Neurobiological Pathways of Romantic Attraction: How do the Neurobiological Pathways Involved in Romantic Attraction Parallel Those Involved in Addiction and Reward?

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Abstract

Romantic rejection is a potentially debilitating condition that many people experience at some point throughout their lives. Whether it is through experiencing a breakup or ruminating over feelings of unrequited attraction, the failure to properly rebound from romantic rejection can have disastrous consequences on one's mental health, such as prolonged feelings of obsession, social anxiety, and suicidal thoughts. To find a potential treatment for romantic rejection, one may observe that romantic attraction is an experience sharing many traits with the reward of addiction, such as the activation of neurotransmitters such as dopamine, serotonin, and oxytocin, as well as the activation of specialized regions in the prefrontal and orbitofrontal cortex, and the nucleus accumbens. Due to the significant role of the brain's reward system in addiction, by considering the similarities this system may share with those salient in individuals experiencing romantic attraction, one may be able to find treatment ideas for romantic rejection. This paper will provide a review of the neurobiological pathways of addiction compared to romantic attraction, a discussion of the similarities between the two, as well as further avenues for research on potential "anti-love" medications that may ease obsessive, fearful, and depressive behavior frequently associated with romantic rejection.

Introduction

A nearly universal human experience has been a romantic attraction (Jankowiak & Fischer, 1992). This being said, another universal experience in human nature has been that of romantic rejection, which is most simply defined as when one is not wanted or liked by a romantic partner (Hsu et al., 2021). Earp et al. (2013) argue that the definition of love can be broken down into three components - lust (characterized by sex drive), attraction (characterized by focused attention, feelings of exhilaration, and intrusive and obsessive thoughts about the desired person), and attachment (characterized by feelings of security and the desire to protect both parties). In this review, we will deal with romantic rejection as it relates to attraction, not to sexual desire. Furthermore, throughout the paper, the terms "romantic rejection" and "heartbreak" will be used interchangeably.

While some instances of heartbreak may be beneficial for a person to develop and mature; intense, stressful rejections characterized by a strong feeling of betrayal and anger can increase the recipient's risk of more grave health consequences, such as depression and grief (Mearns, 1991; Verhallen et al., 2019). Furthermore, Field (2011) notes that romantic rejection can lead to intrusive thoughts, insomnia, and feelings of bereavement. Regarding one's internal reaction, rejection by a romantic partner is interpreted as a painful stimulus in one's brain (MacDonald & Leary, 2005), eliciting a cognitive response of meaningless thought, decreased self-awareness, and excessive lethargy, similar to the response from traumatic physical injury (Twenge et al., 2003).

This plethora of physical and mental impairments surrounding romantic rejection makes it an important avenue of study. Could there be any medical treatments or preventions to this feeling? Because of the partner's tendency to fluctuate between chasing emotional highs and enduring an intense stream of depression, romantic rejection can be seen as a sort of addiction (Peele & Brodsky, 1974). The comparison of the feeling of romantic attraction (and, conversely, rejection) to that of addiction provides a new avenue of research - are there similarities in the neurobiological framework underlying the two? Current research literature has not yet focused on important links between these pathways. If the neural structures and chemicals governing addiction share similar characteristics to those governing romantic attraction, perhaps treatments for substance use can be extended for romantic rejection as well. This article will explore and compare the underlying neurobiological frameworks behind addiction and romantic attraction, as well as provide a new starting point for potential heartbreak treatments.

Review of Literature

The Neurobiological Pathway of Addiction

The neurobiological pathway of addiction is the brain's mesolimbic dopamine (DA) system. There are three main neural structures involved in this pathway - the basal ganglia, the extended amygdala, and the prefrontal cortex (Office of the Surgeon General, 2016). This neurobiological pathway follows three steps: binge/intoxication, withdrawal/negative affect, and preoccupation/anticipation (craving). These steps worsen over time, leading to neuroplastic changes in the brain's reward, stress, and executive function systems (Koob, 2016). To begin, when one consumes an addictive substance there is activity in the nucleus accumbens—particularly the activation of the brain's dopamine and opioid signaling system (Yoshimoto et al., 2000; Weiss & Porrino, 2002).

The reward circuitry of the nucleus accumbens (NA) of the basal ganglia along with dopamine and naturally occurring opioids play significant roles in the pleasurable effects of drugs. It contributes to the triggering of cravings, substance seeking, and substance use in response to cues associated with the substance. As one continues to abuse substances, the dorsal striatum becomes repeatedly activated (Yager et al., 2015). This activation causes the notable impulsive behavior behind substance abuse. Impulsivity is defined as an inability to resist urges as well as the tendency to pursue immediate gratification and reward (Berlin & Hollander, 2014). The involvement of these reward neurocircuitry helps to explain the strong desire for the substance (craving) and the compulsive seeking that occurs when individuals who are previously addicted are exposed to drug-related cues in their environment. At this stage of addiction, the brain's reward systems function less effectively, and stress-related neurotransmitters like corticotropin-releasing factor (CRF) and dynorphin in the extended amygdala become active (Koob & Le Moal, 2001). This combination creates a chemical basis for the negative emotional state experienced during withdrawal. The urge to alleviate these negative feelings reinforces the use of drugs, driving compulsive substance taking (Weiss & Porrino, 2002). This stage of the addiction cycle is characterized by impaired executive function through a compromised prefrontal cortex. The neurotransmitter glutamate becomes more active, leading to substance use habits associated with craving, and disrupting the influence of dopamine on the frontal cortex. The over-activation of the "Go" system in the prefrontal cortex promotes habit-like substance seeking, while the under-activation of the "Stop" system in the prefrontal cortex promotes impulsive and compulsive substance seeking (Tzschentke, 2001).

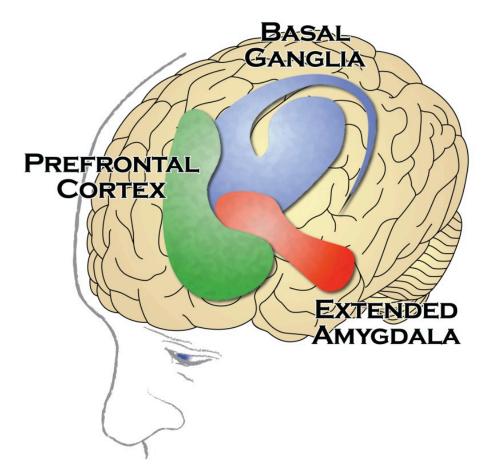


FIGURE 1: Primary brain regions involved in substance use. (The basal ganglia [blue] controls the reward, effects of substance use and is responsible for the formation of habitual substance taking. The extended amygdala [red] is involved in stress and the feelings of unease, anxiety, and irritability that typically accompany substance withdrawal. The prefrontal cortex [green] is involved in executive function i.e., the ability to organize thoughts and activities, prioritize tasks, manage time, and make decisions). Image taken from Office of the Surgeon General (2016).

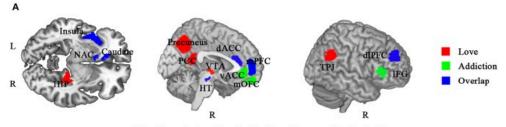
The Neurobiological Pathway of Romantic Attraction To anticipate a potential treatment for romantic rejection, one must first understand how this circuitry runs when the brain is experiencing romantic *attraction*. Namely, this pathway is also the mesolimbic DA system. During experiences of attraction, the brain is associated with higher levels of central DA and norepinephrine (NE), but decreased levels of central serotonin 5-HT (Fisher, 1998). D1 and D2 receptors can be found in the NA, while D3, D4, and D5 receptors are found in the amygdala and hippocampus, where they are primarily linked to feelings of reward and motivation (Seshadri, 2016). Notable characteristics of romantic rejection include a party's obsessive thoughts about their partner, and a party's focus on meeting with them quickly - a short-term benefit. These desires

can be seen as examples of impulsivity. Marazziti et al. (1999) note that this decreased 5-HT transporter may be related to these obsessive preoccupations that one tends to get about their partner in early attraction phases, and consequently during romantic rejection. Key areas where DA is released are the nucleus accumbens and the ventral tegmental area (VTA). The amygdala also plays a major role, particularly in emotional processing. The amygdala enables one to feel emotions such as excitement, arousal, and anticipation (Bozarth, 1994). In general, brain regions associated with romantic attraction are those with high concentrations of dopamine, norepinephrine, and serotonin receptor sites (Fischer et al., 2002). Higher central dopamine levels are associated with several aspects of romantic attraction, such as lovers' focused attention on their subjects or their tendency to relive certain special moments with their partner. Fischer et al. (2002) also note that higher dopamine levels contribute to the euphoric feeling experienced at the start of romantic attraction. When romantic attraction transitions into romantic rejection, the release of certain neurotransmitters, particularly the serotonin 5-HT transporter, significantly decreases (Maserati et al., 1999). Furthermore, Hsu et al. found that the anterior insula (AI), (involved in social rejection) and the ventrolateral prefrontal cortex (vIPFC) (involved in emotional regulation) are specifically activated during romantic rejection (2020). Oxytocin (OT), a neuropeptide, is thought to be involved in coping with social events and regulating social behavior. Romantic rejection is a distressing event and could be considered a social pain. In this regard, OT may have a role in reducing social pain or romantic rejection (Zhang et al., 2021).

Comparison

Romantic attraction and drug addiction activate many similar regions in the brain's mesocorticolimbic dopamine system. Both conditions activate the VTA, NAC, dACC, caudate, and mPFC, as seen in Figure 2 (Zho et al., 2016). The VTA, caudate, and NAC regions are all involved with pleasure, focused attention, and the motivation to pursue rewards (Shultz, 2000). The dACC and mPFC are involved in slightly different functions dACC activation can limit obsessive thinking (Zho et al., 2016), while the mPFC contributes to the feeling of craving. This activation of similar brain regions makes sense when we consider the behavioral similarities between romantic attraction and drug addiction - such as emotional dependency, obsessive thoughts, and craving (Aron et al., 2005). Another important behavioral similarity between romantic attraction and drug addiction is the conditioned reinforcement reaction. A conditioned reinforcement action is defined as "a previously neutral stimulus reinforces or strengthens behaviors through its association with a primary reinforcer and becomes a reinforcer in its own right" (Koob et al., 2016). For drug addiction, the conditioned reinforcement reaction occurs when one is merely anticipating taking drugs, and already feels excited (Goddard et al, 2013). Regarding

attraction, the conditioned reinforcement action could be seen as when one party eagerly anticipates seeing his/her partner, and once this meeting takes place, the party feels a newfound sense of pleasure. Furthermore, both conditions show characteristics of impulsivity as discussed earlier. These two conditions also share several neurotransmitters and neuropeptides - namely, the D1 and D2 receptors, corticotropin-releasing factor (CRF), and oxytocin (OT) (Zhou et al., 2016). The D1 and D2 receptors play a critical role in the feeling of motivation and anticipation of reward (Esch and Stefano, 2005). CRF plays a role in stress responsivity (Bale & Vale, 2004). Finally, OT is involved with social cognition (Hollander et al., 2007). The main difference between the pathways of romantic attraction and those of drug addiction is that romantic attraction is controlled by certain feedback mechanisms that are severely inhibited during drug addiction. These feedback mechanisms activate aversive centers that can prevent romantic attraction from becoming as damaging of addiction as drug addiction (Bozarth, 1994). In general, the DA pathway undergoes both positive feedback (DA system activation) and negative feedback (DA system inhibition). However, continued drug addiction can alter these feedback mechanisms, decreasing their functionality (Stolyarova et al., 2015). This is to say, as one develops a dependence on an addictive substance, he or she will begin to perceive the reward of taking the substance with greater importance than the risks associated with such an action.



Alterations in functional activation (Love and Addiction)

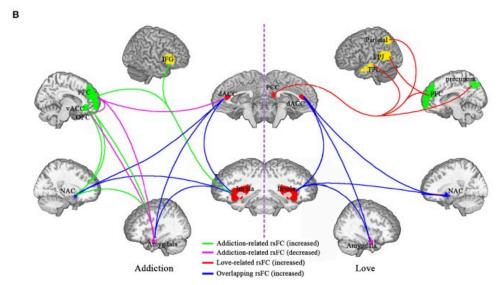


FIGURE 2: Primary brain regions involved in love and addiction (A) and functional connectivity increase or decrease for love and addiction (B). ACC, anterior cingulate cortex; vACC ventral anterior cingulate; dACC, dorsal anterior cingulate cortex; PCC, posterior cingulate cortex; OFC, orbitofrontal cortex; IFG, inferior frontal gyrus; dlPFC, dorsolateral prefrontal cortex; PFC, prefrontal cortex; VTA, ventral tegmental area; NAC, nucleus accumbens; TPJ, temporal-parietal junction; HIP, hippocampus; HT, hypothalamus; TEP, temporal cortex. Image taken from Zho et al (2016).

Romantic Rejection (RR)

RR is an emotionally distressful experience profoundly affecting life, possibly leading to mental illness or suicide. If RR must be studied as a serious condition worth managing or mitigating, a clinically significant romantic rejection can be defined as three or more of the following symptoms being present during the same two-week period and represent a change from previous functioning following recent romantic attraction (or "falling in love"):

- 1- Symptoms of depression -depressed mood, anhedonia, sleep disturbance, change in appetite, energy, psychomotor agitation or retardation, guilt, or suicidal thought.
- 2- Symptoms of obsession Ruminating over feelings and intrusive thoughts.
- 3- Symptoms of anxiety- Fear of losing privacy or difficulty concentrating.

- 4- Symptoms of addiction- craving for restoration of relationship, social impairment, and participation in risky behavior.
- 5- Physical symptoms- painful symptoms or distress, decreased self-awareness, excessive lethargy.
 The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
 The episode is not attributable to the direct physiological effects of a substance or another medical condition.

Conclusion and Future Directions

The main findings of this study are that brain activities related to romantic attraction overlap with those of addiction. Similarly, the mental and physical manifestations of especially early romantic attractions have many features found in subjects with addiction.

Because of the neurobiological similarities these two conditions share, exploring these connections further could enable researchers to develop potential treatment mechanisms for romantic rejection. A further avenue of research would concern the similarities between romantic attraction/rejection and obsessive-compulsive disorder (OCD). Both conditions show characteristics of impulsivity and compulsivity - thus, researching OCD treatments such as SSRIs (known for the emotional blunting effect they produce) (Meyer, 2007) may provide a different avenue into romantic rejection treatments. Additionally, a more comprehensive review of medications such as dopamine antagonists could help try to prevent unhealthy, obsessive cases of romantic attraction. A limitation of this area of study is that while there are standard definitions of characteristics such as impulsivity and compulsivity, there is no standard definition for romantic rejection. Romantic rejection is a more clinically relevant condition. An attempt to define romantic rejection has been made. Standardizing the definition of romantic rejection would provide a consistent framework for researchers looking to study this phenomenon in isolation.

This study contributes by elucidating and putting forward the latest understanding of the relationship between romantic attraction and addiction. The understanding of similarity or dissimilarity between brain regions, specific circuits, and neurotransmitters could help develop therapies for subjects who are significantly affected by romantic rejection.

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