Jennifer Schneider Malamud, 1006257471 WRI307: Science and Writing Prof. Guy Allen December 14, 2022

Article 1C [You Stress Me Out, and my Hypothalamus Loves It]

To survive and reproduce, individuals behave in a matter befitting the acquisition and retention of lust, attraction, and attachment. Lustful behaviour intends to consolidate a sexual union with a fellow adult member of the same species. Attraction means to focus our attention on a select partner to save mating time. Lastly, attachment behaviour consolidates an affiliative connection to complete parental duties. As a result, romantic love develops as a behavioural drive, or a motivation state, to pursue an intimate relationship with a select mating partner.

Across different species, the neurological tasks of forming an attachment encompass behaviours such as approaching a potential partner, learning their identity, and investing in them while rejecting any other potential matches. To consolidate intimacy, humans must first regard another as especial and unique, while focusing their attention on aggrandizing their traits and diminishing their faults.

In his metanalysis about the neuroendocrinology of romantic love, Dr. Krishna Sidrashi claims that during the first stage of a romantic attachment, lovers experience emotional dependence, empathy, willingness to sacrifice, obsessive thinking, sexual desire, possessiveness, and mate guarding. Sidrashi also says that "there is increased ecstasy when things go well, despair when they do not and separation anxiety when apart." Mental arousal is a common symptom of increased stress at the start of a romantic attachment.

Stress Response

Facing feelings of infatuation foster jitters, goosebumps, and palpitations. Falling in love is exhilarating and stressful, activating the *hypothalamo-pituitary adrenal axis*. The hypothalamo-pituitary adrenal axis regulates stress by releasing hormones. When forming an attachment, the hypothalamus will activate the pituitary gland and regulate emotional responses, such as tenderness, joy, and lust. As the brain structure controlling primordial bodily functions and emotional responses, the hypothalamus secretes the stress hormone cortisol and the alertness hormone norepinephrine, prompting physical reactions like trembling, sweating and increased palpitations.



Source: Simply Psychology (Carter, 2017) The hypothalamo-pituitary adrenal axis activates the brain's stress response and reward systems.

The pituitary gland, also known as the brain's master gland, senses the body's physiological needs and uses nerves to communicate to other parts of the brain. By making the adrenal gland bump up perceived feelings of anxiety, the pituitary gland will activate the body's stress response. By linking love with reward mechanisms, the attraction and sentiment hormones dopamine, serotonin, and norepinephrine will then exacerbate feelings of love. In the words of Sedrashi, "stress appears to be the trigger for a quest for pleasure, proximity, and closeness."

Though stress has negative connotations, in the neuroendocrinology of attachment and affection, it reflects the body's reaction to a wide range of positive and negative stimuli.

According to Mercado and Hibel, these stimuli can range from "normative events such as a passionate kiss between new lovers to adverse circumstances such as being chased by a predator." The interplay between the hypothalamus and the hippocampus enhances a positive stress response. As the part of the brain that regulates memory retrieval, the hippocampus interacts with the hypothalamo-pituitiary adrenal axis to connect rewarding, attachment-related emotional memories to the body's neuroendocrine stress response. While the hippocampus activates positive neural pathways, the hypothalamus wills the body's nerve cells and prompts hormonal secretion, in particular, of testosterone and estrogen.

Gonadal Hormones

Gonadal hormones interact with reproductive organs to increase attraction and sex drive. Testosterone supresses the hormone serotonin, decreasing aggression. Both testosterone and estrogen, the male and female sexual hormones, mediate lust and interact with the amygdala, the brain's emotional center. The gonadal hormones will also increase territorial guarding and arousal, by affecting vasopressin and oxytocin, respectively.

At the beginning of romantic attachments, men show increased activity in brain areas related to visual stimuli, while women activate regions associated with attention, memory, and emotion. The effects of gonadal hormones coupled with the hypothalamus-mediated stress response will increase trust, attraction, and feelings of security, leading to pair bonding, the evolutionary antecedent of romantic love.

Sedrashi says that "attraction is mediated by hormones of stress and reward including dopamine, norepinephrine, cortisol and the serotinergic system." Attraction hence reinforces feelings of reward to generate deeper attachments.

Rewards and Reinforcement

When attachment leads to feelings of reward, we call it love. Dopaminergic pathways and influxes of oxytocin –related to reward and trust, respectively– decrease negative emotions and reinforce motivation to maintain intimate romantic attachments. By decreasing emotional judgement and fear, while increasing motivation, our brain rewards and reinforces proximity to our object of affection. The hypothalamus connects to the brain's reward system to reinforce our stress response, prompting us to seek a romantic attachment, and once a monogamous pair bond is achieved, to protect our mate and maintain intimacy.

Sources

Carter, C.S. (2017). The Oxytocin–Vasopressin Pathway in the Context of Love and Fear. *National Library of Medicine*, *8*, 356. doi: 10.3389/fendo.2017.00356

Guy-Evans, O. (2021). *Hypothalamic-Pituitary-Adrenal Axis* [Photograph]. Simply Psychology.

https://www.simplypsychology.org/hypothalamic%E2%80%93pituitary%E2%80%93adrenal-axis.html

Insel, T. R., and Young, L. J. (2001). The Neurobiology of Attachment. *Nature*, *2*, 129-136. <u>https://www.nature.com/articles/35053579</u>

Koelsch, S. (2014). Brain correlates of music-evoked emotions. *Nature*, *15*, 170-180. <u>https://www.nature.com/articles/nrn3666</u>

Mercado, E., and Hibel, L.C. (2017). I love you from the bottom of my hypothalamus: The role of stress physiology in romantic pair bond formation and maintenance. *National Library of Medicine*, *11*(2). doi: 10.1111/spc3.12298

Seshadri, K. G. (2016). The Neuroendocrinology of Love. *National Library of Medicine*, 20(4), 558-563. doi: 10.4103/2230-8210.183479

Article 2B [Love as Conditioned Reward and Motivation]

The doctor enters her husband's warm colored office. He sits hunched over a computer, typing away. The doctor hears the constant thudding of the mouse as she nears her husband's desk. "Guess what?" she asks. He turns around, smiles at his wife's dropping eyelids, and answers "what?" The doctor grabs his hand and says, "I love you." He feels rewarded by the interaction and embraces his wife. "I love you, too."

The interaction is repeated constantly in the following years, always beginning with a muttered "guess what?" One day, the scene unfolds again: The doctor enters her husband's office. "Guess what?" she asks. Now, used to the interaction, her husband feels a pre-emptive sense of reward. Before she can say anything else, he gets up from his chair, embraces his wife, and answers, "I love you, too."

Amber Baillie published this incident as a blog post titled, "I unintentionally classically conditioned my husband." Goldstein, the original writer, had first published the story in a journal of cognitive psychology. According to Goldstein, the repeated pairing of specific stimuli prompted her husband to associate love and intimacy with the phrase "guess what?"

In more depth, the link between different stimuli in the couple's interactions supported feelings of reward, through the secretion of the neurotransmitter dopamine in the process of synapses.

Dopamine, Love and Reward

A synapse occurs when two neurons link to one another and exchange neurotransmitters. Neurotransmitters are chemical signals that transmit information to an immediate nerve cell, muscle cell, or gland. If we take communication theory as an example, neurons act as the sender, the synapses as the channel, the immediate cells as the recipient, and the neurotransmitters as the message.



Source: The Brain from Top to Bottom (McGill, n.d.). Dopamine neurotransmission occurs as a result of the synapses between a neuron and an adjunct cell.

Dopamine is a neurotransmitter that plays a role in feelings of pleasure, motivation, and reward. Neurons secrete dopamine in the processes of learning, remembrance, focus, arousal, and sleep. Thus, the continuous secretion of dopamine strengthens synapses between different stimuli, reinforcing positive emotions and memories. In other words, the constant secretion of dopamine made the doctor's husband create a mental association between the phrase "guess what?" and the word "love."

An experiment by Aron and colleagues set out to find the correlation between dopamineinduced rewards and feelings of romantic love. The researchers tested two hypotheses with the aid of functional MRI (fMRI), an imaging method that shows changes in the brain. The first hypothesis was that romantic love would activate brain regions involved in reward systems and dopamine secretion, such as the ventral tegmental area (VTA) and the nucleus accumbens. The second hypothesis was that romantic love would activate other reward systems like the anterior caudate nucleus, which are involved in goal setting and in detecting expectations for rewards.

Your Brain in Love

To test the brain regions activated in the reward processes, the researchers recruited ten women and seven men from New York State University, ages eighteen to twenty-six, who reported feeling intense love towards their partner. Before the fMRI session, participants completed an interview and two questionnaires about their specific feelings and their romantic relationship.

For the subsequent scanning session, each participant provided a photograph of their partner as positive stimulus, plus a "similar photograph of a familiar, emotionally neutral acquaintance of the same age and sex as the beloved," for a neutral stimulus. Then, the researchers projected the images. They asked participants to think about positive memories with their partners, and to think about neutral events that happened with their acquaintance, when observing the respective pictures. Participants chose these memories beforehand, at the initial interview.

As predicted, the fMRI depicted significant more activation in brain regions that are dopamine rich –or associated with motivation-reward systems– when participants looked at their loved one, versus when they looked at a neutral person. A similar experiment by Takahashi, depicted higher dopamine levels and physical excitement when researchers triggered feelings of attachment, reward, and pair bonding towards the participant's loved ones.



Source: MIT News (Trafton, 2020).

An fMRI of the brain shows higher activation of regions related to dopamine secretion, when participants looked at pictures of their beloved versus when they looked a pictures of acquintences.

Romantic Love as a Motivation State

In their experiment, Aron and colleagues concluded that "intense romantic love is associated with reward and goal representation regions, and that rather than being a specific emotion, romantic love is better characterized as a motivation or goal-oriented state." This reframing of love as a so-called motivation state can explain why people usually want to spend time with and to protect their loved one.

Berridge supports the idea of love as motivation, attributing incentive salience to reward stimuli. Incentive salience means the motivation for rewards, or attention-grabbing wants, as the result of previously learnt associations. In other words, dopamine neurotransmission is associated with this feeling of "wanting something." Incentive salience is the result of a connection –often experienced in classical conditioning– between a cue like your spouse asking "guess what?" and its reward, hearing them say "I love you."

In this sense, it is not far-fetched for Goldstein to claim that she unwittingly classically conditioned her husband. However, the reason why he responded, "I love you, too" when asked "guess what?" is not only because he learnt to associate the two stimuli. The other reason is that the cue of seeing his wife created an influx of dopamine. Then, the reward of hearing "I love you" by his beloved activated the husband's want to spend time with Goldstein, and motivated him to protect his relationship. And so, he responded, "I love you, too."

Sources

Baillie, N.B. (2014, December 9). I Unintentionally Classically Conditioned my Husband. *Penn State*. <u>https://sites.psu.edu/psych256fa14/2014/12/09/i-unintentionally-classically-conditioned-my-husband/</u>

Berridge, K.C. (2006). The Debate Over Dopamine's Role in Reward: The Case for Incentive Salience. *Psychopharmacology* 191, 391-431. https://link.springer.com/article/10.1007/s00213-006-0578-x Cleveland Clinic Medical Professional. (2022, March 14). Neurotransmitters. *Cleveland Clinic*. <u>https://my.clevelandclinic.org/health/articles/22513-</u> neurotransmitters#:~:text=What%20are%20neurotransmitters%3F,muscle%20cell%20or%20a% 20gland

McGill. (n.d.). *The Role of Dopamine* [Photograph]. The Brain from Top to Bottom. Retrieved from <u>https://thebrain.mcgill.ca/flash/i/i_03/i_03_m/i_03_m_que/i_03_m_que.html</u>

Takahashi et al. (2015). Imaging the Passionate Stage of Romantic Love by Dopamine Dynamics. *Frontiers in Human Neuroscience*. https://www.frontiersin.org/articles/10.3389/fnhum.2015.00191/full

Trafton, A. (2020). *How Dopamine Drives Brain Activity* [Photograph]. MIT News. Retrieved from https://news.mit.edu/2020/dopamine-brain-activity-mri-0401

Zhang et al. (2009). A Neural Computational Model of Incentive Salience. *PLOS Computational Biology*.

https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1000437

Article 3C [Oxytocin, Trust, and Investments]

Oxytocin, popularly known as the love hormone, is vastly released during labour, breast feeding, and during the time parents bond with their baby. Other than enabling a child-mother bond since the moment of birth, oxytocin plays a role in other behaviours such as social recognition, orgasm, and bonding. Bonding refers to the process of building trust to further establish social relationships, encourage mating with a monogamous partner, produce offspring, and perpetuate the species.

Trust and Oxytocin

Kosfeld and colleagues performed an experiment to examine the effects of oxytocin on building trust. The researchers hypothesized that oxytocin promoted pro-social behaviours like trust, which contributed to the success of social interactions. In their study, they showed that an intranasal administration of oxytocin could increase trust between share investors. To do so, they compared the behaviour of the group who received an oxytocin dose, versus that of a control group who received a placebo drug.

The groups interacted in a trust game with real monetary stakes. In each game, "two subjects interacting anonymously play either the role of an investor or a trustee." Each investor could choose to give money to a trustee. By transferring the money to the trustee, they had the chance to increase their overall profit. Still, investors carried the risk of the trustee choosing to violate their trust and not return part of their shares.

The researchers concluded that oxytocin causes increased trust in humans, who benefit from social interactions, not due to a readiness to take more risks, but to a willingness to "accept social risks arising through interpersonal interactions." This way, oxytocin, plays a role in people's capacity to form lasting attachments.

Oxytocin supports "physically intimate forms of sociality and nurture," activating neuroendocrine pathways that regulate emotional states. Moreover, oxytocin enhances the effects of dopamine, serotonin, sex steroids and cortisol, which control pleasure, mood, arousal, and stress, respectively. Oxytocin heightens feelings of trust and intimacy, even among strangers. As a result, researchers compared the effects of oxytocin to those of ecstasy, and perfumes containing oxytocin are branded as "love elixirs."



Source: Amazon News (No 9 Bask, 2022) The perfume company No 9 Bask sells oxytocin colognes, marketing them as a pheromone product supposed to acts a "love formula so intense and it's designed to attract & lure anyone."

Risk and Negatives

Oxytocin's potential is both exhilarating and frightening –not unlike ecstasy. Wudarczyk and colleagues researched oxytocin's potential as a relationship enhancer, lowering couple's emotional defenses, while promoting empathy and generosity. However, oxytocin can have some unintended effects, increasing in-group favoritism and outside envy.

Patients with borderline personality disorder might become suspicious and uncooperative.

Patients with anxious attachment styles selectively decreased their own agency. Oxytocin also

alters self-reported perceptions, which users depicting themselves as more extroverted than before. In the ingestion of oxytocin, the context and person *matter*.

Early life experiences influence people's reaction to oxytocin, with people who experienced childhood trauma having decreased levels of the hormone. Ironically, people's oxytocin levels rise when exposed to fearful situations, as a damp to the perceived stress.

Returning to Kosfer and colleagues' investor experiment, oxytocin does *not* change a person's beliefs, such as the likelihood of a good outcome. While users showed more trust in others, they did not change their ideas about others perceived trustworthiness or changed an interaction's level of reciprocity. In other words, while investors became more willing to transfer money, trustees did not necessarily change their behaviour to encourage this trust based on oxytocin intakes.

Future Implications

On a positive note, while a single dose of oxytocin for people with mental health issues might bear negative effects, some studies showed that the long-term administration of oxytocin has potential as a therapeutic treatment. Patients who had ingested oxytocin over long periods of time experienced "attenuated subjective and physiological stress reactivity and improved emotion recognition." Oxytocin also helps regulate chronic pain, by acting as an analgesic.

At the moment, some researchers such as Wudarczyk and colleagues go even further, by arguing *for* the implementation of oxytocin in relationship therapies. In their own words, "we have reviewed a range of preliminary studies that show that the exogenous administration of oxytocin may confer a number of pro-social outcomes, and we have argued that these could serve to enhance at least some romantic relationships."

While a future in which a neurotransmitter with the potential of ecstasy mediates our romantic relationships might not sound appealing, Wudarczyk and colleagues argue that the effects of not forming a pair bonds –social isolation and illness– should frighten us more. If we can be sure about *anything* regarding the so-called love-hormone is that we need more research before moving forward with any kind of therapy. Still, as the investor-trustee experiment shows, when it comes to oxytocin, it is all a matter of *trust*.

Sources

Carter, C. S. (2022). Oxytocin and love: Myths, metaphors and mysteries. *Comprehensive Psychoneuroendocrinology 9*. https://www.sciencedirect.com/science/article/pii/S2666497621000813

Cormier, Z. (2013). Gene switches make prairie voles fall in love. *Nature*. <u>https://www.nature.com/articles/nature.2013.13112</u>

Kosfeld et al. (2005). Oxytocin increases trust in humans. *Nature 435*, 673-676. <u>https://www.nature.com/articles/nature03701</u>

No 9. Bask (2022). *No 9 Bask - 99 Percent Pure Oxytocin Cologne Spray (1.05 oz.) - Lavender Label* [Photograph]. Amazon. <u>https://www.amazon.ca/Bask-Percent-Oxytocin-Cologne-Lavender/dp/B07TW8NLXD</u>

Olff et al. (2013). The role of oxytocin in social bonding, stress regulation and mental health: An update on the moderating effects of context and interindividual differences.

Psychoneuroendocrinology 38(9), 1883-1894. https://www.sciencedirect.com/science/article/pii/S0306453013002369

Shen, H. (2015). Neuroscience: The hard science of oxytocin. *Nature 522*, 410-412. <u>https://www.nature.com/articles/522410a</u>

Wudarczyk et al. (2013). Could intranasal oxytocin be used to enhance relationships?

Research imperatives, clinical policy, and ethical considerations. *Curr Opin Psychiatry* 26(5), 474-484.

https://europepmc.org/backend/ptpmcrender.fcgi?accid=PMC3935449&blobtype=pdf

Article 4B [Love, Heartbreak and Pain]

"We need to talk." Blood pulses inside your head. "It's been a good run, but I don't think things are working out between us, anymore." While mourning the miserable break up, you sit in your room, download a dating app, and your intestines tingle with butterflies as you swipe right.

When love leads to heartbreak, then why do we open ourselves to a new relationship as a cure for our heartache? Does love increase or reduce pain?

In the occasions when love does not lead to a lifelong commitment, it often leads to pain. 93% of students in an American college reported feeling spurned by someone they passionately loved. Researchers have even linked the sensations of heartbreak to the symptoms of withdrawal experienced by drug addicts. Conversely, feelings of enamorament have led people to report decreased symptoms of pain and depression. Then, what explains our proclivity towards infatuation? Might the poison also act as the remedy?

Why don't you gut punch me, instead?

While romantics often associate love with emotional pain, the pain of losing a loved one can show up physically. A behavioural imaging study showed that physical and emotional pain activate the same neurological pathways.

In a 2012 study from the University of Los Angeles department of psychology, Dr. Naomi Eisenberger scanned the brains of 40 participants who reported feeling 'intensely rejected' after breaking up with their romantic partners. Eisenberger conducted the scan under two different conditions: First, she scanned the participants while they observed photographs of their friends and exes. Then, Eisenberger repeated the scan while applying painful thermal stimuli to the participants forearms.

After observing the participants react to both physical and emotional stimuli, Eisenberger concluded that physical and emotional pain activated three different brain regions: The *dorsal anterior cingulate cortex* which mediates conflict with senses and sadness, the *thalamus* which processes behavioural and cognitive sensory input, and the *secondary somatosensory cortex* which regulates sensory recognition and memory.



Source: Bernard J Baars Blog (Bernard J Baars, 2019) Physical and emotional pain activate the dorsal anterior cingulate cortex, the thalamus, and the secondary somatosensory cortex.

If physical and emotional pain activates the same affective and somatosensory brain regions, then that explains why love can act as pain regulator. In a follow up study, Eisenberger decided to further gauge the correlation between these different types of pain, by exploring if Tylenol –a common analgesic drug– could also reduce social pain.

An experimental group took daily doses of Tylenol, while a control group took a placebo drug for three consecutive weeks. Both groups self-reported hurt feelings each evening. Eisenberger also conducted an fMRI imaging scan. In this experiment, Eisenberger concluded that Tylenol reduces hurt feelings, considering that "Tylenol, a physical painkiller, appears to double as a social painkiller."

If Tylenol can reduce symptoms of emotional pain, then an amorous split may develop symptoms of physical pain. Couples feel chest aches when experiencing heartbreak because of a rupture of the neurological pathways that connected thoughts of their partners. Eisenberger supports this idea, arguing that people experiencing a forced separation from their beloved can endure symptoms of withdrawal similar to those undergone by drug addicts, since the chemicals secreted during the formation of romantic attachments, such as oxytocin and dopamine, have addictive and exhilarating properties.

According to Fisher, Xu, and Brown, "like many addictions, romantic rejection can also jeopardize one's health, because abandonment rage stresses the heart, raises blood pressure and suppresses the immune system." The link between depression, heart attacks or strokes, abandonment rage, and hypertension gives biological foundation to the physical pain of heartbreak. Stress cardiomyopathy, also known as the broken heart disease, involves a sudden heart muscle failure due to a sudden emotional stress.



Source: Cleveland Clinic (Cleveland Clinic, n.d.) The broken heart disease, or stress cardiomyopathy, involves forceful contractions and sudden heart failure as a result of emotional stress.

Still, there is some truth to the adage that a new devil helps us forget an old flame. Love can act as a modulator for pain since emotional regulation can lead to a perceived reduction of pain intensity. In the words of Hsu and colleagues, social acceptance increases social motivation and reward, as "dopamine-rich reward areas are also responsible for cravings and addiction."

This might explain why people tend to seek validation from a new romantic prospect after their brain severs a dopamine pathway connected to a past romantic attachment.

Kiss or slap me, but please inject me with dopamine

When your psychologist recommended love as a cure for heartbreak, they probably referred to self-validation rather than asking an external source to confirm your self-perceived attractiveness. However, love *can* act as a propeller for emotional regulation and as a powerful coping mechanism.

Tamam and Ahmad explain that emotional regulation involves an emotional situation that attracts attention and appraisal. This situation arouses a multisystem response involving moods and a reassessment of the self and others. While emotional regulation diminishes pain responses, "heightened awareness and the appraisal of pain can reduce, nullify the effect of or increase pain."

An experiment by Master and colleagues measured the pain perception of 25 women in long term relationships. The researchers observed their brain activity in relation to thermal stimuli, showing that either the physical presence of their partners, or their symbolic presence in the form of photographs, acted as love-induced analgesics.

More than that, these stimuli activated reward brain regions, such as the *nucleus accumbens*, which mediates motivation, the *caudate nucleus* which regulates reward and pair bonding, and the *prefrontal cortex* which modulates social behaviour. These areas are all responsible for dopamine secretion, meditating the neurological pathways of pleasure and reward.



Source: Wikipedia The nucleus accumbes, the caudate nucleus and the prefrontal cortex regulate dopamine secretion.

More impressive still, the secretion of dopamine can regulate chronic pain. Dopamine acts as one type of *monoaminergic pathway*. Monoaminergic pathways refer to the routes that the neurotransmitters –chemicals involved in neural communication– use to connect when regulating mood processes. In patients with chronic conditions, "activating different types of receptors, the descending dopaminergic pathways can exert either facilitatory or inhibitory pain-modulating effects." As many patients with chronic conditions can tell you, emotional pain manifests physically and vice versa.

Love can cause pain. Love can cure pain.

Sources

Baars, B. J. (2019). *The Great "Cortico-thalamic" System: Bidirectional signaling in cortex.* [Photograph]. Bernard J. Baars Blog. <u>https://bernardbaars.com/2019/01/06/the-great-cortico-thalamic-system/</u>

Cleveland Clinic. (n.d.). *Takotsubo Cardiomyopathy*. [Photograph]. Cleveland Clinic. <u>https://my.clevelandclinic.org/health/diseases/22022-takotsubo-cardiomyopathy#management-and-treatment</u>

Eisenberger, N. I. (2012). Broken Hearts and Broken Bones: A Neural Perspective on the Similarities Between Social and Physical Pain. *Association for Psychological for Psychological Science 21*(1). doi: <u>https://doi.org/10.1177/0963721411429455</u>

Fisher et al. (2016). Intense, Passionate, Romantic Love: A Natural Addiction? How the Fields That Investigate Romance and Substance Abuse Can Inform Each Other. *Frontiers in Pscyhology*. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4861725/

- Hsu et al. (2015). It still hurts: altered endogenous opioid activity in the brain during social rejection and acceptance in major depressive disorder. *Molecular Psychiatry 20*, 193-200. https://www.nature.com/articles/mp2014185
- Master et al. (2009). A Picture's Worth: Partner Photographs Reduce Experimentally Induced Pain. Association for Psychological for Psychological Science 20(11). doi: <u>https://doi.org/10.1111/j.1467-9280.2009.02444.x</u>
- Nameroff, C.B. & Goldschmidt-Clermont, P.J. (2012). Heartache and heartbreak—the link between depression and cardiovascular disease. *Nature Reviews Cardiology 9*, 526-539. <u>https://www.nature.com/articles/nrcardio.2012.91</u>
- Tamam, S. & Ahmad, A. H. (2017). Love as a Modulator of Pain. *Malaysian Journal of Medical Sciences 24*(3), 5-14. <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5545613/#!po=86.8421</u>

Wikipedia. (n.d.). *Basal Ganglia*. [Photograph]. Wikipedia the Free Encyclopedia. https://en.wikipedia.org/wiki/Basal_ganglia

Article 5B [Romantic Love as a Drug]

Researchers equate the early stages of romantic love to those of drug addiction. In a 2016 meta-analysis supported by the Natural Science Foundation of China, Zou and colleagues set out to find how the parallels between the effects of drugs and early-stage romantic love can inspire a new treatment for addiction.

For an addiction such as love or drugs to develop, addicts must experiment two levels of *neuroplasticity*. Neuroplasticity refers to the brain's ability to adapt its structure and functioning in response to an experience. For instance, to a drug or a romantic partner.

Addicts initial contact with the stimulant is deliberate and voluntary. Say, a new heroin injection, or a dopamine-infused first kiss with a romantic partner. This deliberate contact is called *regulated relapse*. Each time the user relapses, their neural functioning changes, even when they are going through periods of abstinence. Addiction solidifies. The pleasurable chemicals released during drug consumption and romantic attachment turn regulating relapses from a *want* to a *need*.

On the second stage of neuroplasticity, consumption becomes compulsive, and the brain composition of addict's changes permanently in order to accommodate the new chemicals into its day-to-day operations. Just like drug addicts, people undergoing the early stages of romantic love experience *salience, craving, euphoria and intoxication,* and *tolerance*.

According to Fisher, romantic love mimics addictive behaviour in drug users because addicts, "focus on their beloved (salience); they yearn for the beloved (craving); they feel a "rush" of exhilaration when seeing or thinking about their beloved (euphoria/intoxication). As their relationship builds the lover seeks to interact with the beloved more (tolerance)." If the couple breaks up, each partner will go through symptoms similar to those of drug withdrawal, such as lethargy, anxiety, and insomnia.

Romantic love similarly encompasses two phases: In the initial phase, lovers exhibit excitation and stress, because a part of the brain called the hypothalamus will release the stress hormone cortisol in conjunction with the attachment hormone oxytocin and the reward hormone dopamine, inducing physical reactions like heart palpitations, sweating and trembling. After lovers form a monogamous, intimate attachment –biologically referred to as a pair bond– the relationship turn calm, safe, and balanced.

That is where romantic love differs from drug addiction: The early stages of both romantic love and substance consumption show signs of behavioural addiction. However, as drug use and romantic attachments stabilize, drug addiction magnifies while the addictive characteristics of love disappear to leave a feeling of calm and contentment.

Romantic Love as a Balm for Drug Addiction

Romantic love as a reward can act as a form of therapy for drug addiction. When quitting a form of addictive substance or behaviour, researchers recommend replacing cravings with rewarding behaviours, such as sport activities, new hobbies, or social bonding.

To gauge if new romantic attachments could act a balm for drug addiction, Xu and colleagues performed an fMRI imaging overnight scan over eighteen Chinese nicotine-deprived smokers, who had just fallen madly in love. The men and women of the experiment observed side-to-side pictures of their addiction like a cigarette or their beloved, versus a control picture of a pencil or a stranger. The results showed higher levels of brain activation when participants looked at pictures of their beloved than when they looked at pictures of the cigarettes.

Fisher and colleagues agree, saying that "romantic love could be considered a powerful and primordial natural addiction because it can, under some circumstances, modify brain activations associated with a more contemporary addiction, nicotine." The similarities between the early stages of romantic love and drug addiction can give rise to new treatments against substance abuse.

Potential Treatments for Drug Addiction

External oxytocin administration can improve social cognition in people with addiction, inhibiting drug cravings and reducing the probability of relapse. In an experiment performed in rats, Zou and colleagues observed that exogenous administration of oxytocin in cocaine-tolerant rats reduced the effects of the drug and increased activity in the amygdala, the brain area responsible for emotion and reward responses. Zou and colleagues further explain that oxytocin can "attenuate the development of tolerance for drugs of abuse, as well as mitigate withdrawal symptoms and minimize reinstatement of drug use."



Source: Europe PMC (Fineberg & Ross, 2017) The hypothalamus secretes oxytocin which, in turn, regulates various aspects of social functioning.

The Amygdala

The amygdala affects motivation. Researchers often describe love as a motivation state.

The amygdala modulates behaviour based on negative stimuli such as drugs and positive stimuli such as a partner. As the brain's reward center, the amygdala interacts with stress hormones like cortisol and pleasurable hormones like dopamine to modulate love and addiction.

The amygdala influences emotion, memory, attention, and perception. The release of oxytocin in the amygdala outweighs the impact of negative stimuli like drugs. Long term love and substance abuse have oppositive effects: While drugs cause irritability or emotional outbursts, once the initial stress of romantic love subsides, long term romance fosters better mental health, decreases stress, relieves pain and induces contentment. In the words of Sufi poet Rumi, "lovers are patient and know that the moon needs time to become full."

Sources

Baxter, M.G., & Murray, E. A. (2002). The amygdala and reward. *Nature 3*, 563-573. <u>https://www.nature.com/articles/nrn875</u>

Fineberg, S. K., & Ross, D.A. (2017). *Oxytocin and the social brain*. [Photograph]. Europe PMC. <u>https://europepmc.org/article/pmc/5374331</u>

Fisher et al. (2016). Intense, Passionate, Romantic Love: A Natural Addiction? How the Fields That Investigate Romance and Substance Abuse Can Inform Each Other. *Frontiers in Psychology* 7(687). <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4861725/#B118</u>

Zou, Z., Song, H., Zhang, Y., & Zhang, X. (2016). Romantic Love vs. Drug Addiction May Inspire a New Treatment for Addiction. *Frontiers in Psychology*. doi: <u>https://doi.org/10.3389/fpsyg.2016.01436</u>

Article 6C [The Prairie Vole's Model of Monogamous Pair Bonding]

Fewer than 5% of mammalian species have a monogamous social structure. Prairie voles mate for life. As affiliative social animals, prairie voles seek to foster emotional bonds with a prospective partner. After mating, prairie voles show both less interest in strangers and aggressive behaviour towards newcomers.

Mated prairie voles scurry around picking twigs to build a nest where to guard their children. The furry brown couple hug their offspring. They now share a nest, equal parenting duties, and will stay together for the rest of their lives, which will last the next two to three years. From the moment the prairie voles mated, their genetic makeup changed. Now, the couple has pair bonded.



Source: NPR (NPR Staff, 2014). Prairie voles form monogamous pair bonds and take and egalitarian approach to raising their children.

Pair bonding occurs between members of the same species when two sexually matured adults establish enduring preference. Involving what doctors Yong, Gobrogge, Liu, and Wang call "selective contact, affiliation, and copulation with the partner over a stranger (partner preference)," pair bonded couples guard their mates and help their offspring grow.

But, what differentiates prairie voles from non-monogamous mammals? A group of scientists from the Department of Psychiatry and Behavioral Sciences of Atlanta Georgia set out to answer this question.

Methodology and Testing

The researchers compared the behaviour and brain neurochemistry of prairie voles to that of meadow voles. They chose sexually naïve voles aged two to six months that had grown in laboratories. The scientists performed partner preference tests after the voles cohabited with a female for 24 hours. They put the male in the centre of a three-chambered box, with the female they cohabited with and a female stranger on each of the adjacent chambers. The male vole could freely move between the chambers, and scientists recorded the time spent in each cage and huddling with each female. The researchers performed the experiment twice: After the initial 24 hours and after another two weeks.



Source: Creative Biolab Therapeutics (Creative Biolab, 2014).

The three chambered box allows rodents to move freely, so researchers can gauge their behaviour in forming selective attachment bonds.

The results showed that prairie voles spent significantly more time in contact with their partner than with a stranger. In contrast, meadow voles showed no partner preferences. More than that, prairie voles behave in an affiliative way and spent a lot of time huddling, while meadow voles prefer solitude and spent little to no time huddling with each female.



Source: Nature (Lim et al., 2004)

Meadow voles prefer solitary behaviour and show less levels of vasopressin in their brains, while prairie voles show affiliate behaviour and show higher levels of vasopressin.

Photos of the voles brains showed higher levels of vasopressin in the brains of prairie voles than in those of meadow voles. While both dopamine and vasopressin regulate selective affiliation in adult male species, the photographs reflected no alterations in the dopamine levels. Prairie and meadow voles share 99% of genes, yet the difference in the shift of vasopressin within a part of the brain called the ventral palladium changed the behaviour of prairie voles towards the formation of monogamous pair bonds. Two of the researchers, Wang and Young, decided to do a follow up study about the neurobiology of pair bonding, and the significance of vasopressin.

The Neurobiology of Pair Bonding

Neurotransmitters communicate information between neurons. Dopamine modulates parental bonding, empathy and social recognition, while vasopressin prompts aggression, scent marking and courtship. Dopamine accelerates pair bonding in female voles while vasopressin accelerates pair bonding in male voles. In particular, vasopressin promotes selective social bonding and selective aggression.

After mating, male and female prairie voles get a dose of vasopressin, which makes them want to spend more time with their mate and become aggressive towards strangers. In other words, "as vasopressin increases following mating, the male not only forms a selective preference for the female but also begins to guard access to his mate." The balance between these vasopressin-mediated, affectionate and protective types of behaviour in prairie voles *prompt* monogamous pair bonding. Dopamine helps reinforce the effects of vasopressin by rewarding these behaviours with feelings of pleasure.

What Humans can Learn from Prairie Voles

Pair bonding in voles evolved through evolutionary practices. Mama and papa voles adapted monogamous behaviours to effectively raise their young. The same behaviours that ensure the survival of their offspring facilitate the formation of a monogamous pair bond.

Just as with prairie voles, pair bonding has cross-cultural and evolutionary consequences for humans like us. Young and Wang, this time in partnership with Gobbroge and Liu, analyzed what humans can extrapolate from the love between rodents. They explain that high levels of intimacy decrease negative moods, while increasing immune function and cardiovascular health. Married couples live longer across demographic groups. The children of paired couples experience psychological wellbeing and positive cognitive developments due to bi-parental duties, and children with bonded parents experience lower mortality rates in impoverished communities.

The similarities of the behaviour between prairie voles and humans when mating can greatly aid the neural study of human relationships. The researchers explain it best: "Although study of the bonds formed between prairie vole pairs cannot possibly allow us to fully

understand the intricacies of human relationships, they can certainly offer insights into the basic

neural mechanisms underlying adult attraction and attachment."

Sources

Creative Biolabs. (2022). *Three Chamber Social Test* [Photograph]. Creative Biolab Therapy. https://www.creative-biolabs.com/drug-discovery/therapeutics/three-chamber-social-test.htm

Lim, M.M., Wang, Z., Olazabal, D. E., Ren, X., Terwilliger., Young, L.J. (2004). Enhanced partner preference in a promiscuous species by manipulating the expression of a single gene. *Nature 429*, 754-757. <u>https://www.nature.com/articles/nature02539#citeas</u>

NPR Staff. (2014, February 9). *Learning about love from prairie vole bonding* [Photograph]. NPR. https://www.npr.org/2014/02/09/273811514/learning-about-love-from-the-lifelong-bond-of-the-prairie-vole

Young, K.A., Gobrogge, K.L., Liu, Y., & Wang, Z. (2011). The neurobiology of pair bonding: Insights from a socially monogamous rodent. *Frontiers in Neuroendocrinology 32*(1), 53-69. <u>https://www.sciencedirect.com/science/article/pii/S0091302210000555</u>

Young, L. J., & Wang, Z. (2004). The neurobiology of pair bonding. *Nature Neuroscience 7*, 1048-1054. <u>https://www.nature.com/articles/nn1327#citeas</u>

Article 7C [Emotional Memory and Romantic Pair Bonds]

"Love is so short, forgetting is so long," Pablo Neruda.

The animals mate. Their partner's odor whizzes through their nose into the brain's olfactory nucleus, where neurons filled with the attachment hormone oxytocin rush into the hippocampus to form an emotional memory. Inside the hippocampus, the brain structure that presides over memory and learning, engrams develop to create the social memory. As the neurons representative of memory traces and the physical changes involving remembrance, engrams then interact with the pleasurable hormone dopamine to convert the retrieval of the memory into a rewarding experience.

The interplay between oxytocin, the hippocampus, engrams and dopamine in memory creation and retrieval convert reminiscing into an act of social cognition. Social cognition refers to the way humans process and react to external sensations and social stimuli. It involves attention, perception, action, planning and memory. In the neurobiology of affection and remembrance, social cognition informs how we recall and bond with our loved ones.

Memories of Pair Bonding

"Social cognition is facilitated by oxytocin receptors in the hippocampus, a brain region that changes dynamically with pregnancy, parturition, and parenting experience," said a group of researchers from the University of California in a recent 2020 study about affiliation in titi monkeys. Another 2019 study by the scientists of Kanazawa University in Japan, researched how the movement of oxytocin in the brain facilitates maternal bonding in mice. The investigations draw similar conclusions –that oxytocin rushes in the hippocampus precede emotional memories, unleash feelings of rewards, and induce pair bonds.

Most explorations of pair bonding have involved monogamous rodents known as prairie voles. One such 2018 experiment involving Atlanta's Emory University researchers Hasse Wallum and Larry J. Young describes pair bonding as the "evolutionary antecedent of romantic love." According to doctors Wallum and Young, pair bonding refers to a monogamous intimate relationship between two adults of the same species, that mate and share both parental duties and territory. In humans, love and romantic attachments result from mating and pair bonding.

As a subset of social cognition that facilitates pair bonding, memories of our loved ones occur from a heady potion of oxytocin and dopamine in the hippocampus. While oxytocin modulates parental nurturing, facial recognition, empathetic behaviour and social bonding, dopamine regulates reward perception, reinforcement learning and addiction.

The neural pathways that translate sensory input into romance, whilst allowing us to reflect on past interactions with our partners and on a future together, catalyze in pair bonding. That is, social cognition catalyzes romantic love.

Love in the Hippocampus

Memory enables relationships. As one of the brain regions regulating mood and memory, lesions in the back of the hippocampus impair cognition and memory, while lesions in the front of the hippocampus alter emotional behaviour, social interactions, and stress resilience. We cannot form an attachment without remembering the other person. Without reflecting on our relationships, we cannot develop empathy. According to Rubin and colleagues, "the ability to form and maintain social relationships may also involve contributions from hippocampal representations that support the ability to imagine and reflect upon experiences with other people." The researchers measured empathy through a series of questionaries related to perspective-taking, emotion contagion, emotional responsiveness, and empathetic concern. Patients with hippocampal amnesia exhibited less empathetic responses and difficulty when incorporating emotional memories into prosocial behaviours.

When processing emotional memories, the hippocampus interacts with the amygdala –the brain region that inputs and interprets emotion. While the hippocampus stores memories and enables synapses between neurons, the amygdala gives meaning to emotional cues, allowing for the formation of social engrams. When recovering the memory of our loved ones, the engrams cause the synapses to exchange dopamine and oxytocin, turning the retrieval of the memory into a rewarding experience, offering empathetic responses, and strengthening social bonds.



Source: The Scientist (Catherine Offord, 2020).

The hippocampus interacts with the amygdala to encode and decode emotional memories.

Emotional Memories

Emotion heightens memory. Sharon, Delgado and Phelps say that we remember affecting events in vivid detail, like a camera's flashbulb. Due to their personal significance, flashbulb memories involve the recollection of places, activities, and people during an enduring and affecting experience such as falling in love. In people suffering from memory loss, synapses break yet the emotion remains. Even when they cannot remember the intricacies of the event, the experience leaves "a scar upon the cerebral tissues." There is truth to the old adage, "people will not remember what you said, but they will remember how you made them feel."

Engrams encode emotional stimuli into long term memory. Emotional synapses leave a durable memory scar. Love is hard to forget.

Sources

- Anand, K. S., & Dhikav, V. (2012). Hippocampus in health and disease: An overview. Annals of Indian Academy of Neurology, 15(4). <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3548359/</u>
- Baxter et al. (2020). Oxytocin receptor binding in the titi monkey hippocampal formation is associated with parental status and partner affiliation. *Scientific Reports*, 10(17301). https://www.nature.com/articles/s41598-020-74243-1
- Clark, R.E. (2022). Classical Conditioning. *Encyclopedia of the Human Brain*, 813-827. doi: <u>https://doi.org/10.1016/B0-12-227210-2/00098-4</u>
- Frith, C. D. (2008). Social Cognition. *The Royal Society Publishing*, 363(1499). doi: https://doi.org/10.1098/rstb.2008.0005
- Kennedy, M. B. (2016). Synaptic Signaling in Learning and Memory. *Cold Spring Harbor Perspectives in Biology 8*(2). <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4743082/#:~:text=Memories%20are%20</u> <u>stored%20initially%20in,that%20stores%20a%20new%20memory</u>
- Lee et al. (2015). Oxytocin Protects Hippocampal Memory and Plasticity from Uncontrollable Stress. *Nature* 5(18540). https://www.nature.com/articles/srep18540
- Mercado, E., and Hibel, L.C. (2017). I love you from the bottom of my hypothalamus: The role of stress physiology in romantic pair bond formation and maintenance. *National Library of Medicine*, *11*(2). doi: 10.1111/spc3.12298

- Offord, C. (2020, July 13). *Infographic: What Social Isolation Can Mean for the Brain*. [Photograph]. The Scientist. <u>https://www.the-scientist.com/infographics/infographic-what-social-isolation-can-mean-for-the-brain-67706</u>
- Rubin, R. D., Watson, P. D., Duff, M. C., & Cohen, N. J. (2014). The role of the hippocampus in flexible cognition and social behavior. *Frontiers in Human Neuroscience 30*. doi: https://doi.org/10.3389/fnhum.2014.00742
- Sharot, T., Delgado, M. R., & Phelps, E. A. (2004). How emotion enhances the feeling of remembering. *Nature* 7, 1376-1380.
- Tottenham, N., & Sheridan, M. A. (2009). A Review of Adversity, The Amygdala and the Hippocampus: A Consideration of Developmental Timing. *Frontiers in Human Neuroscience 3*(68). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2813726/
- Walum, H., & Young, L. J. (2018). The neural mechanisms and circuitry of the pair bond. *Nature 19*, 643-654. <u>https://www.nature.com/articles/s41583-018-0072-6</u>
- Yamamoto et al. (2019). Vascular RAGE transports oxytocin into the brain to elicit its maternal bonding behaviour in mice. *Nature* 2(76). <u>https://www.nature.com/articles/s42003-019-0325-6</u>