necessary for their pair-bond formation (Lim & Young, 2004, p. 1).

This distinct distribution of vasopressin receptors in the ventral forebrain seen in monogamous male prairie voles is also seen in monogamous California mice and monogamous marmoset monkeys, whereas promiscuous white-footed mice and promiscuous rhesus monkeys do not express this distribution of V1a receptors in the ventral pallidum (Bester-Meredith, Young, & Marler, 1999; Wang et al., 1997; Young, 1999; Young, Winslow, Nilsen, & Insel, 1997), further suggesting that vasopressin activity in this region of the brain's reward system is directly associated with pair bonding and attachment behaviors (Lim, Murphy, et al., 2004).

Oxytocin also stimulates the bonding process between a mother and her offspring (Carter, 1992; Pedersen, Caldwell, Walker, Ayers, & Mason, 1994) and between mating partners (Lim, Murphy, et al., 2004). When oxytocin is administered intracerebroventricularly, ovariectomized female prairie voles preferred the partner that was present at the time of infusion and formed a pair bond with him (Williams, Insel, Harbaugh, & Carter, 1994). When an oxytocin receptor antagonist is infused directly into the nucleus accumbens of a female prairie vole, it blocks partner preference and pair-bond formation (Lim, Murphy, et al., 2004; Young, Lim, Gingrich, & Insel, 2001).

A specific gene also has been associated with attachment behaviors and pair bonding. When this gene was manipulated to increase V1a receptors in the ventral pallidum, male prairie voles with increased V1aR expression exhibited heightened levels of social affiliation, formed a preference for a specific female, and began to cohabit with her, even though they had not mated with her (Pitkow et al., 2001). When Lim and colleagues introduced this gene into a male meadow vole (a promiscuous species), vasopressin receptors upregulated and the vole began to fixate on a particular female and mate exclusively with her, even though other females were available (Lim, Wang, et al., 2004).

Oxytocin and vasopressin appear to be associated with both partner preference and attachment/pair bonding, whereas dopamine and perhaps other monoamines are related only to partner preference. Thus, Young maintains that when monogamous prairie voles and individuals of other monogamous species engage in sex, they trigger the activity of vasopressin and oxytocin in specific reward centers of the brain; then dopamine in these reward centers enable males and females to prefer their current mating partner, thereby initiating attachment and pair bonding (Lim, Murphy, et al., 2004). Moreover, males of promiscuous species, which lack one link in this chain (V1a receptors in the ventral pallidum), may feel attraction to but do not associate this pleasurable feeling with a specific female and do not initiate an attachment to her.

Data from the Demographic Yearbooks of the United Nations on 97 societies suggest the prevalence of this attachment system in humans: approximately 93.1% of women and 91.8% of men marry by age 49 (Fisher, 1992). Moreover, when Fisher and colleagues examined a subset of their fMRI subjects who were in longer relationships, specifically those who were in love between 8 and 17 months, they found activation in the ventral pallidum, the brain region where activity has been linked with

pair bonding and attachment behaviors in several other monogamous species.

The above studies suggest that a specific brain system is associated with pair bonding in humans and other mammals and that the neural correlates associated with this attachment system are largely distinct from those of the sex drive and romantic love. We propose that this attachment system is also jeopardized by serotonin-enhancing antidepressants.

Attachment and the Sex Drive: Interactions

Oxytocin and vasopressin have complex relationships with the neurochemistry of the sex drive and serotonin. Some animal studies indicate that testosterone can elevate the activity of vasopressin (Delville, Mansour, & Ferris, 1996; Villalba, Auger, & De Vries, 1999; Wang & De Vries, 1995) and oxytocin (Arsenijevic & Tribollet, 1998; Johnson, Coirine, Insel, & McEwen, 1991), thereby increasing attachment behaviors, including mutual grooming, scent marking and defending a nesting site (Winslow & Insel, 1991). Likewise, elevated activity of oxytocin and vasopressin can increase testosterone production (Homeida & Khalafalla, 1990; Sirotkin & Nitray, 1992), and low activity of testosterone can reduce vasopressin activity (Wang & De Vries, 1993).

Given this positive correlation between the chemistry of attachment and the sex drive, serotonin-enhancing antidepressants that inhibit the sex drive can potentially inhibit feelings of attachment as well. Moreover, elevated oxytocin levels can suppress central serotonin activity in the hypothalamus, hippocampus, midbrain, and brainstem (Muir & Pfister, 1998), elevated serotonin can suppress the activity of vasopressin (Ferris & Deville, 1994), and elevated vasopressin can suppress the activity of serotonin (Schwarzberg, Kovacs, Szabo, & Telegdy, 1981). These data also suggest that serotonin-enhancing antidepressants can potentially jeopardize feelings of attachment for a long-term partner.

But other studies conflict with these data. Elevated serotonin levels can stimulate oxytocin release (Van de Kar, Levy, Li, & Brownfield, 1998), potentially stimulating feelings of attachment. Moreover, the sex drive and the attachment system have been negatively correlated. Increasing activity of testosterone can decrease the activity of vasopressin and oxytocin, and elevated activity of vasopressin can decrease the activity of testosterone (Thomas, Kim, & Amico, 1996). This inverse

relationship between lust and attachment is dose dependent; it varies depending on the quantities, timing, and interactions among several hormones (Delville & Ferris, 1995). But elevated activity of testosterone can reduce attachment behaviors.

Evidence of this negative correlation is seen in humans and other species. Men with high baseline levels of testosterone marry less frequently, have more adulterous affairs, commit more spousal abuse, and divorce more often. As a man's marriage becomes less stable, testosterone activity rises. With divorce, male testosterone levels rise even more. Last, single men tend to have higher levels of testosterone than married men (Booth & Dabbs, 1993). This negative relationship between testosterone and attachment behaviors has also been recorded in avian species. Male cardinals and blue jays flit from one female to the next; they do not remain to parent their young. These males have high levels of testosterone. Males of avian species that form monogamous pair bonds and remain with a mate to parent infants have much lower levels of testosterone during the parenting phase of the breeding season (De Ridder, Pinxten, & Eens, 2000; Raouf et al., 1997). But when scientists surgically pump testosterone into monogamous male sparrows, these males abandon their nests, their young, and their mates to court other females (Wingfield, 1994).

This negative correlation between testosterone and attachment behaviors suggest that under some circumstances, serotonin-enhancing antidepressants that suppress the sex drive can strengthen feelings of attachment in a long-term relationship.

Attachment and Romantic Love: Interactions

The biological relationships between the neural mechanisms for attachment and romantic love are equally varied and complex. Central dopamine and norepinephrine can stimulate the release of oxytocin and vasopressin (Ginsberg, Hof, Young, & Morrison, 1994; Galfi et al., 2001), perhaps contributing to one's growing feelings of attachment. But increasing activity of dopamine can also inhibit release of oxytocin (Seybold, Miller, & Lewis, 1978; Vizi & Volbekas, 1980), and increasing activity of oxytocin can interfere with dopamine and norepinephrine pathways (Kovacs, Sarnyai, Barbarczi, Szabo, & Telegdy, 1990; Kovacs & Telegdy, 1983; Schwarzberg et al., 1981; Van de Kar et al., 1998). Hence the chemistry of attachment may potentially jeopardize feelings

of romance, and the chemistry of romance can potentially inhibit feelings of attachment.

The biological relationships among the three brain systems for human mating and reproduction, the sex drive, romantic love, and attachment, are dose dependent and variable, depending on which brain regions are involved and on many other biological and environmental interacting factors. Nevertheless, serotonin-enhancing antidepressants can potentially produce a wide variety of effects on all three neural systems, including suppressing feelings of romantic love and altering feelings of attachment to a long-term partner.

Orgasm as an Attachment, Romance, and Signaling Device

Serotonin-enhancing antidepressants can produce deleterious effects on other complex, largely unconscious (Grammer et al., 2000), adaptive mechanisms for mate selection, pair formation, and pair stability (Thomson & Fisher, 2004).

Orgasm, for example, has many adaptive purposes. Among them, it facilitates feelings of attachment by elevating activity of oxytocin and vasopressin in both sexes (Carmichael et al., 1987). So, when individuals taking serotonin-enhancing antidepressants fail to achieve orgasm, they fail to stimulate in themselves the neural system associated with attachment and pair bonding. In this manner, these antidepressants can endanger emotional bonding with a new partner and the stability of a long-term partnership.

Sexual activity and orgasm may also make an individual more susceptible to falling in love. Genital stimulation and arousal produce elevated activity of dopamine and norepinephrine (Meston & Frohlic, 2000; Pfaff, 2005); orgasm also briefly increases norepinephrine levels in the blood (Meston & Frohlic, 2000). When individuals taking serotonin-enhancing antidepressants fail to initiate sexual activity, fail to become sexually aroused, and fail to achieve orgasm, they fail to activate in themselves and their partner these neurotransmitter systems associated with romantic love.

Orgasm also may function as a device by which women assess potential mates (Miller, 2000). Women do not reach orgasm with every coupling, and the "fickle" female orgasm is currently regarded as an adaptive mechanism by which women distinguish between those partners who are willing to spend time and energy to give them pleasure and

those who are abrupt, impatient, and nonempathetic during intercourse. As the hypothesis is reasoned, those males who are willing to expend time and energy to please a woman sexually are also more likely to be committed, long-term providers (Buss, 2003). When women take serotonin-enhancing antidepressants that inhibit their orgasmic response, they jeopardize their ability to assess the commitment level of a potential long-term provider.

Women also use orgasm to assess an existing partnership. They report greater frequency of orgasm in long-term, committed relationships (Laumann, Paik, & Rosen, 1999), and the onset of anorgasmia in the middle of a long-term mateship may jeopardize the stability of this relationship.

Case study: A 32-year-old woman with recurrent depression and bulimia required relatively high doses of an SSRI to eliminate her chronic binging and purging. The medication led to loss of libido, delayed arousal, and absent orgasm. But her long-term relationship also dissolved, due to the frustrations and conflicts engendered by the sexual side effects of the SSRI medication.

Orgasm serves other purposes. Single women tend to have more orgasms with socially dominant, symmetrical males (Thornhill, Gangestad, & Comer, 1995). Social rank and facial and body symmetry are regarded as markers of fitness and good genes (Gangestad & Thornhill, 1997), so that single women who inhibit their ability to reach orgasm with these biologically fit men can jeopardize their social and genetic future.

Knocking out orgasm with serotonin-enhancing antidepressants can also jeopardize reproductive opportunities among married women engaging in clandestine affairs. Married women report frequent orgasms during their affairs (Baker & Bellis, 1995). In these cases, orgasm may serve as a biological incentive to continue the extramarital relationship, thereby increasing her likelihood of reaping extra resources and benefits for herself and her children or increasing the likelihood of conceiving another child with better genes or different genes.

It has been theorized that orgasm evolved to serve female reproduction in three other ways (Buss, 2003). The paternity confidence hypothesis proposes that female orgasm evolved to enable ancestral women to signal a partner that she was satisfied with him, thereby motivating him to remain with her to help support their forthcoming young. The paternity confusion hypothesis proposes that female orgasm evolved

to motivate ancestral females to copulate with multiple partners, thereby confusing the identity of the biological father of a forthcoming child and obliging each male to contribute to the survival of the infant (Hrdy, 1999). The sperm retention hypothesis proposes that female orgasm evolved to transport sperm through the cervix, enhancing the probability of conception (Fox, Wolfs, & Baker, 1970).

The above data and theories suggest that female orgasm is a multipurpose mechanism designed to promote pair bonding with appropriate males, promote "extra pair copulations" to increase female fecundity, and enable a single woman to identify and win the best possible partner when she seeks a new relationship. All of these functions of female orgasm are jeopardized by serotonin-enhancing antidepressants.

Chemical Clitoridectomy

Women who take serotonin-enhancing antidepressants also disrupt related evolutionary mechanisms for mate selection, pair formation, and pair maintenance. The ring of nerves around the vaginal opening measures penis width and, by distending surrounding muscles, elevates sexual excitement. The clitoris also responds to minor variations in touch and angle, thereby measuring a partner's skill, patience, determination, and sensitivity to her needs (Miller, 2000). By creating a chemical clitoridectomy, serotonin-enhancing antidepressants dull the responses of these devices (Frolich & Meston, 2000), contribute to anorgasmia, and diminish a woman's ability to discern appropriate mating and marital partners. Anorgasmia may also motivate a woman to look beyond her primary relationship, even though this male may have superior genes, resources, and parenting capabilities (Small, 1995).

Serotonin-enhancing antidepressants may affect other subtle female mechanisms for courtship, mating, and reproduction. At midcycle, ovulating women tend to have more erotic fantasies, initiate more sexual activity, and experience a lower threshold for orgasm. They have a better sense of smell (Doty, 1986) and are better able to discriminate healthy from unhealthy available males. At midcycle, women are also more likely to prefer men with higher bodily and facial symmetry and men who are creative, humorous, and display other signs of good genes (Grammer et al., 2003; Miller, 2000; Thornhill et al., 1995). Attraction to individuals with MHC histocompatibility or other immunological profiles may be linked to sex drive and sexual arousal, too. These and many other

courtship mechanisms evolved to aid mate assessment, mate choice, and pair formation, and any and all of these brain responses could potentially be altered by serotonin-enhancing antidepressants.

Like drugs that blur vision, serotonin-enhancing medications may impair myriad female adaptive mechanisms, obscuring a woman's ability to make appropriate mating choices, fall in love, or sustain appropriate long-term reproductive relationships.

Penile Erection, Seminal Fluid, and Antidepressants

Men who take serotonin-enhancing antidepressants also inhibit an array of adaptive mechanisms that evolved to promote mate selection and partnership formation. For example, the penis may function as an internal courtship device (Miller, 2000). With its width, length, and turgidity, it stimulates the vagina to give pleasure; it also advertises psychological and physical fitness (Miller, 2000). When men take antidepressants that produce impotence, they cripple these courtship functions.

The penis also deposits seminal fluid, which contains dopamine and norepinephrine, as well as tyrosine, a building block of these catecholamines (Burch & Gallup, in press). These compounds do not pass through the blood-brain barrier. Nevertheless, when a man taking a serotonin-enhancing antidepressant fails to ejaculate, he fails to deposit these catecholamines in the vaginal tract, neurotransmitters that could contribute to his partner's feelings of romantic attraction to him.

Seminal fluid also contains several other mood-altering hormones, including testosterone, estrogen, follicle-stimulating hormone (FSH), and luteinizing hormone (LH), chemicals that can also affect sexual desire and function (Clayton, 2003). Gallup and colleagues have demonstrated that these and other chemicals in seminal fluid have antidepressant effects on women (Gallup, Burch, & Platek, 2002). When a man fails to ejaculate, he suppresses his ability to stimulate in his partner a positive mood that could potentially change her threshold for romantic attraction or deep attachment to him.

SSRIs and Psychological Barriers to Romance and Marriage

Serotonin-induced sexual dysfunction can adversely affect feelings of romantic love and partner attachment in psychological ways as well. For example, some men and women taking these medications shy away from

a liaison that could become romantic because they are afraid of their own poor performance in bed.

Case study: A 26-year-old man had panic attacks that required high doses of a serotonin-enhancing antidepressant. He soon experienced diminished libido and impotence. A handsome, personable, intelligent man, he was readily sought after by women. However, he ended several relationships because he was too embarrassed about his inability to perform sexually. Although he tried several other medications, he was able to control his panic disorder only with high doses of serotonin enhancers. He eventually retreated into a social life in which he avoided serious dating. When last evaluated, he still confined himself to non-sexual relationships with women.

Due to low libido, other patients on serotonin-enhancing antidepressants fail to become sexually attracted to a potential partner and incorrectly attribute their lack of sexual (and romantic) interest to personality deficits in this potential mate, thereby misappraising the viability of the relationship.

Still others fail to notice potential partners.

Case study: A patient in her late twenties had recurrent major depressions that were being controlled with an SSRI. She reported sexual side effects, including diminished sexual interest and absent orgasm. However, 3–4 weeks after the SSRI medication was reduced and an antidepressant with fewer sexual side effects was added, she noticed an increase in her sexual interest. When asked if she had noticed any change in her feelings of attraction to men, she said, "I notice someone who is attractive now which I hadn't before."

SSRIs and Fertility

SSRI medications can also influence one's genetic future.

Case study: A 35-year-old married woman with recurrent depression and generalized anxiety disorder was placed on an SSRI. She was not told about the potential negative sexual side effects of this medication. The drug relieved her depression and anxiety. However, she soon developed diminished libido and absent orgasm. This led her to conclude that she no longer loved her husband. She decided to divorce him but kept her feelings to herself for several years, planning for the appropriate time to make this major life change. She eventually switched to an

antidepressant with a low frequency of sexual side effects. On this new medication, her sexual desire and orgasmic function returned. She decided not to divorce her spouse. Soon after this, she conceived. Now she and her husband have a child. A serotonin-enhancing medication had affected not only her social life but her fertility.

These medications can also influence one's genetic future in specific biological ways. Serotonin increases prolactin levels by inhibiting dopamine activity and stimulating prolactin-releasing factors. Prolactin can impair fertility through several mechanisms, including suppressing hypothalamic gonadotropin-releasing hormone release, suppressing pituitary FSH and LH release, and suppressing ovarian hormone production (Hendrick, Gitlin, Altshuler, & Korenman, 2000). Also, clomipramine, a strong serotonin-enhancing antidepressant, adversely affects sperm volume and motility (Maier & Koinig, 1994).

The number and range of unconscious psychobiological mechanisms that have evolved to enable men and women to signal mating fitness, assess appropriate mating partners, pursue specific preferred individuals, and form and sustain a pair bond are largely unknown. But it is likely that many of these neural mechanisms are altered by serotonin-enhancing medications.

Conclusion

Homo sapiens has inherited three distinct yet interrelated brain systems for courtship, mating, reproduction and parenting: the sex drive, romantic love, and partner attachment. These neural systems can become active in any sequence. An individual may begin a casual sexual liaison with someone for whom he or she feels only sexual desire, then one evening falls in love with the sex partner, then gradually begins to feel deep attachment to this partner. Some couples begin their relationship with feelings of attachment instead: the man and woman become friends and achieve emotional union in the college dorm, at the office, or in their social circle. With time, this attachment metamorphoses into romantic passion, which then triggers lust. Still others fall in love with someone they hardly know, then they experience lust, and finally they experience feelings of attachment. These three neural systems can also operate independently. An individual can feel deep attachment for a long-term spouse *while* they feel romantic passion for someone else *while* they feel the sex drive for an array of other individuals.

The flexible nature of these three brain mechanisms for reproduction and their complex, dynamic interactions suggest that any medication that changes the chemical checks and balances is likely to alter an individual's courting, mating, and parenting tactics, ultimately affecting that person's fertility and genetic future.

Serotonin is the oldest known monoamine neurotransmitter; it has numerous receptors and many subtle functions. For example, activation of serotonin type 1a (5-HT1a) receptors enhances sexual desire and lowers the threshold for ejaculation; activation of serotonin type 1b (5-HT1b) and 1c (5-HT1c) receptors decreases sexual desire and inhibits orgasm; and activation of serotonin type 2 (5-HT2) and type 3 (5-HT3) receptors impairs all stages of sexual response in both men and women (Meston & Frolich, 2000). Some 90% of these serotonin receptors are located in the body, where serotonin affects the smooth muscle of the vascular system, including the smooth muscle of the genitals.

Individuals vary in the sensitivity of these serotonin receptors (Saks, 2000), as well as in many other aspects of serotonin production, synthesis, and interaction with other bodily systems. Childhood experiences and current circumstances also affect the expression of this monoamine neurotransmitter. Thus, individuals taking serotonin-enhancing antidepressants vary in their response to these medications, including their sexual side effects. In fact, data indicate that under the right circumstances, serotonin-enhancing antidepressants can considerably improve several mental and physical disorders, including disorders that affect one's romantic and marital relationships.

Nevertheless, the Food and Drug Administration has warned Americans that these medications can have potentially harmful side effects, including severe restlessness, anxiety, hostility, insomnia, and/or suicidal thinking, as well as emotional blunting and sexual dysfunction.

Because there is a positive relationship between dopamine (associated with romantic love) and testosterone (linked to sexual desire and arousal) and because there is a negative relationship between serotonin and these catecholamines and the androgens, serotonin-enhancing antidepressants can also inhibit feelings of romantic love. Moreover, because serotonin-enhancing antidepressants have a negative impact on penile erection, sexual arousal, orgasm, and other evolved psychobiological courtship mechanisms, these drugs can also negatively affect one's ability

to signal genetic and psychological fitness, assess and select potential mating partners, pursue preferred individuals, and maintain stable pair bonds.

Harvard Medical School psychiatrist Joseph Glenmullen estimates that 75% of all patients on antidepressants, largely SSRIs, are "needlessly on these drugs"(cited in Morais, 2004, p. 120). Physicians who prescribe serotonin-enhancing antidepressants and individuals who plan to use these drugs should bear in mind the broad, largely unrecognized, and possibly deleterious effects of these medications.

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