Review Article

# Love as a Modulator of Pain

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**Submitted:** 14 Nov 2016
**Accepted:** 21 Feb 2017
**Online:** 30 Jun 2017

To cite this article: Tamam S, Ahmad AH. Love as a modulator of pain. *Malays J Med Sci.* 2017;**24(3)**:5–14. https://doi.org/10.21315/mjms2017.24.3.2

To link to this article: https://doi.org/10.21315/ mjms2017.24.3.2

## Abstract

**Pain is modulated by various factors, the most notable of which is emotions. Since love is an emotion, it can also modulate pain. The answer to the question of whether it enhances or reduces pain needs to be determined. A review was conducted of animal and human studies in which this enigmatic emotion and its interaction with pain was explored. Recent advances in neuroimaging have revealed similarities in brain activation relating to love and pain. At the simplest level, this interaction can be explained by the overlapping network structure in brain functional connectivity, although the explanation is considerably more complex. The effect of love can either result in increased or decreased pain perception. An explanation of the interaction between pain and love relates to the functional connectivity of the brain and to the psychological construct of the individual, as well as to his or her ability to engage resources relating to emotion regulation. In turn, this determines how a person relates to love and reacts to pain.**

**Keywords:** *pain, love, emotion, reward, neuroimaging*

## Introduction

Pain is defined as 'an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage' (1). The perception of pain is determined by nociceptive input and is also dependent on cognitive-affective factors (2–4). While the sensory-discriminative aspect of pain involves the intensity, quality and location of the pain, cognitive-affective factors pertain to the more subjective psychological variables of attention, anxiety, fear, expectation, anticipation and stress (3). Pain is modulated by cognitive and emotional factors (i.e., prior experiences), attention, mood (i.e., anxiety and depression), neurochemical and structural changes in the brain, genetics, and peripheral and central sensitisation (5).

The Oxford English Dictionary (6) defines love as 'a strong feeling of affection', 'a great interest and pleasure in something' and 'a person or thing that one loves'. The term, 'love', is consistent with 'pleasure' in affective neuroscience. However, the pleasure derived from feeling love is different to that obtained when tasting good food or watching a movie, although a significant overlap is involved in the neural circuitry (7). Thus, for the purposes of this study, the context of 'love' in this review was limited to and denoted the emotion felt between two persons.

Since love is an emotion, it is able to modulate pain. The answer to the question of whether it enhances or reduces pain needs to be determined. It has been shown in studies that the effect of love can either result in increased or decreased pain perception. A review was conducted of research in which the neural

  

substrates of this enigmatic emotion were explored and to determine how it potentially interacts with pain.

## The Neural Substrate of Love

A functional magnetic resonance imaging (fMRI) study was performed on 17 individuals identified as being intensely 'in love' (8). The participants were asked to view photographs of their loved one and those of a familiar acquaintance. The performance of activities was separated by a distraction-attention task. Neural mechanisms, associated with romantic love specific to the object of affection, were identified in the right ventral tegmental area and right caudate nucleus; two areas known to process reward and motivation. The right anteromedial caudate correlated with the questionnaire scores used to quantify the intensity of romantic passion. Similar results were found when the study was conducted on a Chinese population sample (9).

A number of neurotransmitters has been associated with the experience of love. The rewarding and pleasurable feeling of love results from the release of dopamine tied to the brain reward system (10, 11). Oxytocin and vasopressin are the most prominent hormones implicated in pair bonding, as studied in monogamous animals (12), and those implicated in love; not just between partners, but also between friends, or a mother and her child (13, 14). Vasopressin, the attachment hormone, increases the fear and stress response and induces partner bonding in males. Oxytocin has anxiolytic and stress-reducing effects and expedites partner bonding in females (14, 15). With the binding of oxytocin and vasopressin, the subcortical dopaminergic reward-related system is activated and extends to the medial insula, anterior cingulate cortex, hippocampus, striatum and hypothalamus, thereby contributing to the rewarding experience of love (16).

The initial phase of love, characterised by unreasonably obsessive behaviour, is the result of a reduction in serotonin levels, similarly seen in patients with obsessive-compulsive disorder (13). Reduced activity is observed in the frontal cortex. This explains why people who are 'in love' exhibit lack of judgement and irrational behaviour (14). Elsewhere, the parietal cortex and parts of the temporal lobe, linked to negative feelings and depression, were also shown to be deactivated (17).

## The Neural Substrates of Pain

Electrophysiological and haemodynamic studies on the human infant brain reveal that the newborn brain is capable of processing noxious and skin-breaking stimulation of the body surface, suggestive of the early establishment of a somatosensory pain network at birth (18, 19). Research on the mature pain network has demonstrated that there are two aspects to pain processing; either sensory-discriminative or cognitive-affective (20–22). The sensory-discriminative component involves the intensity, quality and location of pain (23) and is served by the thalamus and somatosensory cortices (SI and SII), while the cognitive-affective component processes psychological variables, such as attention, anxiety, fear and stress, in areas such as the anterior insula and anterior cingulate (21, 23, 24).

It was shown following a connectivity analysis that the brain regions that serve the two pain components are structurally connected to (25, 26) and hence influence each other (22). In turn, these pain-related areas are modulated by higher cortical areas, such as the prefrontal cortex, through the descending pain control system (2). While the neurotransmitter most commonly associated with descending pain modulation is opioid, others [such as dopamine (27) and cannabinoids (28)] also play a role. Interestingly, the activation of dopamine neurotransmission in different parts of the basal ganglia results in the components of pain being coded differently. Dorsal striatal (caudate and putamen) activation is associated with the sensory aspects of pain, and nucleus accumbens activation with the emotional response to it (29).

## The Pain of Love Lost

It has been demonstrated in studies that the figurative expression 'heartbreak' has a literal meaning too as the pain of heartbreak may actually have a biological basis. Stress cardiomyopathy ('broken heart syndrome' or 'takotsubo cardiomyopathy') is a condition that mimics a sudden heart attack and involves heart muscle failure due to sudden emotional stress, e.g., the death of a loved one (30). While heartbreak is distressing, it is not usually associated with injury.

The distinction between emotional and physical pain has been blurred following neuroimaging research as activation of the pain-

related brain regions has been demonstrated with both conditions (31). Similar areas of the brain were observed to be activated in a study when the participants felt either physical or emotional pain. The brains of 40 participants, who had broken up with their romantic partners six months prior to the study and who felt 'intensely rejected', were scanned while they viewed photographs of their friends and exes (32). A scan was also performed of their brains while painful thermal stimuli were applied to their forearms with the objective of comparing the neural similarities between physical and emotional pain. Feeling emotional pain was shown to activate the affective brain regions, such as the dorsal anterior cingulate cortex, as well as areas that code the somatosensory aspects of pain, i.e., the secondary somatosensory cortex (SII neurons) and thalamus.

It was demonstrated in another study that acetaminophen, a painkiller used to treat physical pain, was also effective in lessening emotional pain (33). The pain of heartbreak also seems to last longer than that of physical pain, with recollections of the hurt caused by a breakup with a loved one being more vivid than those of previously experienced physical pain, as shown in the study by Chen et al. (34).

## Love as a Modulator of Pain

While it is painful to lose a loved one, both emotionally and physically, being 'in love' invokes feelings of pleasure that have been shown to modulate pain. A behavioural study was performed on 25 women in long-term relationships of ≥ 6 months. A comparison of their pain response to thermal heat was assessed while they held hands with their partners and while viewing photographs of them (35). Ironically, while pain perception was reduced in both situations, viewing photographs of their partners produced greater analgesia than that achieved while holding their hands directly. The authors concluded that due to variability in the abilities of their partners to provide support, a symbolic representation, of the support in the form of a photograph, had greater efficacy in reducing pain.

To elicit the neural correlates of love-induced analgesia, an fMRI study was performed on undergraduates in the early stages of romantic love to assess their response to pain (36). The participants were asked to view photographs of their romantic partners while simultaneously having thermal heat applied to their skin. The task was interspersed with viewing photographs of a familiar acquaintance and another used to distract attention (the control), again while thermal heat was applied. Pain reduction achieved during the task to distract attention was found to be comparable with that accomplished when viewing images of their romantic partners. However, only love-induced analgesia was associated with activation of the brain areas that code reward, i.e. the caudate nucleus, nucleus accumbens, orbitofrontal cortex, amygdala and dorsolateral prefrontal cortex (dlPFC). These areas were not associated with analgesia resulting from distraction, suggesting that there is a link between analgesia and the positive emotion produced by viewing photographs of a loved one.

The effect of an attachment figure on safety signalling was assessed in another fMRI study. Women participants in long-term relationships were shown photographs of their partners while receiving painful stimuli (37). A reduction in the recorded pain score corresponded with a reduction in activity in the pain-related areas of the brain (dorsal anterior cingulate cortex and anterior insula) and the area associated with safety signalling [the ventromedial prefrontal cortex (vmPFC)]. In addition, greater vmPFC activity in response to images of their partners was associated with relationships of a longer duration and greater perceived partner support, further highlighting the role of the vmPFC in relation to the women's perceptions of their partners as a source of 'safety'. Interestingly, giving support to a partner in pain also activates the ventral striatum, the site of the nucleus accumbens within the reward system.

In a study on empathy for a loved partner, Cheng et al. (38) scanned the brains of male and female participants while showing them images of themselves, their romantic partners, and a stranger in pain. Viewing pictures of themselves and their romantic partners in pain activated areas known to relate to pain, i.e., the dorsal anterior cingulate cortex and anterior insula, more so than when they viewed pictures of a stranger in pain.

The above studies, however, only addressed the effect of romantic love on pain. Another study used laser-induced pain delivered while the subject was in the presence or absence of a 'loved-one' (39, 40) who was either a romantic partner, family member or best friend. The all-female participants who received pain

stimulation demonstrated varying responses to laser heat pain, with a resultant increase and decrease in their pain threshold when accompanied by a romantic partner, compared to when they were unaccompanied. A decreased pain threshold in the presence of a romantic partner was associated with the activation of the thalamus, parahippocampal gyrus and hippocampus, while an increased pain threshold when accompanied by a romantic partner was associated with activation of all parts of the cingulate cortex (Figure 1). The cingulate cortex plays an important role in processing anticipation (41) and expectation (42) in relation to pain, as well as positive emotions in the social context (43). Therefore, it is likely to be involved in processing expectations regarding romantic partners.

It was also found that the personality of the individual and the type of relationship with the partner who was present during the pain stimulation determined the directionality of the pain response—as either more or less painful. Participants who had extraversion type of

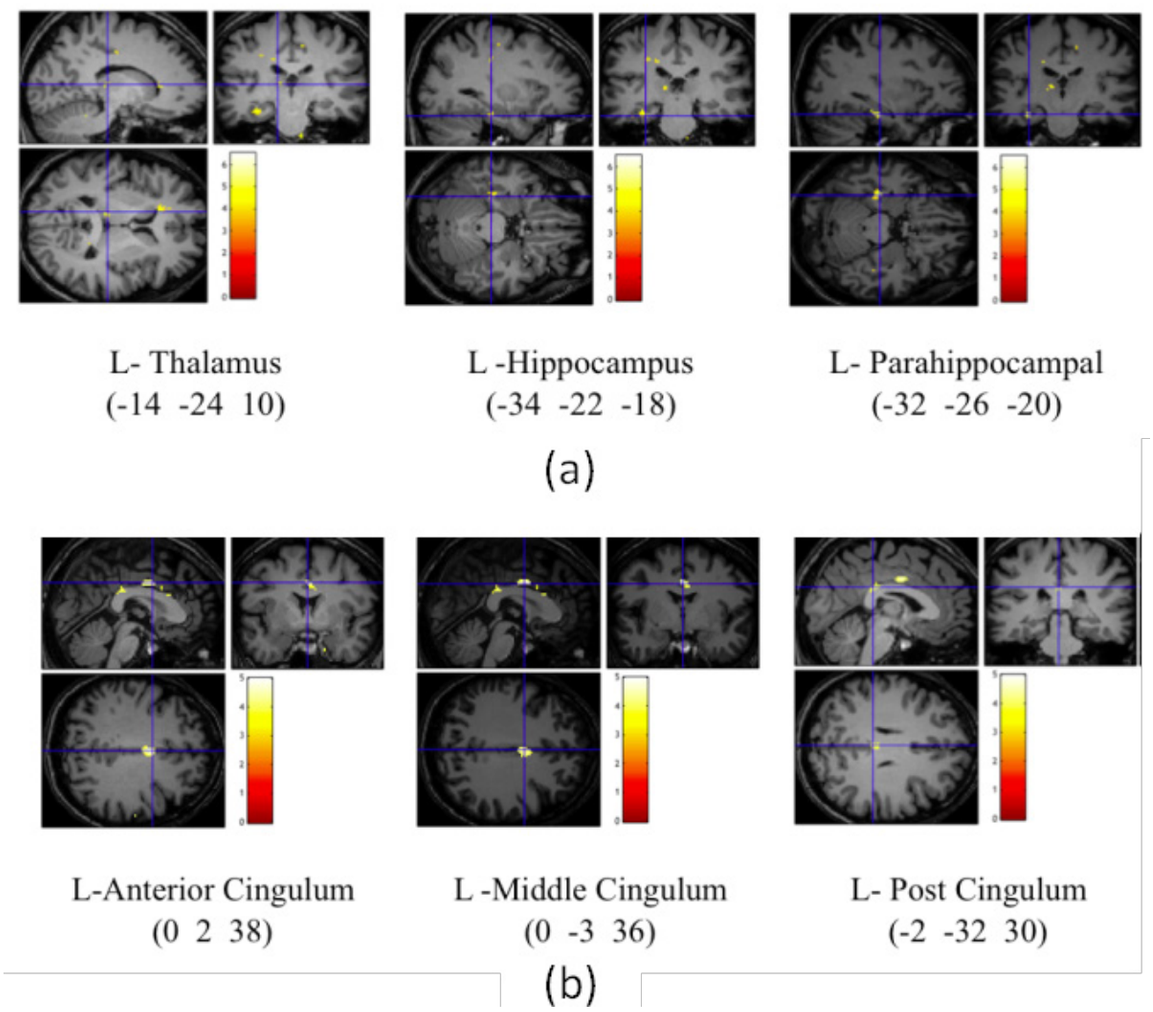


**Figure 1.** Brain activations in female participants associated with decreased pain threshold (a) and increased pain threshold (b) during laser pain stimulation while being accompanied by a loved one. The coordinates are in standard stereotaxic space of the Montreal Neurological Institute (MNI) template. Images are in neurological convention (left is left). The colour bar represents *t*-statistics of brain activations corrected with significance threshold of $P < 0.05$.

personality and accompanied by their romantic partners experienced a reduction in their pain threshold, whereas those who were escorted by their parents, siblings or best friends had an increase therein. These results highlight the influence of personality traits and the quality of relationships between individuals on emotion regulation and behavioural response to pain.

## Emotion Regulation

Emotion regulation (44) refers to the 'processes by which individuals influence which emotions they have, when they have them, and how they experience and express these emotions', i.e., the alteration of emotional processes for coping purposes. Emotions result from a person-situation transaction that attracts attention, has a valenced meaning and eventually give rise to a multisystem response (45). Emotion generation may be bottom-up, i.e., elicited by the presentation of a stimulus, or top-down, i.e., elicited by the activation of an appraisal that a situation is relevant (46). Emotion regulation begins with an emotionally relevant situation that commands attention and appraisal. These three processes (situation, attention and appraisal) are known as 'antecedents' and subsequently give rise to a multisystem response (47).

Effective emotion regulation involves skills relating to awareness appraisal, regulation and the adaptive use of emotions, not only of the self but also of others (48). Awareness appraisal of the self and others triggers response tendencies towards modulating emotions (49). The negative and positive emotions of the self and others are managed through emotion regulation. Emotion utilisation involves the use of moods to solve personal and interpersonal challenges. Successful emotion regulation reduces pain intensity (50) and negative effects. However, heightened awareness and the appraisal of pain can reduce, nullify the effect of or increase pain.

The most commonly implicated brain areas in emotion regulation include the orbitofrontal cortex (OFC), dlPFC, ventrolateral prefrontal cortex (vlPFC), dorsomedial prefrontal cortex and anterior cingulate cortex (ACC) (51). The ventromedial aspects of the prefrontal cortex (PFC) (the OFC, dorsomedial PFC and ACC) are generally associated with the control of emotional behavior, while the lateral aspects, i.e., the dlPFC and vlPFC, are involved in higher executive functioning (51). The use of emotion regulation in the control of pain has been widely demonstrated using strategies such as attentional manipulation and reappraisal (52–54). However, data on the modulation of pain in specific relation to love remain sparse.

## The Overlap of Love and Pain

The role of the opioid system in relieving social pain, and specifically separation and distress, has been highlighted in the extant literature (55). More recently, it was found in a study by Hsu et al. (56) that social acceptance increased social motivation, positively correlating with μ-opioid receptor activation in the nucleus accumbens, also a reward structure. This suggests that the opioid system plays a role in modulating feelings of love and rejection. However, this effect was absent in patients with major depressive disorder.

Neural similarity within the pain and love networks may explain the manifestation of social pain and the modulation of pain by love. Both the opioid and dopamine systems have been recognised as systems that have a major influence on pain (57, 58).

While pain and hedonism (Greek for 'pleasure') have long been considered to be opposites, a considerable overlap between the two in terms of brain areas that process pain and pleasure (59) was identified following recent advances in neuroimaging. Feelings of pleasure, which can be brought about by receiving a reward or being in love, activate reward areas in the brain. Neural activity in the striatum, comprising the caudate nucleus, putamen and nucleus accumbens, has consistently been shown to scale with anticipated rewards, whereas a regional limit exists between reward and motivation. This is because the response in the caudate nucleus and putamen increases with motivation, while activity in the nucleus accumbens increases with the anticipation of reward (60). These subcortical, dopamine-rich reward areas are also responsible for cravings and addiction (61).It is little wonder then that intense, passionate romantic love has been identified as a natural addiction, with similar manifestations to substance, non-substance and behavioral addiction, for example, euphoria, craving, tolerance, emotional and physical dependence, withdrawal and relapse (62). The dopamine brain reward centre is involved in mood and motivation (63) and includes the ventral tegmental area. Neurons in the ventral

tegmental area also project to the nucleus accumbens and prefrontal cortex (64). The OFC is another area that is notably associated with pleasure functioning (63).

The mesolimbic dopamine circuit modulates responsiveness to the opioids and antidepressants used in chronic pain treatment (64). In addition, aberrant functioning of the circuit has been linked to the development of chronic pain states (65, 66). An example is the disruption of the reward pathway by chronic pain in multiple sclerosis (67). Pain relief that is induced by treatment with pregabalin causes dopamine release in the nucleus accumbens of rats in the early phase of neuropathic pain (68). Elsewhere, dopamine release that was induced by sucrose solution intake (given as a reward) was found to be suppressed in rats with neuropathic pain, indicating that dopamine plays a role in the underlying mechanism of chronic pain (69).

A motivational role of dopamine in pain modulation, either to avoid or endure pain, was found following a recent review of animal and human studies by Taylor et al. (27). Depending on the circumstances, dopamine is posited to mediate the motivation to avoid or endure pain in exchange for a greater reward (57). This finding is in keeping with that in a study by Woo et al. (70) in which the mediation of the cognitive self-regulation of pain was demonstrated by the functional connectivity between the ventromedial PFC and nucleus accumbens. Taken together, the roles of dopamine and the reward structure may not be in pain processing per se, but rather in the evaluation and learning of the pain experience (22). Reward circuitry dysfunction was shown to predispose the development of acute pain to chronic pain in recent research (71).

The value of the applicability of an interaction between the 'love' and 'pain' networks is becoming apparent in therapeutics, as demonstrated by the 'love hormone', oxytocin, which, when administered exogenously, demonstrates the potential to modulate the pain experience (72).

## Conclusion

The interaction between love and pain is by no means straightforward. However, it has been demonstrated through recent advances that the interconnection of this relationship could be attributed to the way in which the brain is functionally connected, as well as to the neurotransmitters involved. The personality type of the individual, interindividual relationship structure and the ability to utilise emotion regulation in relation to the self and others contributes to interindividual variability in the response to love-related pain. This warrants further investigation.

## Acknowledgement

This work was supported by Universiti Sains Malaysia RUI grant 1001/PPSP/812130.

## Authors' Contributions

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Critical revision of the article for important intellectual content: AHA
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