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 Mashek3

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

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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 rejector 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.
relationships were heterosexual. All participants preferred their right
hand (Oldfield 1971), and none were taking antidepressant medica-
tions. 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 stim-
ulus 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 nega-
tive. 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 scan-
ing and digitized, cropped, and sized to show the head only. Image
quality was inspected by an experimenter so that it was not pixelated,
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 inter-
spersed 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.

Intructions 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 participant, for example, said that she had dreamed of the rejecter saying, “I want a letter from him, or a phone call; I want some respect.”

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 20 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-weighted 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 IMRI 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 ≤ 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 ≤ 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 ≤ 0.05, FDR correction). Included were midbrain activation consistent with the right and left ventral tegmental area (VTA; Fig. 1A 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. 1E and Table 1), medial prefrontal cortex (Fig. 1H and Table 1), left dorsolateral prefrontal cortex (Fig. 1F 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).
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), 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.
(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 (Camarca 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 (Kringlebalb 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

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

ROI analysis. P ≤ 0.01, uncorrected. All clusters were 15 or more voxels. MNI coordinates (x,y,z) for the highest intensity voxel in a cluster.
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 (Kringlebach 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-
may have value for survival and reproduction, namely to win 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.

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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, Tallahassee, FL 32306.

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DISCLOSURES

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