J Neurophysiol 104: 51–60, 2010.
First published May 5, 2010; doi:10.1152/jn.00784.2009.

Reward, Addiction, and Emotion Regulation Systems Associated With Rejection in Love

Helen E. Fisher,[1] Lucy L. Brown,[2] Arthur Aron,[3] Greg Strong,[3] and Debra Mashek[3]

[1]*Department of Anthropology, Rutgers University, Newark, New Jersey;* [2]*Departments of Neurology and Neuroscience, Einstein College of Medicine, Bronx, New York; and* [3]*Department of Psychology, State University of New York, Stony Brook, New York*

Submitted 24 August 2009; accepted in final form 1 May 2010

Fisher HE, Brown LL, Aron A, Strong G, Mashek D. Reward, addiction, and emotion regulation systems associated with rejection in love. *J Neurophysiol* 104: 51–60, 2010. First published May 5, 2010; doi:10.1152/jn.00784.2009. Romantic rejection causes a profound sense of loss and negative affect. It can induce clinical depression and in extreme cases lead to suicide and/or homicide. To begin to identify the neural systems associated with this natural loss state, we used functional magnetic resonance imaging to study 10 women and 5 men who had recently been rejected by a partner but reported they were still intensely "in love." Participants alternately viewed a photograph of their rejecting beloved and a photograph of a familiar, individual, interspersed with a distraction-attention task. Their responses while looking at their rejecter included love, despair, good, and bad memories, and wondering why this happened. Activation specific to the image of the beloved occurred in areas associated with gains and losses, craving and emotion regulation and included the ventral tegmental area (VTA) bilaterally, ventral striatum, medial and lateral orbitofrontal/prefrontal cortex, and cingulate gyrus. Compared with data from happily-in-love individuals, the regional VTA activation suggests that mesolimbic reward/survival systems are involved in romantic passion regardless of whether one is happily or unhappily in love. Forebrain activations associated with motivational relevance, gain/loss, cocaine craving, addiction, and emotion regulation suggest that higher-order systems subject to experience and learning also may mediate the rejection reaction. The results show activation of reward systems, previously identified by monetary stimuli, in a natural, endogenous, negative emotion state. Activation of areas involved in cocaine addiction may help explain the obsessive behaviors associated with rejection in love.

INTRODUCTION

Our overall hypothesis is that early-stage romantic love is a developed form of a mammalian drive to pursue preferred mates (Fisher 1998). In a previous investigation (Aron et al. 2005a), we used functional magnetic resonance imaging (fMRI) to study 10 women and 7 men who were happily in love and concluded that it was a goal-oriented motivational state (rather than an emotion) that uses subcortical mammalian reward/survival systems, helping to explain why early-stage romantic love affects behavior so profoundly. These results were consistent with our hypothesis. In the present study, we used fMRI to study 10 women and 5 men who had recently been rejected by a romantic partner to examine the systems involved in this negative state of romantic love.

Rejection in love is a common phenomenon that causes severe distress in many individuals. The trauma of romantic rejection has been recorded in the poetry, songs, stories, myths, and legends of the ancient Sumerians, Greeks, Romans, Arabs, Aztecs, Japanese, Chinese, Indians, Polynesians, Kung Bushmen of Namibia and Botswana and many other historical and contemporary societies (Baumeister et al. 1993; Fisher 2004; Jankowiak and Fischer 1998). In a study of 114 men and women who had been rejected by a partner within the past 8 wk, 40% experienced clinically measurable depression; of these, 12% displayed moderate to severe depression (Mearns 1991). In a study of American college students, 93% of both sexes reported that they had been rejected by someone they passionately loved; 95% said they had rejected someone who was deeply in love with them (Baumeister et al. 1993); and cross-culturally, some rejected lovers commit suicide or homicide (Meloy and Fisher 2005; United-Nations 1995; Wilson and Daly 1992).

Romantic love is a "universal. . .or near universal" human phenomenon (Jankowiak and Fischer 1998). In a survey of 166 societies, Jankowiak and Fischer (1998) found evidence of romantic love in 147 of them. There was no negative evidence; in the 19 remaining cultures, no data were available due to ethnographic oversight.

Current overall theories of romantic love either consider it one of many emotions (Shaver et al. 1996), or as a factor in the biological imperative for human reproduction (Aron et al. 2005a; Fisher 2004; Lewis et al. 2000; Xu et al. 2010). Research has focused on predictors of "falling" in love and initiating a relationship, cultural influences, the expression of romantic love (reviewed in Aron et al. 2006), special characteristics associated with feelings of intense romantic love, relationship processes that emphasize the reward value of romantic partners (e.g., Aron and Aron 1986; Kelley 1983), individual differences in ways love is experienced and expressed (e.g., Mikulincer and Shaver 2007), the cognitive construction of how love is recognized as such (Fehr 1988), typologies distinguishing different types and functions of love (Hendick and Hendrick 2003; Sternberg 1986), and biologically based studies focusing on the role of romantic love in selective mating and pair bonding (Fisher 1998; Fisher et al. 2006).

Several psychologists regard romantic love as an addiction because it shows addiction characteristics such as the lover's intensely focused attention on a preferred individual, mood swings, craving, obsession, compulsion, distortion of reality, emotional dependence, personality changes, risk-taking, and loss of self-control (Griffin-Shelley 1991; Halpern 1982; Liebowitz 1983; Mellody et al. 1992; Peele and Brodsky 1975; Schaef 1989; Tennov 1979). Romantic love is likely to be a constructive form of addiction when one's love is returned but a destructive form of addiction when one's love is rejected

Address for reprint requests and other correspondence: L. L. Brown, Dept. of Neurology, Einstein College of Medicine, 1410 Pelham Pkwy S., Rm. 912C, Bronx NY 10461 (E-mail: brown@einstein.yu.edu).

(Fisher 2004). Brown has suggested that romantic love and cocaine addiction behaviors share survival system activation in the brain, helping to explain the strength of the obsession (Frascella et al. 2010).

However, little is known about the process of unreciprocated love and romantic rejection (Aron et al. 1998; Baumeister et al. 1993; Fisher 2004). Investigators have divided separation from a parent during development into two general phases: "protest" and "despair" (Bowlby 1969). This is reminiscent of observed behavior following romantic rejection (Lewis et al. 2000). During a protest phase, romantically rejected individuals often obsessively try to win back the beloved. As resignation sets in, they give up and slip into despair. However, these general phases of rejection grief are not yet substantiated. In light of the potentially severe consequences of romantic rejection, as well as its cross-cultural incidence, strong behavioral effects, and association in the literature with addictive behaviors, it is notable that there is only one brain-systems study of this common, intense, life experience (Najib et al. 2004).

In our study, we tested four predictions. First, romantic rejection would activate subcortical reward systems that mediate motivation and reward, specifically the ventral tegmental area (VTA), because previous studies (Aron et al. 2005a; Bartels and Zeki 2004) indicate that these areas are involved in feelings of romantic love, and adversity tends to heighten feelings of romantic love (Hatfield and Rapson 1996). Activation of the VTA in rejected individuals would provide further evidence that the VTA is involved in romantic love, even in this different context. Second, romantic rejection would activate subcortical and cortical areas associated with drug craving, particularly the nucleus accumbens and prefrontal cortex, because others have noted the similarity between romantic love and addiction (Fisher 2004; Frascella et al. 2010). Third, romantic rejection would engage forebrain areas activated by losses and gains as well as gain anticipation (Camara et al. 2008; Kable and Glimcher 2007; Schultz 2000; Tobler et al. 2009; Tom et al. 2007), and cognitive and emotion regulation systems (Wager et al. 2008). Fourth, romantic rejection would activate brain regions associated with the autonomic nervous system, such as the insular cortex, because rejected individuals express a range of intense emotions.

If romantic love is a factor in a biological system associated with reward and reproduction, then it becomes more understandable why it shares behavioral characteristics with addiction (Frascella et al. 2010) and why it is so devastating when it is lost. Importantly, the study of love also provides an opportunity to investigate neural systems associated with reward and emotion within the context of a natural life situation as opposed to a laboratory-induced response. Investigating the neural systems associated with romantic rejection may also contribute understanding to the costly psychological, social, reproductive, and medical consequences of romantic rejection worldwide (Meloy and Fisher 2005; United-Nations 1995; Wilson and Daly 1992).

METHODS

Participants

Ten women and five men were recruited from the State University of New York at Stony Brook, Rutgers University, and the New York area by word of mouth and with flyers. The flyer highlighted the sentence: "Have you just been rejected in love but can't let go?" All relationships were heterosexual. All participants preferred their right hand (Oldfield 1971), and none were taking antidepressant medications. The average age was 19.8 ± 1.0 (SD) yr (range, 18–21 yr); the average length of relationship before breaking up was 21 mo (range, 4–48 mo); the average time since initial rejection was 63 days (range, 1–32 wk), and the average score on the Passionate Love Scale (Hatfield and Sprecher 1986) was 8.0 ± 0.6 (on a 1–9 scale). Thus the age of the participants and love intensity were similar to Aron et al. (2005), but the average length of the relationship was 21 mo compared with 7 mo in Aron et al. (2005). All participants gave informed written consent and each received $50 for his or her participation. The institutional review boards at Stony Brook and Rutgers approved all procedures.

Each participant's degree of obsessive thinking and craving for emotional union was recorded during the prescan interview, during which the interviewer (HEF) asked each participant, "what percentage of the day and evening do you think about your sweetheart?" All participants responded that they thought about their rejecter >85% of their waking hours. All participants also reported that they yearned for the rejecter to return to them and reestablish emotional union. They all also reported signs of lack of emotion control on a regular basis since the initial break up, in all cases occurring regularly for weeks or months. This included inappropriate phoning, writing or e-mailing, pleading for reconciliation, sobbing for hours, drinking too much, and/or making dramatic entrances and exits into the rejecter's home, place of work or social space to express anger, despair or passionate love.

Questionnaire

Just prior to the scanning session, each participant completed the Passionate Love Scale (PLS).

Stimuli

The *rejecter* stimulus was a photograph of the beloved. To begin to study this complex emotion state, participants were instructed to use photographs that effectively stimulated in them feelings of intense romantic passion; all reported that they complied. The *neutral* stimulus was a photograph of a familiar individual of the same sex and approximate age as the beloved with whom there had been no emotionally close relationship. The photos were obtained for the express purpose of the experiment or borrowed and copied. To control for facial familiarity, we used photos of a roommate's partner, a co-resident of their dormitory, a current classmate, or an individual at their place of work. We used a relatively neutral, familiar face rather than a friend or an individual in a positive or negative context because we had used this control in our previous study and because the emotions expressed toward the rejecter were both positive and negative. Future studies will benefit from including more specific controls. Because of the kind of control we used, the effects obtained by the comparison in our study represent a wide range of experiences, including aspects of closeness that might be associated with friendship because our comparison of rejected versus familiar neutral did not control for closeness or friendship.

The photographs were received from the participants before scanning and digitized, cropped, and sized to show the head only. Image quality was inspected by an experimenter so that it was not pixilated or blurred. The stimuli were presented using in-house software. An angled mirror was mounted on the RF coil, enabling the participant to view each image, which was projected on a screen placed directly outside the MRI tube, subtending a visual angle of 17°.

Because it is difficult to quell feelings of intense romantic love, we devised a protocol (Mashek et al. 2000) to decrease the carry-over effect after the participant viewed the rejecter stimulus. We interspersed the rejecter stimulus and neutral stimulus with an attention-distraction count back task. This task involved viewing a number such

as 9,247 on the screen and mentally counting backward in increments of seven, beginning with this number. A randomly selected different starting number was presented each time the task was given. Mashek et al. (2000) established that 40 s of the countback task effectively erased feelings associated with the previous rejecter stimulus in most individuals. To provide a similar distraction after the neutral stimulus (but reduce experiment duration), participants did the countback task for 20 s. The different lengths of the countback task preceding the rejecter and neutral stimulus presentations was a possible confound (20 vs. 40 s). However, the length of the stimulus presentation block was likely great enough to reduce any carryover effects from the countback task. Indeed inspection of the data showed that the rejecter and neutral conditions began at the same response magnitude rather than different response magnitudes, which would be indicative of carryover effects from the previous block.

Instructions to participants, prescanning, and exit interviews

The instructions to the participants were to think about events that occurred with the rejecter while they viewed the rejecter photograph and to think about neutral events that occurred with the neutral individual, like watching TV, while they viewed the neutral photograph. The events recalled for the rejecter photo were all emotionally charged.

During the prescanning interview, the interviewer (HEF) and participant discussed events that the participant might think about while looking at each photograph. For the rejecter, the participants started with their feelings of disappointment and their list of injustices. One participant, for example, reported, "I found a letter that he had written to another person at work. . . ." Another planned to think about a particular fight she had had with her would-be partner during which he gave her a watch, then took it back, then gave it again; they began fighting verbally and throwing the watch back and forth at one another. Finally she walked across the street, he threw it at her, and she never found it again. When talking about the rejecter, all participants also said words to the effect of, "he/she would have been perfect for me." Thus participants expressed both negative and positive feelings during the prescan interview. For the neutral stimulus, one subject planned to recall the hours she spent "with a boring guy in my dorm who just sat there and watched TV."

Participants described a mixture of feelings associated with their rejection experience, including obsession, intense romantic passion, protest, anger, hope, regret, and despair. They also reported an inability to function in their daily lives and talked about making inappropriate phone calls. As an example of the obsession expressed, one participant said, "I think about him constantly." As an example of the romantic passion expressed, one said, "We try to be friends, but this doesn't work. I'm too attracted to him." As an example of protest, one reported that she had recently said to her rejecter, "You can't just break up with me on a whim." Regarding hope, one reported, "I don't want to break up until I have exhausted every possibility of getting back together." Regarding anger, one said, "I want a letter from him, or a phone call; I want some respect." Another said, as she handed one of us the photo to be used during the experiment, "Here's the jerk." Many wondered why the break-up happened. One said, "He hasn't even bothered to explain the situation. I feel so angry." Another said, "Why the hell did she leave me?" Another reported, "I can't sleep; I just lie there, wondering about what happened and what could have been." Another said, "I don't know what I did wrong." Many also reported despair. One said, "It hurts so much. I crumble. I just start crying." Another said, "What's the point, without her." All displayed conflicting emotions. One reported, "I hate what he did to me, but I still love him."

Our design did not enable us to confirm that participants followed our instructions for the separate stimuli except by a postscan verbal report, which is limited by the participants' memory and motivation. However, the postscan reports enabled us to judge to some extent whether a participant successfully carried out the alternating tasks or should be eliminated. All participants indicated verbally to one of the investigators (HEF) that they had followed the instructions, including The Countback task, to the best of their ability.

In the postscanning interview, individuals showed mixed expressions of romantic love, agitation, anger, and despair. Most recounted *both* happy and unhappy memories. One said that the experience was "powerfully intense, as if I just started to feel all the rejection again. And it just got worse. I began to shake. My chest hurt. I had to breathe deep. I was scared I would die of my feelings." Another said, " I kept thinking, I love you, I hate you; how could you do this." Another said, "I kept anticipating the hurt."

When asked about their feelings as they looked at the neutral photograph, several reported that they felt "bored." One said, "I wanted to get out of there; it was boring." Another found the neutral photo and the countback task "a relief." Another reported, "I would keep counting after the neutral photo appeared, but when "she" appeared, my entire focus would go straight to her." (Inspection of this individual's data showed no significant carryover effect from countback to neutral.) Another said that as he looked at the neutral photo he "just listed in my mind things about the woman, such as the fact that she was standing near a horse, that she was wearing red. . ." All reported that they did the countback task. One reported, "I started to get the hang of it. I began to focus on the numbers and subtract first by five and then by two." Another said, "at one point I was able to do over five of them." Several reported that it was hard to do the countback task after viewing the rejecter stimulus but not after looking at the neutral stimulus, which suggests that they carried out these tasks.

Most participants expressed the wish to resolve their pain. One participant called the next day and said that he thought the experience had helped him to get over "her."

Experimental design and procedures

The protocol consisted of four tasks presented in an alternating block design. First for 30 s, the participant viewed the rejecter stimulus; for the following 40 s, the participant performed the countback distraction task; for the following 30 s, the participant viewed the neutral stimulus; and for the following 20 s, the participant performed the countback task. The starting image was either the neutral stimulus or rejecter stimulus and was counterbalanced across participants. The four-part sequence was repeated six times; the total stimulus protocol was 720 s (12 min).

Image acquisition and analysis

Data were acquired using a 1.5 T Marconi (Phillips) Edge MRI system. We measured the blood-oxygen-level-dependent (BOLD) response and took in-plane anatomical data for each participant. The images were: *1*) anatomical, axial T1-weighed spin-echo scans: 14 ms TE, 600 ms TR, 90° flip angle, 24 cm FOV, 4 mm slice thickness, 0 mm gap, 256 × 256 matrix size, 20 slices; *2*) functional, T2-weighted gradient-echo EPI scans: 70 ms TE, 5,000 ms TR, 90° flip angle, 24 cm FOV, 4 mm slice thickness, 0 mm gap, 64 × 94 matrix size (0 filled into 128 × 128 before FFT and the resulting 128 × 128 images were averaged into 64 × 64 before analysis), 20 slices. Voxel size for the functional images was 3.75 × 3.75 × 4.00 mm. The amygdala, fusiform gyrus, hippocampus, cerebellum, and most of the temporal and dorsal parietal lobe were not covered by the twenty slices in all participants, thus these areas could not be included in the group analysis. We were limited by the field of view, variability in brain size, and storage capacity of the system at the time.

The fMRI data analyses were performed using Statistical Parametric Mapping software (SPM2; The Wellcome Trust Centre for Neuroimaging at University College London; //www.fil.ion.ucl.ac.uk/spm/software/spm2). Functional images were realigned, smoothed

with a Gaussian kernel of 8 mm and normalized to the SPM EPI template brain. (Seventeen participants were recruited, but 2 were dropped from the study because they moved >2 mm.) We treated each of the stimulus types (rejecter, neutral, countback 1, countback 2) as a separate regressor, modeled as a boxcar function convolved with the canonical hemodynamic response. We created contrast images for rejecter versus neutral for each participant and inspected the individual results. We then analyzed the contrast images across participants using a mixed-effects general linear model, treating participants as a random effect and conditions as a fixed effect.

For planned comparisons (hypothesis-driven analyses), we applied a region of interest (ROI) analysis using a sphere [radius, 4–15 mm; $P \leq 0.05$, false discovery rate (FDR) correction for multiple comparisons]. We placed the center of the ROIs from Table 1 of Aron et al. (2005a) and from their results; also from other studies of romantic love, studies of craving, emotional regulation, and attachment (Bartels and Zeki 2000, 2004; Breiter et al. 1997; Eisenberger et al. 2003; Ortigue et al. 2007; Strathearn et al. 2008; Wager et al. 2008). To explore unpredicted regions of activation, we thresholded the images at $P < 0.001$, uncorrected for multiple comparisons. All clusters were ≥15 voxels. There were no significant activations when we analyzed the whole brain corrected for multiple comparisons.

To directly test the difference between happily and unhappily in love, we used a two-sample *t*-test in SPM2 and compared the data from participants in the report of Aron et al. (2005a) with the present data. Both data sets were collected on the same scanner using the same parameters. We accepted a threshold of $P < 0.001$, uncorrected.

Using SPM2, we tested ROIs for statistical correlations between participant brain responses and questionnaire scores for the PLS, time in the relationship, and time since the last break-up. To reinvestigate previous results, we placed the center of the ROIs (radius, 4–15 mm) on the coordinate locations from our previous study that performed the same correlations (Aron et al. 2005a) and from Ortigue et al. (2007). To look for associations with craving, the PLS and time since the break-up, we used ROIs from the results of Breiter et al. (1997) and Risinger et al. (2005). Because all these correlation analyses were replication attempts or hypothesis-driven, we accepted $P \leq 0.01$, uncorrected for multiple comparisons. All clusters were ≥15 voxels. All correlations were carried out within the rejecter-versus-neutral contrast.

RESULTS

Rejecter stimulus-specific activations

For the rejecter-versus-neutral contrast, predicted ROI measurements of subcortical areas associated with reward, romantic love, cocaine craving, attachment, and emotion reappraisal showed significant group effects ($P \leq 0.05$, FDR correction). Included were midbrain activation consistent with the right and left ventral tegmental area (VTA; Fig. 1*A* and Table 1); right ventral striatum in the region of the nucleus accumbens core, ventral globus pallidus (Fig. 1, *A–D,* and Table 1) and ventral putamen; right pulvinar (Fig. 1, *B* and *D,* and Table 1). Cortical areas that showed significant group effects were the middle orbitofrontal cortex, right lateral prefrontal cortex (Fig. 1, *A* and *E,* and Table 1), the angular gyrus deep in the sulcus (Table 1), right middle/ inferior frontal gyrus (Fig. 1, *B, D,* and *G*), left ventral sulcus (Fig. 1*E* and Table 1), medial prefrontal cortex (Fig. 1*H* and Table 1), left dorsolateral prefrontal cortex (Fig. 1*F* and Table 1), right anterior and left posterior insular cortex (Fig. 1, *A, E,* and *G,* and Table 1), bilateral anterior cingulate, and left posterior and retrosplenial cingulate (Table 1).

We compared these data on rejected individuals with the results from our study of 17 happily-in-love individuals (Aron et al. 2005a). Rejected lovers expressed significantly greater activity in the right nucleus accumbens core and ventral putamen/pallidum than did those who were happily-in-love ($P <$ 0.01).

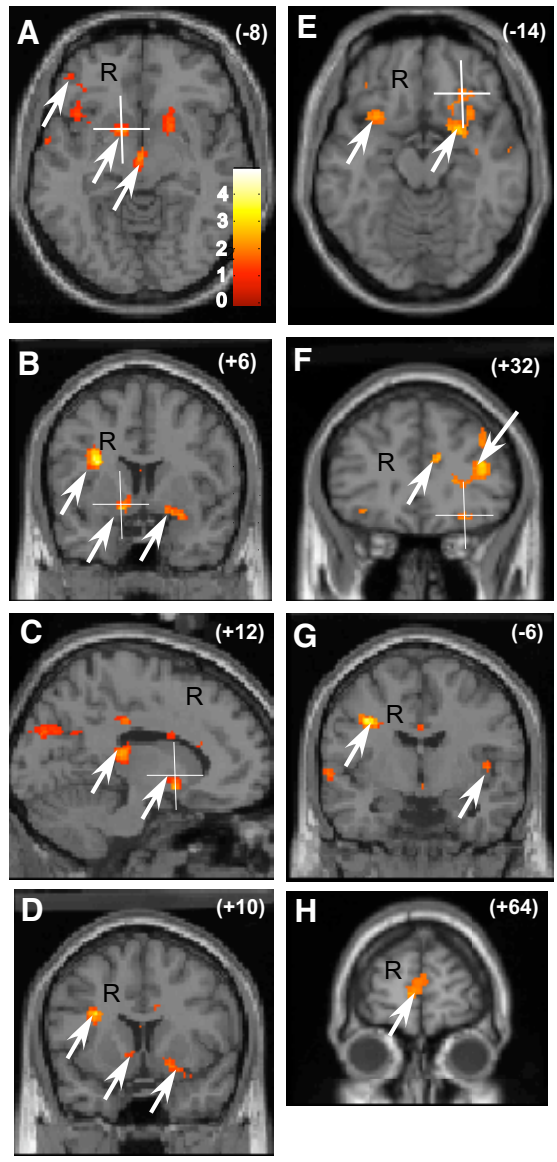

FIG. 1. Group regional activation specific to the rejector stimulus in reward systems and other areas. *A*: axial view. Ventral tegmental area (VTA, right arrow). The VTA regions overlap those affected when looking at a lover while happily in love (Aron et al. 2005a). The cross hair (middle arrow) marks an area of activation that includes the nucleus accumbens and ventral pallidum. The cross hair marks the same region in axial, coronal and sagittal views in *A–C.* The right ventrolateral prefrontal cortex (far left arrow) region shown by others (e.g., Wager et al.) to mediate successful emotion regulation. *B*: coronal view. The nucleus accumbens (middle arrow), ventral putamen (right arrow) and the fundus of the sulcus between the inferior and middle frontal gyri, in premotor cortex (left arrow; see also left arrow in *D* and *G*). *C*: sagittal view. The accumbens and ventral pallidum (right arrow and cross hair). An activation of the pulvinar is marked by the left arrow. *D*: coronal view. Right nucleus accumbens core (left arrow) and left ventral putamen activation (right arrow). *E*: axial view. The cross hair marks the same middle orbitofrontal region in *E* and *F*. The right anterior insula (left arrow) and left lateral ventral sulcus (right arrow) were affected. *F*: the left middle orbitofrontal cortex (crosshair), the left dorsolateral prefrontal cortex (right arrow) and anterior cingulate (left arrow). *G*: left insular cortex (right arrow) and middle frontal gyrus (left arrow). *H*: medial prefrontal cortex (arrow). Color scale shows *t*-test values and applies to all panels. R, right side.

TABLE 1. *Regional activations and deactivations specific to the picture of the beloved rejecter compared to a picture of a familiar, neutral acquaintance*

Brain Region	Left				Right			
	x	*y*	*z*	*P*	*x*	*y*	*z*	*P*
Activations								
Ventral tegmental area	−0.5	−16	−9	.02	2	−16	−9	.05
Ventral striatum* (Accumbens core/vGP)					11	6	−6	.002
Ventral striatum* (Accumbens core)					6	10	−4	.001
Ventral striatum* Putamen	−21	7	−11	.001	21	7	−11	.003
Middle orbitofrontal cortex	−28	31	−16	.05	37	33	−12	.03
Ventrolateral prefrontal cortex					40	37	−9	.002
Lateral ventral sulcus	−25	7	−15	.02				
Medial prefrontal cortex	−2	64	8	.03				
Dorsolateral prefrontal cortex	−42	32	16	.01				
Middle frontal gyrus					30	8	23	.001
Anterior cingulate	−10	40	16	.04	7	38	16	.02
Posterior cingulate	−6	−52	28	.02				
Retrosplenial cingulate	−12	−40	10	.01				
Anterior insula					26	19	7	.05
Posterior insula	−46	−8	4	.03				
Angular gyrus/sulcus					44	−48	26	.0001
Pulvinar					14	−30	14	.001
Deactivations								
Posterior ventral pallidum	−20	−8	0	.02				
Anterior dorsolateral striautm	−20	17	12	.04				
Orbitofrontal cortex					19	34	−6	.01

Region of interest analysis, false discovery rate (FDR) multiple comparison correction. Coordinates are at the maximum value for the cluster, which may be elongated in any direction. All clusters were 15 voxels or greater. x,y,z: MNI coordinates; vGP, ventral globus pallidus. *Different from happily in love (Aron et al. 2005a $P < 0.01$).

Rejecter-specific deactivations

Activity related to the rejecter decreased relative to the neutral stimulus in the left globus pallidus, left anterior dorsolateral striatum, and right orbitofrontal cortex (Table 1).

Self-report of degree of passionate love

A positive association between brain activity and individual scores on the PLS occurred in the body of the caudate nucleus ($r = 0.61$, $P = 0.01$) and septum/fornix area ($r = 0.46$; $P = 0.01$; Table 2). Associations with activation in these same regions occurred among the happily-in-love participants in Aron et al. (2005a) (caudate: $r = 0.60$, septum/fornix: $r = 0.54$). Thus the magnitude of the PLS correlation in the two studies was the same for the caudate ($r = 0.61$; $r = 0.60$) and similar for the septum/fornix ($r = 0.46$; $r = 0.54$). Additional cortical regions were associated with the PLS that were also activated in studies of cocaine craving (subcallosal gyrus and middle orbitofrontal cortex, Table 2) (Breiter et al. 1997; Risinger et al. 2005) or risk aversion and switch versus stay learning (Cohen et al. 2008; Tobler et al. 2009).

Length of relationship and number of days since break-up

The length of the relationship was not positively associated with degree of activation in any of the regions measured. Thus this group was different from the happily-in-love participants in Aron et al. (2005a), who showed greater activity in the left ventral putamen/pallidum as the relationship increased in duration. Instead, the reverse occurred: in this rejected-in-love group, the *greater* the number of days since break-up was associated with *less* activity in the right ventral putamen/pallidum area (Table 3), suggesting that attachment-related responses might be decreasing across time. In addition, the number of days since break-up was positively associated with increasing activity in the right anterior cingulate gyrus (BA 24, Table 3), an area linked with cocaine craving (Risinger et al. 2005).

DISCUSSION

Reward/loss/motivation systems and rejection during romantic love

Romantic love has been associated with a specific set of physiological, psychological, and behavioral characteristics

TABLE 2. *Regional brain activity associated with the Passionate Love Scale scores*

Passionate Love Scale	Left				Right			
	x	*y*	*z*	*P*	*x*	*y*	*z*	*P*
*Caudate body, anteromedial					12	4	22	.01
*Septum/fomix	−2	−1	17	.01	2	−2	20	.01
Subcallosal gyrus	−7	21	7	.001				
Middle orbitofrontal cortex					23	31	−12	.01

ROI analysis. $P \leq 0.01$, uncorrected. All clusters were 15 or more voxels. *The same area where happily-in-love participants' scores were correlated with the Passionate Love Scale scores in Aron et al. (2005a).

TABLE 3. *Regions of brain activity associated with number of months since the break-up of the relationship*

	Left				Right			
	x	*y*	*z*	*P*	*x*	*y*	*z*	*P*
Positive association								
Cingulate cortex BA32	−12	20	38	.001				
Cingulate cortex BA24	−2	−7 to +6	34	.01				
Negative association								
Insula, posterior	−42	−14	6	.01	40	−12	16	.01
Ventral Putamen					20	2	−8	.01

ROI analysis. $P \leq 0.01$, uncorrected. All clusters were 15 or more voxels. MNI coordinates (*x,y,z*) for the highest intensity voxel in a cluster.

(Fisher 1998; Gonzaga et al. 2001; Harris and Christenfeld 1996; Hatfield and Sprecher 1986; Tennov 1979). These characteristics include focused attention on the preferred individual, rearrangement of priorities, increased energy, mood swings, sympathetic nervous system responses including sweating and a pounding heart, emotional dependence, elevated sexual desire, sexual possessiveness, obsessive thinking about him or her, craving for emotional union with this preferred individual, affiliative gestures, goal oriented behaviors, and intense motivation to obtain and retain this particular mating partner. Three studies of individuals who were happily in love in London, New York, and Beijing indicate that this suite of characteristics is associated with activity in dopamine rich midbrain regions in the vicinity of the VTA and striatum (Aron et al. 2005a; Bartels and Zeki 2004; Xu et al. 2010). A fourth study has also found midbrain activation consistent with the VTA in association with romantic love intensity, measured using PLS scores (Ortigue et al. 2007).

Thus our first prediction was that rejected lovers who continue to be "in love" with their rejecting partners would show activation when viewing the person who rejected them in areas that mediate motivation and reward, specifically the midbrain area of the VTA and the striatum. We predicted this partly because adversity tends to heighten feelings of romantic love (Fisher 2004; Hatfield and Rapson 1996) and because when a reward is delayed in coming, reward-expecting neurons in the reward system prolong their activity (Schultz 2000). This prediction was supported. Our subjects showed greater activation in the midbrain area of the VTA during viewing of the rejecter than during viewing the neutral face in a region that overlaps with the area activated in our study of happily-in-love individuals (Aron et al. 2005). Our study also replicates the involvement of the angular gyrus in romantic love (Ortigue et al. 2007). These data lead us to speculate that despite separation and a negative emotional state, activity mediating intense romantic love is maintained in the midbrain area of the VTA and angular gyrus.

However, our participants also showed greater activation during the viewing of the rejecter face relative to the neutral face in forebrain regions of the reward system: the ventral striatum and region of the nucleus accumbens core, ventral/pallidum/putamen, and orbitofrontal/prefrontal cortex. These brain regions are associated with the dopaminergic reward system (Hollerman et al. 2000; Pessiglione et al. 2006; Porrino et al. 1984; Schultz et al. 2000; Wise and Hoffman 1992), expected value (Palminteri et al. 2009), and anticipatory affect that "promotes approach toward uncertain outcomes" (Knutson and Greer 2008). Several studies have shown that the accumbens, prefrontal and orbitofrontal cortex are associated with responses to both gains and losses (Camara et al. 2008; Carter et al. 2009; Tom et al. 2007). In particular, Carter et al. (2009) have found that the VTA and accumbens regions are engaged by both gains and losses, and they argue that activation in these regions generally reflects motivational relevance (see their introduction for a current review of the varied ventral striatal activation results). Thus an image of the rejecter and thoughts about the rejection experience activated brain regions that have been associated with *both* gains and losses in laboratory settings and may best be interpreted to reflect the high motivational relevance of the rejecter.

The forebrain reward system results also lead us to speculate that our rejected participants employed cognitive, experience-based reward systems while viewing their rejecter and that they might be engaged in a learning process that uses such systems, which could have been adaptive. These areas have been implicated in feedback-guided decision-making (Cohen et al. 2008). Kable and Glimcher (2007) propose that regions where we found increased activity, including regions of the accumbens core, medial prefrontal cortex, and posterior cingulate, together assist in the subjective evaluation of immediate and delayed rewards and during reinforcement learning (Schonberg et al. 2007). Liu et al. (2007) propose that these striatal and middle orbitofrontal cortex regions are associated with evaluating the choice one has made. The mid-orbitofrontal cortex where we found activity when our subjects viewed the rejecter relative to the neutral has also been correlated with evaluating punishers (Kringelbach and Rolls 2004) and implementing appropriate adjustments in behavior (Ridderinkhof et al. 2004a,b). Because this extended system was activated when our subjects viewed their rejecter, we speculate that these romantically rejected men and women were engaging reward evaluation systems to assess their situation and adjust their behavior accordingly, an adaptive response.

Passionate Love Scale correlation

The magnitude of the PLS score correlation with the BOLD signal in this and our previous study of romantic love (Aron et al. 2005a) was the same for the caudate ($r = 0.61$; $r = 0.60$) and similar for the septum/fornix ($r = 0.46$; $r = 0.54$). This satisfies a suggestion offered by Vul et al. (2009) that fMRI correlations with behavioral measures be replicated because the value of the Pearson *r* appears to be unusually high in many fMRI studies. Vul et al. specifically cited the study by Aron et al. (2005a) as showing an unusually high *r* for the correlation with the PLS that they doubted could be valid. Thus it is important to note that the magnitude of the *r* value remained the same in a second study. Additional areas in the cortex were

correlated with PLS scores in the present study with rejected subjects. These included the subcallosal gyrus and middle orbitofrontal cortex, which have been associated with cocaine craving (Breiter et al. 1997; Risinger et al. 2005), risk aversion, and switch versus stay learning (Cohen et al. 2008; Tobler et al. 2009).

"Addiction" to the rejecting romantic partner

Second, we predicted that rejected men and women would express neural activity in cortical and subcortical areas associated with craving and addiction when they viewed the rejecter relative to the neutral photograph, particularly the nucleus accumbens and orbitofrontal/prefrontal cortex because our rejected participants reported that they thought about their rejecter obsessively and craved emotional union with their rejecting partner. Our prediction was supported. Breiter and colleagues (1997) report that the nucleus accumbens is activated during cocaine administration and activity in this region is positively correlated with craving for cocaine. Volkow et al. (2006) report that craving for drugs is associated with a significant increase of dopamine in the striatum, including the dorsal (core) of the nucleus accumbens where we found activation. Risinger et al. (2005) report that cocaine craving during self-administration is positively correlated with activity in the same regions of the nucleus accumbens, prefrontal/ orbitofrontal gyrus and middle frontal gyrus where we found activity. Risinger et al. (2005) also report that activity in the pulvinar and retrosplenial cingulate near where we found activation is associated with a cocaine "high." Experiments with rodents suggest that the accumbens core mediates delayed reinforcement learning, or self-controlled choice (Cardinal and Everitt 2004; Cardinal et al. 2004), and that neural mechanisms in this region may be the basis of the persistence of addictive drug effects, including craving (Jacobs et al. 2005a,b). Interestingly, the angular gyrus, associated with romantic love in this and another study (Ortigue et al. 2007), has also been associated with cigarette craving (Brody et al. 2007). These previous findings suggest that the experience of romantic rejection involves the same neural systems that underlie various addictions.

Emotion regulation

Third, we predicted that when viewing the rejecter relative to the neutral photograph, rejected men and women would express activity in brain regions associated with emotion regulation because all participants sought ways to resolve their strong, conflicting feelings and control their despair. Previous studies suggest that the orbitofrontal cortex where we found activation is involved in emotion-related learning and behavior control (Kringelbach and Rolls 2004; Watanabe et al. 2007). So this hypothesis was supported. In addition, the ventrolateral prefrontal cortex activation that we found among our rejected participants when viewing the rejecter relative to the neutral photograph may be particularly involved in *successful* cognitive reappraisal of difficult emotional situations. Wager et al. (2008) found that successful emotion reappraisal of aversive images activated the ventrolateral prefrontal cortex, and the strength of its connections to the accumbens was associated with reappraisal success compared with a path through the amygdala where activity was associated with reduced reappraisal success. This same ventrolateral prefrontal cortex region was correlated with reduced distress following social exclusion in an experimental setting (Eisenberger et al. 2003). Also the lateral ventral sulcal area activated in our romantically rejected individuals when viewing the rejecter relative to the neutral photograph was involved in reappraisal success (Wager et al. 2008). This further suggests the possibility that the responses while looking at a rejecter in this group of participants might have been adaptive.

General emotion and grief

Fourth, we predicted that when viewing the rejecter relative to the neutral photograph, rejected individuals would express activity in neural regions associated with emotions because our participants expressed psychological pain and sadness in both the preinterviews and exit interviews. Several found it difficult to sleep, or trembled, cried, sighed, or got angry as they discussed their rejecter. We expected that these behaviors would involve the insular cortex. This prediction was supported. The insular cortex regions where we found activity have been associated in other studies with physical pain and/or distress (Brooks et al. 2005; Dube et al. 2009; Treede et al. 2000). Also a large area of the anterior cingulate where we found activity is involved in pain regulation (e.g., Petrovic et al. 2002). Thus among our rejected individuals some regions associated with general emotional responses and pain were activated.

Our study is the second investigation of romantic rejection. Najib and colleagues studied nine women who expressed "acute grief" over a romantic relationship that ended within the preceding 4 mo (Najib et al. 2004). Comparisons between the two studies uncovered few commonalities; only some small areas of the basal ganglia and orbitofrontal cortex were similar; in several regions where we found activations, Najib et al. (2004) found deactivations. Among these was the ventral striatum/accumbens.

A major difference in experimental design may contribute to the different results of these two studies. Najib et al. (2004) required their participants to lie in the scanner and "ruminate" about their "grief." No external stimuli were provided. Our participants, on the other hand, looked at a photograph of their rejecter and were required to actively remember incidents with this rejecting individual. These different approaches need further investigation because they may produce important differences in how the brain processes rejection and could potentially lead to considerably different therapeutic approaches to recovery from romantic rejection.

Many of our participants expressed hope that their participation in this project would help them learn more about their rejection experience as well as recover from it faster and/or more effectively. Our postscan interviews suggest that the experiment process did encourage participants to evaluate the gains and losses and learn from their rejection experience. We speculate that this learning experience occurred because as participants looked at the photograph of their rejecting partner and reflected on their rejection, they were activating the nucleus accumbens, ventrolateral prefrontal cortex, and medial prefrontal/orbitofrontal cortex, all regions involved in positive reassessment of negative emotional stimuli and learning (Ca-

mara et al. 2009; Cohen et al. 2008; Wager et al. 2008). Also activity in the nucleus accumbens related to reward expectation can be modulated with cognitive strategies (Delgado et al. 2008). We further speculate that forms of therapy that encourage recently rejected individuals to actively recall the events that led to the dissolution of the relationship, rather than "ruminating" on their pain (Najib et al. 2004), could be a more effective mechanism for recovery.

Last, in the context of loss and grief over the death of a beloved, O'Connor et al. (2008) found that activity in the anterior nucleus accumbens, where we also found activation when our subjects viewed the rejecter relative to the neutral photograph, was correlated with self-reported yearning as an individual mourned the death of a mother or sister. The accumbens appears to be consistently involved in reward craving and motivational relevance under a variety of circumstances.

Attachment and pair-bonding

We had not predicted that our rejected participants would show activation when viewing the rejecter compared with a neutral in the anterior ventral pallidum. Activity in this region, associated with a specific distribution pattern of vasopressin (V1aR) receptors, has been linked with pair-bonding and attachment behaviors in monogamous prairie voles (Lim and Young 2004; Lim et al. 2004). Promiscuous white-footed mice and promiscuous rhesus monkeys do not express pair-bonding/attachment behaviors or this distribution of V1a receptors in the ventral pallidum (Bester-Meredith et al. 1999; Wang et al. 1997; Young et al. 1997, 1999b). When the V1a receptor of the prairie vole is transgenically inserted into a nonmonogamous species, monogamous social behavior is generated (Young et al. 1999a). Importantly, variability in the human V1a receptor affects pair-bonding behavior in men (Walum et al. 2008). It is possible that this brain system initially evolved for other purposes (Lebreton et al. 2009), and further investigations need to be made to establish the relationship between these neural substrates and human pair-bonds; however, we speculate that activity in this region in humans is likely to be related to feelings of attachment. We regard these data to be of possible importance to the overall mapping of neural mechanisms associated with human reproductive strategies, specifically the formation, trajectory, and dissolution of human pair-bonds. Interestingly, in an adjacent area of the ventral pallidum, where activity has been associated with *increased* duration of a romantic relationship in humans (Aron et al. 2005a), we found *decreased* activity associated with the number of months since the break-up. So we speculate that the sensorimotor responses associated with daily interactions with the rejecting individual become less strong over time, resulting in less activity in this posterior sensorimotor area, whereas the emotional attachment remained strong, as reflected in the anterior limbic area of the globus pallidus.

Conclusion

We identified group regional activations related to a naturally occurring, emotionally chaotic, motivational state that may have value for survival and reproduction, namely to win back a mate. We do not know whether the activation in the VTA, nucleus accumbens, and an extended forebrain gain/loss system in this group of individuals was adaptive or maladaptive for them, but it indicates the motivational relevance of the rejecter. Also the involvement of the dopamine-rich mesolimbic regions suggest behavior associated with romantic rejection has a basis in mammalian, (not only human) drives. Thus this brain imaging study of individuals who were still "in love" with their rejecter supplies further evidence that the passion of "romantic love" is a goal-oriented motivation state rather than a specific emotion (Aron and Aron 1991; Aron et al. 2005). Moreover, the fMRI results of the study show that looking at a romantic rejecter and cocaine craving have several neural correlates in common. The findings are consistent with the hypothesis that romantic rejection is a specific form of addiction (Fisher 2004). The perspective that rejection in love involves subcortical reward gain/loss systems critical to survival helps to explain why feelings and behaviors related to romantic rejection are difficult to control and lends insight into the high cross-cultural rates of stalking, homicide, suicide, and clinical depression associated with rejection in love.

ACKNOWLEDGMENTS

We are grateful for the technical expertise provided during the scanning by H. Li, Department of Radiology State University of New York at Stony Brook. We are also grateful to D. Smith for help with preparation of the figure.

Present addresses: D. Mashek, Dept. of Humanities, Social Sciences, and the Arts, Harvey Mudd College Claremont, CA 91711; G. Strong, Dept. of Family and Child Sciences, Florida State University, Tallahasse, FL 32306.

GRANTS

This study was supported in part by National Science Foundation Grant 9910420 to A. Aron.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

REFERENCES

Aron A, Aron EN. *Love and the Expansion of Self: Understanding Attraction and Satisfaction.* New York: Hemishphere, 1986.

Aron A, Aron EN. Love and sexuality. In: *Sexuality in Close Relationships,* edited by McKinney K. and Sprecher S. Hillsdale, NJ: Erlbaum, 1991, p. 25–48.

Aron A, Aron EN, Allen J. *Motivations for unreciprocated love*. *Pers Soc Psychol Bull* 24: 87–796, 1998.

Aron A, Fisher H, Mashek DJ, Strong G, Li H, Brown LL. Reward, motivation, and emotion systems associated with early-stage intense romantic love. *J Neurophysiol* 94: 327–337, 2005a.

Aron A, Fisher H, Strong G. Romantic love. In: *The Cambridge Handbook of Personal Relationships*, edited by Vangelisti A, Perlman D. New York: Cambridge, 595–614, 2006.

Bartels A, Zeki S. The neural basis of romantic love. *Neuroreport* 11: 3829–3834, 2000.

Bartels A, Zeki S. The neural correlates of maternal and romantic love. *Neuroimage* 21: 1155–1166, 2004.

Baumeister RF, Wotman SR, Stillwell AM. Unrequited Love: on heartbreak, anger, guilt, scriptlessness and humiliation. *J Pers Soc Psychol* 64: 377–394, 1993.

Bester-Meredith JK, Young LJ, Marler CA. Species differences in paternal behavior and aggression in peromyscus and their associations with vasopressin immunoreactivity and receptors. *Horm Behav* 36: 25–38, 1999.

Bowlby J. *Attachment and loss.* New York: Basic Books, 1969.

Breiter HC, Gollub RL, Weisskoff RM, Kennedy DN, Makris N, Berke JD, Goodman JM, Kantor HL, Gastfriend DR, Riorden JP, Mathew RT, Rosen BR, Hyman SE. Acute effects of cocaine on human brain activity and emotion. *Neuron* 19: 591–611, 1997.

Brody AL, Mandelkern MA, Olmstead RE, Jou J, Tiongson E, Allen V, Scheibal D, London ED, Monterosso JR, Tiffany ST, Korb A, Gan JJ, Cohen MS. Neural substrates of resisting craving during cigarette cue exposure. *Biol Psychiatry* 62: 642–651, 2007.

Brooks JC, Zambreanu L, Godinez A, Craig AD, Tracey I. Somatotopic organisation of the human insula to painful heat studied with high resolution functional imaging. *Neuroimage* 27: 201–209, 2005.

Camara E, Rodriguez-Fornells A, Ye Z, Münte TF. Reward networks in the brain as captured by connectivity measures. *Front Neurosci* 3: 350–362, 2009.

Cardinal RN, Everitt BJ. Neural and psychological mechanisms underlying appetitive learning: links to drug addiction. *Curr Opin Neurobiol* 14: 156–162, 2004.

Cardinal RN, Winstanley CA, Robbins TW, Everitt BJ. Limbic corticostriatal systems and delayed reinforcement. *Ann NY Acad Sci* 1021: 33–50, 2004.

Carter RM, Macinnes JJ, Huettel SA, Adcock RA. Activation in the VTA and nucleus accumbens increases in anticipation of both gains and losses. *Front Behav Neurosci* 3: 21, 2009.

Cohen MX, Elger CE, Weber B. Amygdala tractography predicts functional connectivity and learning during feedback-guided decision-making. *Neuroimage* 39: 1396–1407, 2008.

Delgado MR, Gillis MM, Phelps EA. Regulating the expectation of reward via cognitive strategies. *Nat Neurosci* 11: 880–881, 2008.

Dube AA, Duquette M, Roy M, Lepore F, Duncan G, Rainville P. Brain activity associated with the electrodermal reactivity to acute heat pain. *Neuroimage* 45: 169–180, 2009.

Eisenberger NI, Lieberman MD, Williams KD. Does rejection hurt? An FMRI study of social exclusion. *Science* 302: 290–292, 2003.

Fehr B. Prototype analysis of the concepts of love and commitment. *J Pers Soc Psychol* 55: 557–579, 1988.

Fisher HE. Lust, attraction, and attachment in mammalian reproduction. *Hum Nature* 9: 23–52, 1998.

Fisher HE. *Why We Love: The Nature and Chemistry of Romantic Love.* New York: Holt, 2004.

Fisher HE, Aron A, Brown LL. Romantic love: a mammalian brain system for mate choice. *Philos Trans R Soc Lond B Biol Sci* 361: 2173–2186, 2006.

Frascella J, Potenza MN, Brown LL, Childress AR. Shared brain vulnerabilities open the way for non-substance addictions: Craving addiction at a new joint? *Ann N Y Acad Sci* 1187: 294–315, 2010.

Gonzaga G, Keltner D, Londahl E, Smith M. Love and commitment problems in romantic relations and friendship. *J Pers Soc Psychol* 81: 247–262, 2001.

Griffin-Shelley E. *Sex and Love: Addiction, Treatment and Recovery.* Westport, CT: Praeger, 1991.

Halpern HM. *How to Break Your Addiction to a Person.* New York: McGraw-Hill, 1982.

Harris CR, Christenfeld N. Gender, jealousy and reason. *Psychol Sci* 7: 364–366, 1996.

Hatfield E, Rapson RL. *Love and Sex: Cross-Cultural Perspectives.* Needham Heights, MA: Allyn and Bacon, 1996.

Hatfield E, Sprecher S. Measuring passionate love in intimate relationships. *J Adolesc* 9: 383–410, 1986.

Hendick C, Hendrick SS. Romantic love: measuring cupid's arrow. In: *Positive Psychological Assessment: A Handbook of Models and Measures*, edited by Lopez SJ, Snyder CR. Washington, DC: Am. Psychol. Assoc., 2003, p. 235–239.

Hollerman JR, Tremblay L, Schultz W. Involvement of basal ganglia and orbitofrontal cortex in goal-directed behavior. *Prog Brain Res* 126: 193–215, 2000.

Jacobs EH, Smit AB, de Vries TJ, Schoffelmeer AN. Long-term gene expression in the nucleus accumbens following heroin administration is subregion-specific and depends on the nature of drug administration. *Addict Biol* 10: 91–100, 2005a.

Jacobs EH, Wardeh G, Smit AB, Schoffelmeer AN. Morphine causes a delayed increase in glutamate receptor functioning in the nucleus accumbens core. *Eur J Pharmacol* 511: 27–30, 2005b.

Jankowiak WR, Fischer EF. A cross-cultural perspective on romantic love. *Ethnology* 31: 149–155, 1992.

Kable JW, Glimcher PW. The neural correlates of subjective value during intertemporal choice. *Nat Neurosci* 10: 1625–1633, 2007.

Kelley HH. Love and commitment. In: *Close Relationships*, edited by Kelley HH, Berscheid E, Christensen A, Harvey JH, Huston TL, Levinger G, McClintock E, Peplau LA, Peterson DR. New York: Freeman, 1983, p. 265–314.

Knutson B, Greer SM. Anticipatory affect: neural correlates and consequences for choice. *Philos Trans R Soc Lond B Biol Sci* 363: 3771–3786, 2008.

Kringelbach ML, Rolls ET. The functional neuroanatomy of the human orbitofrontal cortex: evidence from neuroimaging and neuropsychology. *Prog Neurobiol* 72: 341–372, 2004.

Lebreton M, Barnes A, Miettunen J, Peltonen L, Ridler K, Veijola J, Tanskanen P, Suckling J, Jarvelin MR, Jones PB, Isohanni M, Bullmore ET, Murray GK. The brain structural disposition to social interaction. *Eur J Neurosci* 29: 2247–2252, 2009.

Lewis T, Amini F, Lannon R. *A General Theory of Love.* New York: Random House, 2000.

Liebowitz MR. *The Chemistry of Love.* Boston: Little, Brown, 1983.

Lim MM, Wang Z, Olazabal DE, Ren X, Terwilliger EF, Young LJ. Enhanced partner preference in a promiscuous species by manipulating the expression of a single gene. *Nature* 429: 754–757, 2004.

Lim MM, Young LJ. Vasopressin-dependent neural circuits underlying pair bond formation in the monogamous prairie vole. *Neuroscience* 125: 35–45, 2004.

Liu X, Powell DK, Wang H, Gold BT, Corbly CR, Joseph JE. Functional dissociation in frontal and striatal areas for processing of positive and negative reward information. *J Neurosci* 27: 4587–4597, 2007.

Mashek D, Aron A, Fisher HE. Identifying, evoking, and measuring intense feelings of romantic love. *Representative Res Soc Psychol* 24: 48–55, 2000.

Mearns J. Coping with a breakup: negative mood regulation expectancies and depression following the end of a romantic relationship. *J Pers Soc Psychol* 60: 327–334, 1991.

Mellody P, Miller AW, Miller K. *Facing Love Addiction.* New York: HarperSan Francisco, 1992.

Meloy JR, Fisher H. Some thoughts on the neurobiology of stalking. *J Forensic Sci* 50: 1472–1480, 2005.

Mikulincer M, Shaver PR. Attachment, group-related processes, and psychotherapy. *Int J Group Psychother* 57: 233–245, 2007.

Najib A, Lorberbaum JP, Kose S, Bohning DE, George MS. Regional brain activity in women grieving a romantic relationship breakup. *Am J Psychiatry* 161: 2245–2256, 2004.

O'Connor MF, Wellisch DK, Stanton AL, Eisenberger NI, Irwin MR, Lieberman MD. Craving love? Enduring grief activates brain's reward center. *Neuroimage* 42: 969–972, 2008.

Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9: 97–113, 1971.

Ortigue S, Bianchi-Demicheli F, Hamilton AF, Grafton ST. The neural basis of love as a subliminal prime: an event-related functional magnetic resonance imaging study. *J Cogn Neurosci* 19: 1218–1230, 2007.

Palminteri S, Boraud T, Lafargue G, Dubois B, Pessiglione M. Brain hemispheres selectively track the expected value of contralateral options. *J Neurosci* 29: 13465–13472, 2009.

Peele S, Brodsky A. *Love and Addiction.* New York: Taplinger, 1975.

Pessiglione M, Seymour B, Flandin G, Dolan RJ, Frith CD. Dopamine-dependent prediction errors underpin reward-seeking behaviour in humans. *Nature* 442: 1042–1045, 2006.

Petrovic P, Kalso E, Petersson KM, Ingvar M. Placebo and opioid analgesia—imaging a shared neuronal network. *Science* 295: 1737–1740, 2002.

Porrino LJ, Esposito RU, Seeger TF, Crane AM, Pert A, Sokoloff L. Metabolic mapping of the brain during rewarding self-stimulation. *Science* 224: 306–309, 1984.

Ridderinkhof KR, Ullsperger M, Crone EA, Nieuwenhuis S. The role of the medial frontal cortex in cognitive control. *Science* 306: 443–447, 2004a.

Ridderinkhof KR, van den Wildenberg WP, Segalowitz SJ, Carter CS. Neurocognitive mechanisms of cognitive control: the role of prefrontal cortex in action selection, response inhibition, performance monitoring, and reward-based learning. *Brain Cogn* 56: 129–140, 2004b.

Risinger RC, Salmeron BJ, Ross TJ, Amen SL, Sanfilipo M, Hoffmann RG, Bloom AS, Garavan H, Stein EA. Neural correlates of high and craving during cocaine self-administration using BOLD fMRI. *Neuroimage* 26: 1097–1108, 2005.

Schaef AW. *Escape From Intimacy: The Pseudo-Relationship Addictions: Untangling the "love" Addictions, Sex, Romance, Relationships.* New York: Harper and Row, 1989.

Schonberg T, Daw ND, Joel D, O'Doherty JP. Reinforcement learning signals in the human striatum distinguish learners from nonlearners during reward-based decision making. *J Neurosci* 27: 12860–12867, 2007.

Schultz W. Multiple reward signals in the brain. *Nat Rev Neurosci* 1: 199–207, 2000.

Schultz W, Tremblay L, Hollerman JR. Reward processing in primate orbitofrontal cortex and basal ganglia. *Cereb Cortex* 10: 272–284, 2000.

Shaver PR, Morgan HJ, Wu S. Is love a "basic" emotion? *Pers Relationships* 3: 81–96, 1996.

Sternberg R. A triangular theory of love. *Psych Rev* 93: 119–135, 1986.

Strathearn L, Li J, Fonagy P, Montague PR. What's in a smile? Maternal brain responses to infant facial cues. *Pediatrics* 122: 40–51, 2008.

Tennov D. *Love and Limerance: The Experience of Being in Love in New York.* New York: Stein and Day, 1979.

Tobler PN, Christopoulos GI, O'Doherty JP, Dolan RJ, Schultz W. Risk-dependent reward value signal in human prefrontal cortex. *Proc Natl Acad Sci USA* 106: 7185–7190, 2009.

Tom SM, Fox CR, Trepel C, Poldrack RA. The neural basis of loss aversion in decision-making under risk. *Science* 315: 515–518, 2007.

Treede RD, Apkarian AV, Bromm B, Greenspan JD, Lenz FA. Cortical representation of pain: functional characterization of nociceptive areas near the lateral sulcus. *Pain* 87: 113–119, 2000.

United-Nations. *Human Development Report.* New York: Oxford, 1995.

Volkow ND, Wang GJ, Telang F, Fowler JS, Logan J, Childress AR, Jayne M, Ma Y, Wong C. Cocaine cues and dopamine in dorsal striatum: mechanism of craving in cocaine addiction. *J Neurosci* 26: 6583–6588, 2006.

Vul E, Harris C, Winkielman P, Pashler H. Puzzlingly high correlations in fMRI studies of emotion, personality, and social cognition. *Persp Psychol Sci* 4: 274–290, 2009.

Wager TD, Davidson ML, Hughes BL, Lindquist MA, Ochsner KN. Prefrontal-subcortical pathways mediating successful emotion regulation. *Neuron* 59: 1037–1050, 2008.

Walum H, Westberg L, Henningsson S, Neiderhiser JM, Reiss D, Igl W, Ganiban JM, Spotts EL, Pedersen NL, Eriksson E, Lichtenstein P. Genetic variation in the vasopressin receptor 1a gene (AVPR1A) associates with pair-bonding behavior in humans. *Proc Natl Acad Sci USA* 105: 14153–14156, 2008.

Wang Z, Young LJ, Liu Y, Insel TR. Species differences in vasopressin receptor binding are evident early in development: comparative anatomic studies in prairie and montane voles. *J Comp Neurol* 378: 535–546, 1997.

Watanabe M, Hikosaka K, Sakagami M, Shirakawa S. Reward expectancy-related prefrontal neuronal activities: are they neural substrates of "affective" working memory? *Cortex* 43: 53–64, 2007.

Wilson M, Daly M. The man who mistook his wife for a chattel. In: *The Adapted Mind: Evolutionary Psychology and the Generation of Culture*, edited by Barkow JH, Cosmides L, Tooby J. New York: Oxford, 1992.

Wise RA, Hoffman DC. Localization of drug reward mechanisms by intracranial injections. *Synapse* 10: 247–263, 1992.

Xu X, Aron A, Brown LL, Cao G, Feng T, Weng X. Reward and motivation systems: a brain mapping study of early-stage intense romantic love in Chinese participants. *Hum Brain Map* In press.

Young LJ, Nilsen R, Waymire KG, MacGregor GR, Insel TR. Increased affiliative response to vasopressin in mice expressing the V1a receptor from a monogamous vole. *Nature* 400: 766–768, 1999a.

Young LJ, Toloczko D, Insel TR. Localization of vasopressin (V1a) receptor binding and mRNA in the rhesus monkey brain. *J Neuroendocrinol* 11: 291–297, 1999b.

Young LJ, Winslow JT, Nilsen R, Insel TR. Species differences in V1a receptor gene expression in monogamous and nonmonogamous voles: behavioral consequences. *Behav Neurosci* 111: 599–605, 1997.