Troubled love: The downside of love and possible ways to fix it

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Abstract

Love is an interesting topic, often romanticized by literature and movies, that can bring feelings of joy but also leads to problems. How is love, from all the euphoric feelings, the breathtaking experiences to sweating hands translated to neurobiology? How comes that people have the tendency to be unfaithful to their partners? And is there a specific type that is more prone to cheating than others? Moreover, how is it possible that some are unable to experience that love-bond that others talk about, despite them liking a person very much? Possibly, it would be desirable if you could manipulate love in some kind of way. Is it possible to manipulate love, and if yes, is it something that we as humans should want to influence our lives?

Biologically seen, love can probably best be described as a series of behaviors that lead to the formation of a long-term bond between two partners. Most likely, this is an evolutionary mechanism to promote reproduction, survival and support in species where bi-parenting is beneficial involving different neurotransmitters and hormones such as testosterone, estrogen, dopamine, serotonin, oxytocin and vasopressin. Overall, some of the highest risk-factors for why people involved in infidelity were low satisfaction in the relationship and low commitment to the relationship. When approached more biological, cheating individuals often show avoidant attachment, which is associated with mental disorders that involve deviant signaling in dopamine pathways. More grounded is the theory of Sue Carter, that claims monogamy does not include sexual exclusivity. That is, in most non-human animals that show monogamous behavior, it is rare to observe total sexual exclusivity. There are signs that levels of some biological agents, for example testosterone in men, can be a predictor of infidelity. Although not a lot of literature is known about neurobiology on why victims of an abusive relationship stay with their spouses, when considering the neurobiology of love it is likely that the dopamine reward-system and the attachment-system keeps the victims bound to their abusive spouse. There are no studies yet that describe a specific neurobiological profile for all people that claim to be unable to feel love. When taking the neurobiology of love into consideration, it could be likely that, similar to the not-monogamous montane voles, they show lower densities of the neuropeptides oxytocin and vasopressin. Lastly, currently a lot of different substances are shown to be capable of manipulating at least a part of love. Though none of them have successfully altered love as a whole, and thereby it raises the question if future use of “love-drugs” is ethically acceptable.

Inhoud

1. Introduction

"*Hello, I am a man of 40 years old, married for 12 years and I have three children ranging from 6 to 11 years old. I used to be very respectful and loving towards my wife. Wrote poems, brought her flowers, booked surprise trips etc. I really missed her when I was away from home for a while. We have an amazing house and to the outside we are the perfect family. However, something happened… By coincidence I met a woman that I match with on all interests: humor, sports, taking initiative, taste in music, upraising, being adventurous, loving the outdoor life etc. Something I miss with my current wife. We know each other for a year now and are still very much in love. I told everything to my wife, and despite everything she wants to work on our relationship. Now I don't know what to do. Do I choose for my marriage and fight for it? I have a fantastic house and my children are my everything. I would die for them. Or do I choose for the woman I have a connection with that I never experienced with my current wife?*" *– Viva 2019*

Above confession is found on a forum of the Dutch magazine *Viva*. It is a good example of the trouble that love can bring along. Love, a subject that is most of all associated with a load of positive feelings and emotions. People might say it is a breathtaking and euphoric experience. If you ask the Cambridge Dictionary for their definition of love they will say love is: '*to like another adult very much and be romantically and sexually attracted to them, or to have strong feelings of liking a friend or person in your family*'.

But is love solely that abstract, romanticized, breathtaking phenomenon brought by an arrow of Cupid? Love is also a concept that is regulated by biology and neurobiology. So how is love, from all the euphoric feelings, the breathtaking experiences to sweating hands translated to neurobiology? Apart from all the positive feelings and happiness that comes along with love, there is also a more negative side to it. The example at the start of this chapter, about the man being in love with another woman than his wife while having a family of three children, shows how love can also get you into trouble. How comes that people have the tendency to be unfaithful to their partners? And is there a specific type that is more prone to cheating than others? Moreover, love can even get you in dangerous situations. Think of all the partners that are caught in an abusive relationship, but refuse to leave their partner because they claim to still be in love with them. Love can also get you in trouble by being absent. Some people are unable to feel love at all. So, how is it possible that some are unable to experience that love-bond that others talk about, despite them liking a person very much? All of these examples have negative impacts on the person themselves and on the people around them. When someone cheats, most of the time the partner is hurt emotionally. In the case of being stuck in an abusive relationship, the individual is hurt emotionally and/ or physically, which could even be dangerous for someone's life. Individuals that are not able to love at all are very likely to hurt other person's feelings for not getting back the love that they expect. Moreover, they can hurt their own feelings too if they want to love, but just are unable to. For all this cases it would desirable if you could manipulate love in some kind of way. Is it possible to manipulate love, and if yes, is it something that we as humans should want to influence our lives? All the questions that are asked so far is where this thesis will try to find an answer for.

2. What is love?

Love is a strong emotion,
That connects two hearts,
It is a new beginning,
A great new start,
Love is a feeling, that cannot be expressed,
There is a good vibe, a great zest
True love survives till the end of time
I am glad I found you,
You are truly mine!
- *Wishafriend.com*

In love poems as such, love is often described as something magical and romanticized. Metaphors such as a connection between two hearts, a bond that outlasts time and space or a bond between two souls are not strange to the literature. When searching the dictionary for the meaning of love, you will find a description as: 1. *A profoundly tender, passionate affection for another person.* 2. *A feeling of warm personal attachment or deep affection, as for a parent, child or friend.* and as 3. *Sexual passion and desire.* (*Dictionary.com*)
So according to this dictionary, love is a phenomenon that includes passionate affection, personal attachment and sexual passion and desire. However, is this in line with love if you look at it from a more biological and neurological perspective?

Over the whole human population, romantic love is something ubiquitous[1]. This is a good indication that the necessity for romantic love is evolutionary preserved and that there is some sort of biological basis for it.[2] Evolutionary seen, romantic love is a series of emotions and behaviors that are needed for reproduction of a species, in this case humans.[3] It is even debatable if the kind of romantic love we experience is known among other non-human species too, or that it is a human brainchild. Pair bonding is a more general term referring to the process of forming an enduring (romantic) relationship between two individuals, either human or non-human species. Interestingly, pair bonding is shown by only <5% of all mammals[4]. Species that form an enduring relationship with their partner are often considered monogamous, including humans. Monogamy is mostly described as "the habit of having only one partner"[5]. In humans being monogamous normally means you are together with one person and not being involved in sexual activities with others. This same definition for monogamy was used in the field of biology too. Lately however, the definition of monogamy is debated. A research by Solomon et al. found that sexual exclusivity is actually very rare in species that are considered "monogamous", such as the prairie vole.[6] Solomon and her group had previously found evidence that prairie voles might not be genetically monogamous. Therefore they examined allelic polymorphisms in microsatellite loci in different litters of wild prairie vole females. They collected nine pregnant prairie vole females from a natural population in east-central Illinois and sacrificed them to obtain their litters. Maternal as well as embryotic tissue was collected. Genomic DNA was extracted from the maternal liver and embryotic tissue for the microsatellite analysis. Five different loci were examined via heterologous microsatellite primer pairs and the samples were amplified via PCR. The samples of a single mom and her offspring were ran on the same gel for a multiple paternity analysis. To see if one female was impregnated by multiple males, the number of different alleles per loci were counted. If there were more than two different paternal alleles for one loci, this indicated that the female prairie vole had mated with more than one male (fig. 1). Five out

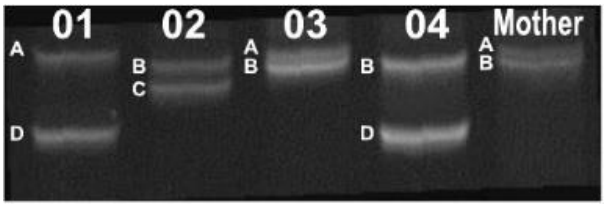

Figure 1. Electrophoresis gel with the amplified PCR-products of the AV13 locus of a female prairie vole (Mother) and her four littermates offspring (O1-O4). The letters mark the different alleles present in each individual. As non-maternal allele, offspring O1 and O4 have D, O2 has C and O3 has either A or B. Three different paternal alleles indicates the female prairie vole mated with more than one male. *Source: Solomon et al.,2004, fig 1.*

Table 1. Results of the multiple paternity analysis per female prairie vole. The minimum number of fathers per litter and number of loci indicating multiple paternity are shown. *Source: Solomon et al.,2004, table 2.*

Female	Number of embryos	Minimum number of fathers	Number of loci indicating multiple paternity
20A	3	1	0
21A	5	1	0
23A	5	2	2
25A	4	2	1
26A	6	2	1
27A	6	2	3
31A	4	2	1
33A	5	1	0
35A	5	1	0

of the nine examined female prairie voles produced litters that showed a number of loci indicating multiple paternity (table 1). This shows that among species that are considered "monogamous", sexual exclusivity is not self-evident. Therefore nowadays the more specific term of *social* monogamy is more common in the field of biology to refer to species that exhibit some or all of the following traits: Selective social interaction with an opposite-sex mate, selective aggression towards unfamiliar animals, biparental care, communal living within the family group, alloparental care and reduced sexual dimorphism.[5] Though, if not for sexual exclusivity, what is the evolutionary benefit of monogamy in animals? As being a widely discussed topic, different explanations are given in current literature. First of all, the forming of enduring relationships is considered evolutionary beneficial for animals that produce offspring in need of bi-parental raise.[2,3] Furthermore, monogamy increases the access of the individual to the partner's reproductive potential. However, at the same time this is a disadvantage as access to other potential partners is strongly reduced.[4] In animals, living in one-male one-female pairs does have the benefit of maximum protection of resources needed for reproduction. Besides the reproduction potential of the male, the female needs a territory that may contain essential nutrients and nesting sites. Constant availability of the males territoriality increases chances of a suitable territory for reproduction.[7] So, even though not yet completely understood, monogamy can probably be seen as '*a social system, and one that offers the advantages of shared parenting, protection of resources, and social support,*' as Sue Carter very nicely formulated[5]. Romantic love in humans might be a similar social system that is focused on reproduction, survival and support, made a lot more complicated by the human brain.

In biology, love is not considered as being solely an emotion, but also as a motivation system[8]. Despite not completely understanding the exact biologic basis for romantic love in humans, now it is quite clear that it can be divided in three different sub emotion-motivation systems. All three subtypes operate in tandem to achieve romantic love, but are also able to act independently of each other[3]. Lust, or sex drive, is the most primitive subtype of love. It is the main cause for attraction to the opposite sex and sexual desire in humans as a primitive motivation for reproduction.[9,10] Even though lust is often the first step towards romantic love, it is not inseparable from the other two emotion-motivation systems, as people can have sex with people they do not feel attraction or attachment for. Lust motivates an individual to mate with any suitable partner, where attraction and attachment more cause the focusing of mating energy towards one single partner.[3] Attraction is the emotion-motivation system that is involved with the euphoric feeling of being in love, together with the strongly, almost obsessive, focused attention on one partner[3,10–12]. The extremely positive, euphoric feelings might be explained by the brain reward-systems that are involved in the attraction system[13],

which will be explained in the next chapter. The strong euphoric feelings of the attraction-system are mostly experienced in the initial phase of romantic love, and often decrease overtime during a long-term relationship. Attachment is the emotion-motivation system that causes the phenomenon of pair-bonding[3,14]. Feelings of attachment often increase in intensity the longer two partners are together. The systems of attachment are the basis for the formation of selective social and/or emotional bonds, which are important for an enduring relationship. Attachment is not only seen in romantic relationships, but also in maternal relationships with their offspring[14], which might not be too surprising as the bond between mother and child is also supposed to be a long-lasting one. Even though being three very distinct systems, they all intertwine somehow and together they form the recipe for human romantic love. Lust is causing the initial opposite-sex attraction and the sexual desire aimed at an individual, where attraction triggers the reward system and is the culprit for euphoric feelings when being together and the obsessive, focused attention towards one individual, and finally attachment makes that the love-couple wants to stay together forever.

3. Neurobiology of love

In the previous chapter, the phenomenon of love was somewhat rationalized by introducing the three biological emotion-motivation systems of human romantic love. Here I will further dive into the biology of love by discussing the neurobiology underlying these systems.

Most often, falling in love starts with lust, or the feeling of sexual attraction towards someone. The gonadal hormone testosterone is considered important for the existence of this sex drive, or libido, in humans. Men appear to have a 10-to-20 fold higher concentration of testosterone[15]. In general men also have a higher sex drive than women.[16] Assuming that testosterone is the hormone influencing the arousal threshold, this could indicate that higher levels of testosterone mean a higher urge for sex. This statement is supported by research showing increased testosterone levels in women correlates with a higher sexual desire, more sexual thoughts and anticipation of sexual activity.[17] In men, decreased levels of testosterone cause erectile dysfunction and decreased libido. Increasing the levels of testosterone with testosterone therapy restores the libido to normal levels.[18] When looking at testosterone levels of individuals that were in the initial stage of falling in love (relationships of <6 months), women showed increased testosterone levels, but men showed lowered levels of testosterone.[19] Possibly, falling in love requires the two sexes to become more alike, with softening of male features in men and enhancing them in women.[19] In men, lower levels of testosterone probably make him more relationship orientated than being “on the market”, as lowered testosterone also decreases his libido and mating effort.[20] The exact reason for this difference in testosterone levels between the two sexes is, however, not yet quite known. Estrogen, the feminine counterpart of testosterone also seems to influence sex drive. In research regarding sex drive of women over their menstrual cycle, it was observed that women in their ovulatory phase showed a stronger reaction towards sexual stimuli than in other phases of their cycle. And let the ovulatory phase be the phase where women have a peak in their estrogen levels.[21] An interesting phenomenon to add to that is the fluctuation of what a woman finds attractive in a man during her menstrual cycle. During their ovulatory phase, they appear to show a preference for men with very masculine traits, which would indicate fit genes.[22,23] Remarkably they show higher preference for more feminine faces in their low estrogen luteal phase of the cycle. A more feminine face in men indicates lower levels of testosterone and lower levels of testosterone are often associated with higher parental investment.[24,25] This indicates that testosterone, estrogen and possible other androgens may not only influence the sex drive of individuals, but may also influence towards which person this sexual desire is directed.

Then, the attraction-system, the mechanism responsible for the strong feelings of euphoria when being around the romantic partner and the uncontrollable obsessive thoughts about that one person. As was already mentioned briefly in the previous chapter, the reward-system has a large share in the attraction-phase of love, especially in the euphoric feeling of love. One of the main culprits here is dopamine. Dopamine is a neurotransmitter that is involved in various mechanisms including motor coordination, emotions, memory and thus the most important in this respect, the reward mechanism[26]. The dopamine-pathway of the reward system in the brain begins at the ventral tegmental area (VTA). The VTA is where dopamine is produced in nerve cell bodies and plays a role in memory, attention, motivation and thus reward.[27,28] From there it is released into the nucleus accumbens (NAcc), often referred to as the center of reward and considered the neural interface between motivation and action.[28,29] The pathway continues to the prefrontal cortex (PFC), which, next to reward, is involved in attention and goal-directed behaviors.[28,30] When shown pictures of their romantic partners while still being in their "passionate" phase of the relationship, a significant increase of dopaminergic activity was also observed in the medial orbitofrontal cortex[31], which interestingly is involved in reward-guided learning[32]. Possibly activation of dopamine in this area is one of the reasons people "learn" they get a reward from being with that one person. The concentration of dopamine in the NAcc strongly increases during sexual as well as feeding behavior[33], as is also shown by the studies of Bassareo & Di Chiara and Damsma et al. Bassareo & Di Chiara investigated the influence habituation to a certain food had on the dopamine reward response.[34] Therefore Sprague-Dawley rats were presented with cheesy corn-flour snacks called Fonzies and allowed 20 minutes to eat them. Dopamine response was measured through an probe implanted in the NAcc. Presentation of Fonzies led to an increase of dopamine in the NAcc, reaching almost 150% of the basal neuron activity (fig. 2A). On the same note, Damsma et al. looked at the influence of locomotion, exposure to a novel chamber, exposure to sex odors and sexual activity on dopamine transmission in the NAcc of rats.[35] Dopamine response was measured via a microdialysis probe, while they were exposed to locomotor activity, novelty and sexual behavior. For sexual behavior the rats were exposed to bedding used during sexual activity training sessions for sex odor, then to a sexually receptive female behind a vertical mesh screen, and lastly the mesh screen was removed to allow sexual interaction. Specifically the dopamine response during sexual behavior is of interest for this

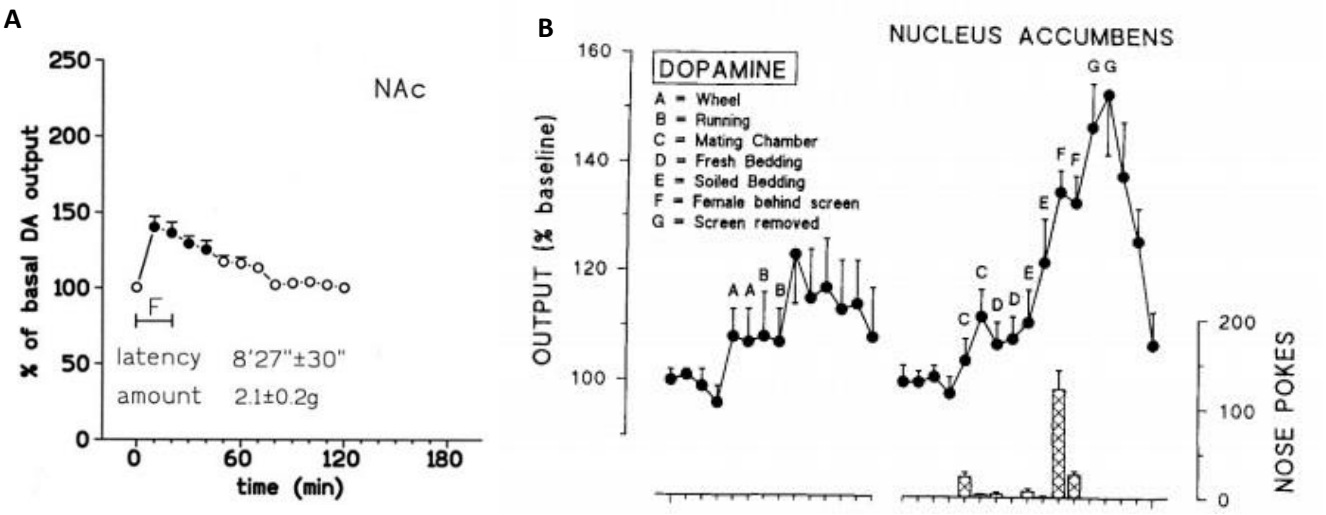

Figure 2. Dopamine activity in the nucleus accumbens (NAc) in feeding and sexual behavior. A)The dopamine response in the NAc of rats increases upon presentation of a cheesy corn-flour snack (F). *Source: Bassareo & Di Chiara, 1997, fig.1.* B)The dopamine response increases upon anticipation on and during sexual interaction in the NAc of rats. *Source: Damsma et al. 1992, fig.3.*

story. Dopamine in the NAcc showed a strong increase in anticipation to and during sexual interaction peaking at 153% of the basal dopamine output(Fig 2B). Looking at both studies, this indicates that sexual activity is just as rewarding as feeding behavior. This strong involvement of the reward system that causes the euphoric, positive feelings you get from being together and having sex with the one you love, enhancing the desire for and frequency of sexual activities, enforces the idea that romantic love is a biological mechanism to promote reproduction.

An interesting element of the attraction system is serotonin. In contrast to the previous mentioned substances, levels of serotonin are strongly reduced during the initial phases of love.[40] This drop in serotonin shows a striking resemblance to the reduction of serotonin in patients with obsessive-compulsive disorder (OCD)[40,41]. In both, patients with OCD and individuals that have recently fallen in love, the function of the serotonin-transporter is reduced. It is therefore believed that the shared symptoms of obsessive and intrusive thoughts are due to similar operating on a neurochemical level of early phase love and OCD.[42] Furthermore, when people are highly in love, deactivation is seen of the frontal, parietal and middle temporal cortex, together with the amygdala. The frontal cortex is not only deactivated by romantic love, but also by sexual arousal alone.[41] Social cognition and judgement is regulated in amongst others these cortices and the amygdala is involved with social judgement and fear.[41,43] That taken together might explain why people are often described as being 'blind in love'. They are genuinely blind to the flaws of their partner because their social judgement and fear is, at least temporally, suspended.

Lastly, I will discuss the neurobiology of attachment, which is the basis for pair-bonding and long-term monogamous relationships. Some even go as far as stating that true love cannot exist without attachment. In couples with long-term relationships, amongst others the right anterior and posterior cingulate cortex show increased activity[44] together with an increase of activity in the ventral pallidum[45]. The exact function of the cortex-areas is still highly discussed. Currently, it is believed that the anterior cingulate cortex (ACC) is linked to commitment to a course of action.[46] The posterior cingulate cortex (PCC) is associated with amongst others cognitive functioning and the focusing of attention.[47] Aron et al.[48] studied the link between activation of brain areas in romantic love, among which the ACC and PCC. Participants were questioned by one of the researchers to establish the duration, intensity and range of the participant's romantic love. Additionally, the participants were exposed to pictures of their loved ones and neutral pictures, while their brain activity was monitored via fMRI. When plotting activity in the ACC against the duration of the relationships revealed a correlation between the two. Activity in the ACC and PCC increased with lengthening of relationships (fig. 3). The process of attachment similarly shows a dynamic increase, indicating the role of the ACC

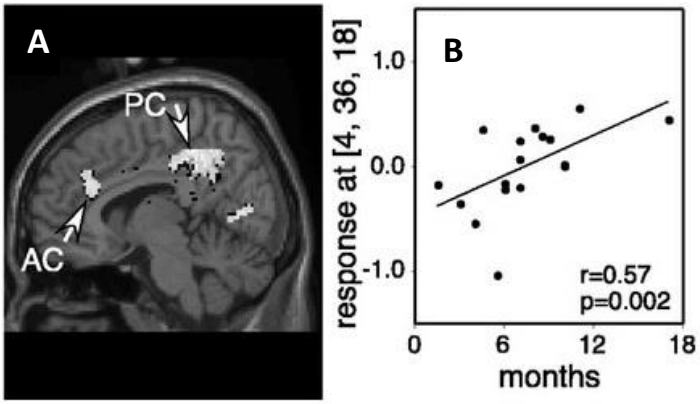

Figure 3. Correlation of length of time in love with activation of anterior cingulate cortex (AC) and posterior cingulate cortex (PC). A) Voxel clusters corresponding to length of relationship in AC and PC (arrows). B) Graph of correlation between length of relationship and AC activity. *Source: Aron et al. 2005, fig.5 C&D.*

and PCC in this process. While the functions of commitment to a course of action and focusing of attention, that are described above, are rather general, increased activity in these areas indeed adds up with the phenomenon of increasing commitment and focus towards one person in a long-term relationship. The function of the ventral pallidum is more clear. The ventral pallidum is very important for regulating motivated behaviors.[49] Interestingly, there are projections of dopaminergic neurons from the NAcc to the ventral pallidum and it has been shown that dopamine directly alters ventral pallidum signaling.[50] This suggests that there is a role for dopamine in the system of attachment, which will be further discussed below.

The main players for pair-bonding are oxytocin and vasopressin. Oxytocin and vasopressin are small peptides that are chemically very alike. The function of the two is also similar, although not entirely identical.[14] The paraventricular nucleus (PVN) and supraoptic nuclei (SON), that are located within the hypothalamus, are the prevailing sources for oxytocin and vasopressin production.[51] Oxytocin is involved in pregnancy and nursing and in the bonding process between mother and infant[52]. Furthermore, it is released upon sexual activity, orgasm[53] and skin-to-skin contact[54]. The feeling of attachment between two people is thus likely increased after having sex. The analogous involvement of oxytocin in parental bonding leads to think that the romantic bonding between two individuals might have come from the evolutionary base of the mother-infant attachment. Oxytocin also seems to play a role in the building of trust, as intranasal administering of oxytocin increased trust of people in others, even strangers, when playing a money game[55]. Pair-bonding and the function of oxytocin and vasopressin has been widely studied in voles (rodents). These studies brought some interesting insights, as there are substantial contrasts in mating strategies within the species. Prairie voles are animals that form life-long socially monogamous bonds, induced by mating. Once they found their mate, they show the typical partner preference, selective aggression towards conspecific strangers and bi-parental raising that is associated with monogamous pair-bonding.[56] Their cousins, the montane voles, are genetically very similar to the prairie voles, but do not form these life-long bonds with one mate and do not show any monogamy at all[57]. This made these two animals very suitable for research regarding the neurobiology of monogamy. What they found out was that oxytocin and vasopressin are the critical factors. Keebaugh et al.[58] suspected that knocking down of the oxytocin receptor (OXTR) in the NAcc would affect monogamous behavior in female prairie voles. They used RNA interference to selectively knock-down (but not knock-out) OXTR's in the NAcc. At 21 days of age the animals were infused with adeno-associated viral vectors that contained the sequence for short hairpin RNA (shRNA) targeting OXTR mRNA in the NAcc (shRNA-vOxtr). As a result they observed a 45% reduction of binding capacity in the OXTR's (Fig. 4A) . Partner preference testing was performed when the animals were adults. For the partner preference test the animals were first placed together in a cage with a sexually experienced adult male for 24 hours. Hereafter, the females were examined if they had mated or not and only animals that had mated were used for the partner preference test. The partner preference test was performed in a three-chambered testing arena with the familiar male partner in one chamber and a second novel sexually experienced male in the other. For 3 hours the time spent in immobile contact (huddling) with both males was analyzed. In animals that were treated with shRNA, no preference was observed between huddling with the familiar vs. the stranger male (Fig. 4B). Inhibiting the effect of vasopressin in male prairie voles gave similar results. Blocking the V1aR vasopressin receptor in the ventral pallidum of male prairie voles lead to a loss of monogamous behavior.[59] So blocking of oxytocin and vasopressin leads to a loss of monogamous behavior in prairie voles. However, injecting oxytocin and vasopressin in montane

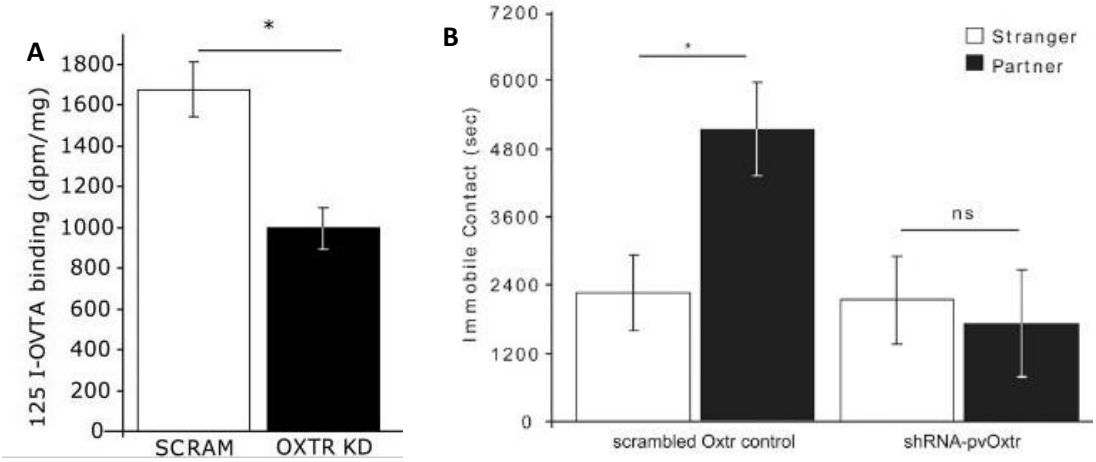

Figure 4. Partner preference behavior in shRNA-pvOxtr and scrambled Oxtr control female prairie voles. A) Oxytocin receptors of female prairie voles that were infused with VAA containing shRNA-pvOxtr showed a decrease of 45% in binding capacity. B) Only scrambled Oxtr control females showed a preference for a familiar male partner during the partner preference test. *Source: Keebaugh et al. 2015, Fig. 1E & Fig. 3A*

voles does not automatically lead to monogamous behavior in these animals.[41] This is explained by a lack of receptors for both substances in the montane vole.[41] Thus, in order to be sensitive for the monogamy-inducing effects of oxytocin and vasopressin it is crucial that their receptors are also present in the relevant areas.

As was suggested earlier, next to oxytocin and vasopressin, dopamine also plays an important role in monogamous relationships. Despite dopamine not being directly responsible for the feeling of attachment, it might have a crucial role in the origin of monogamy. The dopamine reward system communicates with the system of oxytocin/vasopressin, amongst others via the ventral pallidum[3,49] Through this communication, people will likely associate the feeling of reward with one specific person. This interaction could therefore actually be the foundation of monogamy. Oxytocin and vasopressin are thus the key mediators of the attachment-process, which is necessary to form long-lasting social monogamous bonds between romantic partners. Communication with the dopamine reward-system appears to be crucial for the development of monogamy. However, not every species has a biological dependency on these social monogamous bonds, which is demonstrated by a lack of oxytocin and vasopressin receptors in the relevant brain areas in this species.

4. Why do humans cheat?

As is seen in the *Viva*-story showed in the introduction, it is not guaranteed for couples that have fallen in love to stay together 'till death does them part'. The numerous break-ups and divorces are a witness of this. The man from the story is married for 12 years and has three children, but describes to be in love with another woman. In this particular story the man has not involved in infidelity yet, however infidelity is unfortunately not uncommon in supposedly monogamous relationships and marriages. Around 20% of all married spouses and around almost 70% of unmarried couples admitted to have engaged in an extra-relational affair[60]. This while 99% of all individuals that claim to be in a monogamous relationship expect total sexual exclusivity from their partner[61]. So how comes extramarital sex (EMS) is still such a common phenomenon? If we look at current literature, different risk-factors for infidelity are put forward. Low satisfaction in the relationship, domestic violence, having excess alternatives to their partner in their working and/or private environment and low

commitment to the relationship are regularly mentioned examples.[60,62–64] Low commitment to the relationship is often appointed to an avoidant attachment style. Individuals showing avoidant attachment often avoid interdependence in the relationship and are hesitant in seeking proximity with the partner. It is said that attachment style originates from insecurities in the individual, who is usually skeptical about the other partners' intentions and anxious to lose self-independency.[65,66] However, maybe the reason for avoidance attachment is not only insecurity and mistrust, but listens to a more biological explanation. The phenotype of avoidant attachment is often associated with different mental disorders such as schizophrenia and depression[65]. Of schizophrenia it is known that there are complications with dopamine signaling[67], The exact abnormalities with dopamine-receptors that are observed in schizophrenic patients are very heterogenous. Hess et al. discovered one of them.[68] They performed a radioligand binding assay on D1 and D2 receptors in the caudate nucleus of postmortem brains of schizophrenic patients. Affinity and density of the D1-receptors was assessed by binding of the D1 dopamine receptor antagonist radioligand [^{3}H]SCH23390. Affinity and density of the D2-receptor was assessed through radioligand [^{3}H]Spiperone binding, a D2 dopamine receptor antagonist. For the D1 receptor they found a significant decrease in affinity as well as the density of the receptor in the caudate nucleus when compared to a control group. For the D2 receptor there was no significant difference in affinity, but schizophrenic patients had a higher density of the receptor in their caudate nucleus. (Fig. 5) Although this is one example of how dopamine signaling is dysregulated in schizophrenia, many other different abnormalities were found in other studies.[69,70] Nevertheless, all of these dopamine dysregulations might possibly affect the attraction system. Not all individuals that have an avoidant attachment style will be classified as having a mental disorder. Nevertheless, in people without mental disorders this attachment style may be caused by similar miss-signaling of dopamine pathways. Moreover, it might be possible that these people, mental disorder or not, show similar abnormalities in oxytocin/vasopressin signaling, which influences their feelings of attachment. But the reason for the existence of infidelity might actually be more simple. As was mentioned previously, Sue Carter argued that the definition of being 'monogamous' is debatable.[5] Where the first assumption of monogamy in animals was that the formed pair-bonds were sexually exclusive, this turned out to be false. Of all mammals showing "monogamy", the majority did involve in promiscuous sex, while still being socially-monogamous

	D_1 Receptor		D_2 Receptor	
	[^{3}H]SCH23390 Binding		[^{3}H]Spiperone Binding	
	K_D (nM)	B_{max} (fmol/mg protein)	K_D (nM)	B_{max} (fmol/mg protein)
CONTROL	2.13±0.19	281.5±20.5	0.06±0.004	119.8±13.7
SCHIZOPHRENIC	1.10±0.19**	161.4±22.1**	0.35±0.19^{NS}	186.7±33.0*
%CHANGE FROM CONTROL	−48%	−43%		+56%

NS, $p > 0.05$ (one tail)
* $p < 0.05$ (one tail)
** $p < 0.005$ (two tail)

Data represent means ± S.E.M. for the affinities (K_D) and densities (B_{max}) determined by saturation analyses of [^{3}H]SCH23390 binding and [^{3}H]spiperone binding (n = 8/group). Asterisks denote significant difference from control values, Student's t test.

Figure 5. Binding characteristics of the D1 and D2 dopamine receptors in the caudate nucleus of postmortem brains of controls and schizophrenic patients.

with their partner. If we project this to humans, who are just mammals with pants after all, maybe it is not that odd that there is such a high tendency for infidelity. Even though it is not socially accepted, and does more harm than good to people, from a biological perspective EMS might be something that is 'in our nature'.

5. Does cheating has a type?

If infidelity is something that is 'in our nature', that raises the question if certain personal characteristics or maybe even certain biological characteristics can predict the risk of someone involving in cheating. First of all, despite both sexes being involved in EMS, it appears that being male is associated with an increased risk of extra-dyadic activities.[61] In general, men indeed show a higher urge for sex and have less difficulties with seeing sex apart from love, which could possibly explain this increased risk.[16,71] Recently, Klimas et al. have linked higher levels of testosterone within men to a higher chance of infidelity.[72] Testosterone in men has also been linked to aggression and competitive, dominant behavior[73]. Does this mean that the most manly "alpha-males" are the ones most likely to cheat? Interestingly, narcissism, the having of an idealized egocentric self-image, is associated with the avoidant attachment style[65] that was previously mentioned as a substantial risk factor for infidelity. Furthermore, a grandiose sense of sexual skill and partners' sexual entitlement, two facets of narcissism, were directly associated with infidelity[74]. Narcissism often leads to exceptional high levels of self-confidence which could translate to behavioral patterns that are generally classified as typically "alpha-male". Dare devils, they who involve in extreme or even dangerous activities to seek excitement or attention, show behavior that can be classified as being 'very manly'. But does this also mean that men that practice extreme activities for their excitement have a higher tendency for infidelity?

Even though it is not a direct link, a polymorphism in one of the dopamine-receptor genes has recently been linked to a higher incidence of infidelity by Garcia et al.[75] This same polymorphism was associated with sensation-seeking behavior[76]. Additional researches had lead Garcia and his colleagues to the hypothesis that genes modulating dopamine neurotransmission and therefore mediating behavioral phenotypes associated with sensation-seeking behavior, possibly could also be involved with a higher chance of infidelity. Their candidate gene was that for the dopamine D4 receptor (DRD4), which has been linked to sensation-seeking behavior[76]. This gene contains a variable number tandem repeat (VNTR), with a range from 2 to 11 repeats on one allele. Individuals with more than 7 repeats on this allele (7R+) have a higher predisposition for sensation-seeking behavior. To

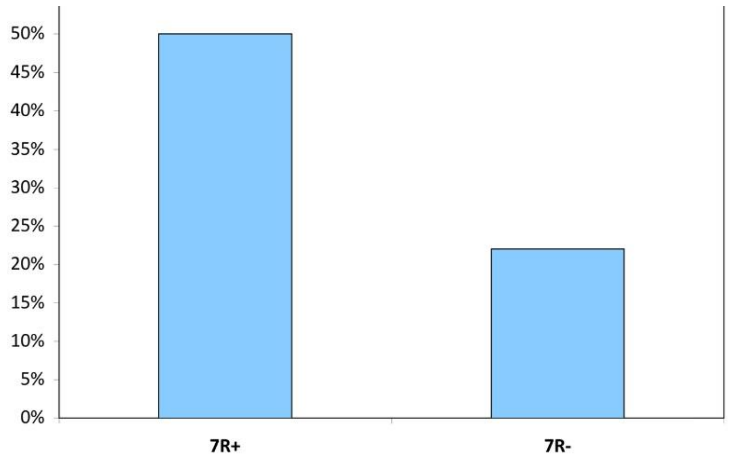

Figure 6. Percent of participants reporting extra-relationship sexual experiences, by DRD4 genotype group. *Source: Garcia et al., 2010, Fig.2*

find a correlation with this gene and extra-dyadic behavior, DNA-samples were collected from the participants and they had to fill in a questionnaire. In the questionnaire they had to answer questions about their past sexual behavior, sexual expectations and preferences. DRD4 VNTR was genotyped from DNA collected via buccal samples. They found a correlation (although not significant) between individuals with at least one 7R+ allele and higher reporting of extra-relationship sexual experiences (Fig. 6). Individuals with two 7R+ alleles show a lower density of dopamine receptors in the corticomesolimbic reward pathway in the brains. The receptors that are present show a lower binding affinity.[75] Lower quantities of receptors with a lower affinity to bind dopamine, probably means these people need a higher frequency of stimulation, or a stimulation of higher intensity to experience the same rewarding sensation as individuals with less than 7 repeats. Hence the sensation seeking or the seeking of sexual attention outside the relationship. Not only polymorphisms in a dopamine receptor gene, but also polymorphisms in a gene for vasopressin receptors have been associated with an increased risk of infidelity. Specifically, AVPR1A, the gene coding for vasopressin receptor V1aR. The region of this gene contains three polymorphic repetitive sequences, of which the repetitive sequence named RS3 is relevant in this respect. Men carrying the 334 allele for AVPR1A showed a significant lower score on the partner bonding scale (PBS). When carrying two copies of the 334 allele, the PBS score was even lower.[77] Possibly, similar to the polymorphism in the dopamine receptor, the 334 allele interferes with quantity and/or affinity of the vasopressin receptors, however this is not yet known. It is known though, that presence of the 334 allele influences activity of brain regions such as the hippocampus and amygdala, thus affecting social brain function.[77] Taken together, there is not one specific characteristic that will guarantee infidelity from an individual, but there are many factors, personal or biological, that contribute to a higher risk of involvement in extra-dyadic activities. All previous risk-factors create the image that men that are generally considered more 'manly', e.g. showing sensation-seeking behavior and/or being loud, dominant and overly self-confident, are the individuals most at risk of cheating.

6. Love in an abusive relationship

Suzanne (34): "The first time Robin hit me I was convinced it was a one-time thing. That he was só upset, he couldn't control his aggression. It did scare me a lot. I always knew he had a short temper, but that he would hit me was something I could never imagine. But it did not stay at that one time.." –Flair 2019

Unfortunately, domestic violence as such is not very rare amongst romantic couples. Domestic violence is seen in various forms, e.g. physically, sexually, mentally, and is also seen among all types of relationships, e.g. married, un-married, same-sex and heterosexual.[78] Despite domestic violence being present in all possible relationships, the man to woman violence in a heterosexual relationship is the most frequent seen form.[79] A shocking 10 to 50 percent of all woman worldwide, have reported experiencing some sort of domestic violence during their lifetime.[79] Being in a bad abusive relationship can influence a person's health, physically and mentally.[80] It has been shown that being in a bad relationship increases the chance on developing a major depressive disorder. Depression on its own promotes inflammation, which may lead to numerous other physical health issues.[81] Some victims develop a post-traumatic stress disorder, and having a low self-esteem and suicidal thoughts are other possible results of domestic violence.[82] Other physical health issues that are not directly caused by mental issues are chronic pain, cardiovascular problems, gastrointestinal disorders and neurological problems.[83] Apart from all the medical health problems, domestic violence can be very dangerous and even end deadly for the victim as lethal domestic violence is not a rare phenomenon.[84] Despite all the negative health influences and dangers of being in a violent relationship, often the victim will refuse to leave the relationship. Usually the reason for this is that they genuinely believe

the abusive partner will change, and they still claim to love their spouse. Or that they do not dare to end the relationship, because they are afraid the violence will only get worse from that.[85] Moreover, some researchers suggest that women in an abusive relationship develop a state of learned helplessness, where they will just accept that the abuse is happening to them and they will have little control over that.[85,86] Clearly an abusive relationship is affecting one's mind. Maybe we can also partly explain why people do not leave such a relationship using neurobiology. How is it possible that these people allegedly still love their partner, despite the violence they are confronted with?

So let's look back at the neurobiology of love that was explained previously. In the spectrum of love, dopamine is important for the feeling of reward when being around the loved one. When these people say they still love their abusive spouse, it is likely that, despite the violence, they still experience the euphoric, rewarding feeling when seeing their partner. Intimate partner violence (IPV) often occurs in a cycle of different phases. Tension building and the acting out period, where the actual abuse takes place, and afterwards the 'honeymoon' period and calm period where the abusive partner will very likely apologize for its actions and swear it will never happen again.[85] It is possible that all the sweet acts of the violent partner during this last phases to make up for the violent behavior keep triggering the dopamine system. Therefore, they will keep getting the feeling of reward when being with their partner. When you combine this with the genuine believe their partner will change, gives an understandable view of why they do not leave the abusive spouse. Furthermore, it has been addressed that in the initial states of love the frontal, parietal and middle temporal cortex, together with the amygdala, have a decreased activity. These are the areas in the brain that regulate social judgement and fear.[41,43] When deactivated, this allows for unreasonable judgement of the partner and his actions. In this state of mind the victim can judge the acts of violence, that are evidently wrong, as being 'not so bad', or claim 'he doesn't mean it'. Both forms of denial could explain why these victims genuinely believe the abuse will not happen another time. Possibly, the attachment system, involving oxytocin and vasopressin, also plays a role in why abused spouses remain with their abusive partner. Oxytocin and vasopressin cause the monogamous bond between partners, creating loyalty of both partners to each other. Victims of domestic violence appear to remain very loyal to their spouses. Imaginably, this loyalty is induced by oxytocin and vasopressin. In that case, the oxytocin/ vasopressin signaling is so strong, that despite all the violence and abuse the affected partners still have the feeling they 'belong together' with the abusive spouse. All of these love-mechanisms could possibly be the or a part of the explanation why victims of an abusive relationship do not leave their partner. Apart from these possible neurobiological mechanisms, there seems to be a trend for women that have been exposed to IPV in their youth. Women that were victimized by or have witnessed domestic violence during their childhood, seem to have developed a state of 'learned helplessness', increasing the risk of being victimized by IPV themselves as an adult.[87] So even though the actual underlying neurobiology of refusing to leave an abusive relationship has not yet been investigated very thoroughly and remains speculative for now, it appears that there is a high-risk profile for women that have a history of IPV in their environment, with or without one of the proposed neurobiological mechanism discussed above.

7. If you can't fall in love

My boyfriend told me that he can't feel love for girls, or fall in love with anyone, is that true?
- Quora 2018

On the contrary of people that love too much and therefore involve in infidelity, some people report not being able to love at all. Sometimes this can be addressed to mental disorders such as sociopathy and psychopathy (anti-social personality disorders). For individuals suffering from these disorders, it

is often reported they are not able to feel love.[88,89] Others do not suffer from a mental disorder, but simply have a hard time feeling love somehow. It can be especially painful for the people surrounding the individuals that are not able to love. In absence of love, for example, children can suffer from neglect. Furthermore, romantic partners are hurt because they do not get the love back that they give themselves. In patients suffering from psychopathy, brain areas that regulate emotional processing and social decision making are deviant from healthy individuals.[89] Amongst these areas are the prefrontal and orbitofrontal cortex, which are active in the dopamine pathway of the reward-system. Since the connection between dopamine and oxytocin and vasopressin is so important to form the association between reward (dopamine) and attachment to one person (oxytocin & vasopressin), this might explain why psychopaths are unable to feel love. While they are able to feel sexual attraction and get the reward for having sexual interactions, they do not link that reward to one specific person. A possible other explanation for the absence of love could be found in the differences between the prairie and montane voles. Prairie voles are described as monogamous animals where montane voles do not show any monogamy. In prairie voles, oxytocin and vasopressin are the main mediators of "love" and monogamy. Montane voles, however, lack receptors for these substances.[41] As the density of oxytocin and vasopressin receptors differs between species, it might be possible that the receptor density is also variable between humans. Possibly, the individuals that do not feel love, lack or have lower levels of the receptors for oxytocin and vasopressin. In that case, they will be unable to develop attachment to someone. Not being able to fall in love could thus be explained by neurobiology, however the exact mechanism is yet unknown.

8. Can you manipulate love?

Love is considered a very positive experience by most of the people. Even though the beginning of being in love can be stressful, when the love is answered by both partners, most people feel ecstatic and safe when being together. However, as we learned from the previous chapters, love is not always that rose colored. Partners cheat, fall in love with someone else, get violent or are not able to love at all. Furthermore, not all initial loves get answered, which also provides a source of emotional pain. Previous chapters showed troubles in love can lead to sadness, unhappiness and even mental and physical health problems. Since there is a neurobiological base for love, it is likely these neurobiological pathways can also be manipulated to manipulate feelings of love. In this chapter I will address the possibility of manipulating love. Is it possible to turn love on or off like a light switch? And do the benefits of manipulating love weigh up to the ethical constraints?

Giving someone a love potion that makes them fall in love with you might sound like something from a sci-fi movie. However, in reality the number of studies that involve manipulation of love components are surprisingly high. Love can be divided into three different motivation-systems [3]. Since all three motivation-systems have different neurobiological mechanism and mediators, different strategies are needed to influence them. Lust, the feeling of sexual attraction towards someone, is mainly mediated by the gonadal hormones testosterone and estrogen.[16,21] Currently, there are already substances that cause a reduction in a person's sex drive. A couple examples are almost all blood pressure pills, opiates such as morphine, anti-androgens and cholesterol drugs containing statin. Most of them, however, are substances used for other conditions and the libido-reducing effect is an unwanted side-effect. Only anti-androgens are deliberately used as a chemical-castration drug, but can also be administered for prostate cancer.[12] From the gonadal hormones, testosterone has the strongest association with the libido. Therefore, current researches that are searching for a specific libido-reducing drug focus on reducing testosterone levels. For example by long term administration of a gonadotropin-releasing hormone (GnRH) agonist analogue called

triptorelin. Triptorelin interferes with the secretion of luteinizing hormone (LH), reducing the synthesis of testosterone.[90] In other studies, levels of testosterone are lowered through the androgen deprivation therapy that was described previously,[91] sometimes combined with substances that inhibit testosterone-triggering hormones.[92] Often these researches were performed on man that were voluntarily hospitalized for paraphilic tendencies such as pedophilia, public masturbation and sex addiction. Although these treatments have shown positive results, they still cause serious unwanted side-effects. The study of Krueger and Kaplan[92] described different side-effects such as nausea, inability to ejaculate or to get an erection at all. Apart from these minor effects, all patients that had a prolonged exposure to the medication reported bone mineral density loss, which puts them at risk for osteoporosis. Furthermore, with the use of testosterone-reducing drugs, there is no selective decrease of one's libido. An overall heard side-effect was an absence of any sexual feelings in general. Thus, it is already possible to completely shut-off the lust motivation system, however currently it is still accompanied by severe side-effects. Furthermore, a more selective shutting-off of sexual feelings is preferable as this is less invasive for someone's normal sex life.

A different strategy of manipulating love is via the attraction-system. Earlier it was described that in the initial stages of love, levels of serotonin are strongly decreased. According to Marazitti and her colleagues, individuals that have recently fallen in love show similarities to patients with OCD. Both show lowered levels of the serotonin transporter protein, hence decreased serotonin.[93] The lowered levels of serotonin probably cause the obsessive thinking patterns that are seen in both people fallen in love and people with OCD. Serotonin reuptake inhibitors (SSRI's) are drugs that are currently administered to patients with OCD, to control their obsessive thoughts. As a side-effect they show diminishing effects on feelings of love. SSRI's influence sex drive[12] and can lead to "blunting" of other emotions that are involved with romantic love. This effect is thought to be caused through the interference of SSRI's with the release of dopamine[94], hence a decrease of dopamine, which is involved with the euphoric feelings when falling in love. Other strategies of manipulation attraction are more theoretical. As SSRI's appear to influence feelings of love by interfering with dopamine, targeting dopamine directly could be a promising approach. Studies have been performed that showed activity of dopamine and the reward-system in romantic love. However, to my knowledge, no studies yet have been focusing on the effect of manipulating dopamine directly on romantic love. Durand-de Cuttoli et al. recently did show that firing of dopamine neurons in the VTA could be influenced by acetylcholine (ACh) receptors.[95] In their study they wanted to figure out the mechanism of nicotinergic ACh receptors (nAChR's) and nicotine in tuning the activity of dopaminergic (DA) neurons and how they mediate the activities leading to nicotine addiction. nAChR's consist of different α and β subunits. Almost all nAChR's in the VTA contain the β2-subunit. The group therefore designed a photosensitizable receptor with a single extra cycline-substitution (β2E61C). This single cycline-substitution is used to attach the photoswitchable ligand Maleimide-Azobenzene-Homocholine (MAHoCl). MAHoCl switches conformation under different photo-circumstances, blocking the function of the receptor at 380 nm and leaving the receptor available for interaction at 500 nm. WT mice got β2E61C transduced in their VTA via a viral vector, and recordings were performed three to four weeks after transduction. The MAHoCl was infused in the VTA at least one hour prior to recording. They found that most MAHoCl-treated DA-neurons of transduced animals showed a decrease in activity when exposed to light of 390 nm and a transient increase with 520 nm (Fig. 7B), where control WT animals did not show this change,(Fig. 7A) indicating ACh-receptors influence firing of DA-neurons. A side note to this study is that they used genetically manipulated mice to generate these photo-reactive ACh-receptors, and this is not applicable in humans. Nevertheless, this gives very interesting perspectives for future research. This study indicates

manipulating ACh-receptors in the VTA could influence DA-neuron firing, which is involved in the reward-system that is so important in the development of attraction in love.

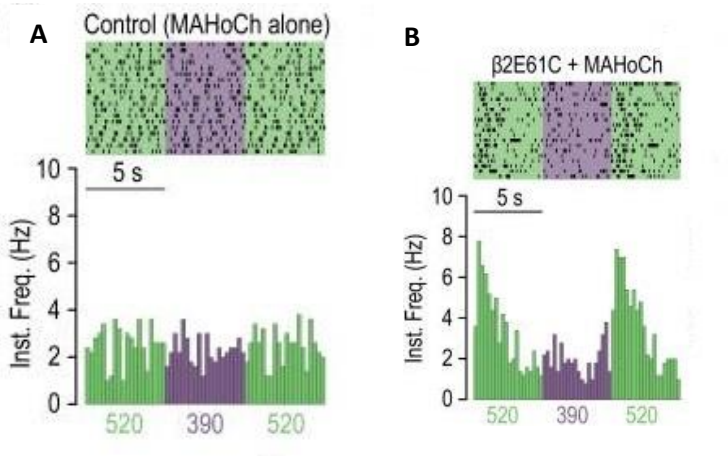

Figure 7. Influence of different light intensities on firing of dopamine (DA)neurons. A) Firing of control WT neurons is not influenced by 320 nm or 590 nm light. B) Most DA-neurons of β2E61C-transduced, MAHoCh treated animals showed a decrease of activity when exposed to 390 nm light and increase of activity when exposed to 520 nm light. *Source: Durand-de Cuttolli et al., 2018, fig.3C&E*

Then, by influencing the neuropeptides oxytocin and vasopressin, the attachment-system can be manipulated. The research that has been performed with different types of voles have provided valuable insights for attachment manipulation. Normally oxytocin and vasopressin mediate the formation of monogamous pair bonds. In prairie voles, that are considered social monogamous animals, blocking oxytocin and vasopressin lead to loss of this monogamous behavior. After blocking these neuropeptides they showed promiscuity and lack of long-term attachment similar to their non-monogamous cousins montane voles.[41,58,59] Interestingly, inducing of attachment also appears to be possible through oxytocin and vasopressin. Normally attachment is formed after sexual interaction, but Insel and Hulihan believed that it could also be induced by solely administering oxytocin without sexual intercourse.[96] They ovariectomized female prairie voles without sexual experience to preclude sexual receptivity. Two weeks after the ovariectomy, the females were infused with either artificial cerebrospinal fluid (CSF), vasopressin or oxytocin via an osmotic minipump for 6 hours. During this infusion period the females were exposed to a sexually experienced male. Then the pump was removed and the female was tested for partner preference in a three-chambered testing area, with the familiar male (partner) tethered on one side and a novel, sexually experienced male (stranger) tethered on the other side. The female was able to move around freely for 3 hours, and her time in contact with the different males during this time was monitored. Females infused with CSF or vasopressin did not develop a partner preference. Of females infused with oxytocin, however, 10/11 did develop a partner preference, which is defined as twice as much time spent in contact with the partner over the stranger. (Fig. 8) Similarly, injection of vasopressin in male prairie voles could induce pair-bonding without sexual interaction.[97] Thus, it appears that pair-bonding, or attachment, can be induced by injecting either oxytocin in females or vasopressin in males. Likewise, blocking of dopamine in the nucleus accumbens caused prairie vole males to be more receptive to sexual interactions with unknown females.[98] These studies, however, are all performed in non-human animals. It is therefore not guaranteed that the mechanisms that work in these voles, will also work

the same way for humans. It is believed though that mechanisms for attachment are highly conserved within species[99], giving it a higher probability this approach can work for humans too.

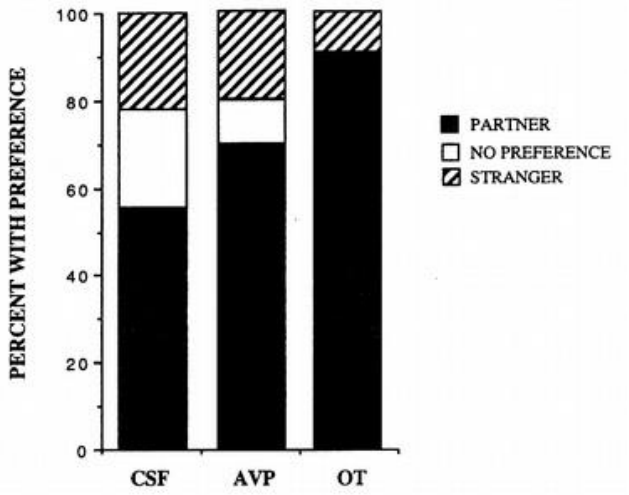

Figure 8. Partner preference in prairie vole females infused with cerebrospinal fluid (CSF), vasopressin (AVP) or oxytocin (OT) via osmotic minipump infusion. *Source: Insel & Hulihan, 1995, fig.2*

With all this options that could possibly influence love, it is not so weird to think a 'love potion' will be invented in the future. Or maybe a pill that stops the feeling of love to help get over a break-up. However, this also raises the question if it is ethically acceptable to use this kind of luxury medication. In the case of individuals suffering from paraphilic tendencies, this kind of drugs is already applied. Personally, I think that is a good cause, as their behavior can be dangerous and harmful for other individuals. However, in situations with more general love, the right point of view is less clear. Some authors claim some couples have the 'duty' to use love-enhancing drugs. As an argument they use that parents have the duty to protect their children for harm, and they qualify a divorce as being harmful to children. Using love-enhancing drugs would save their marriage and protect their kids for harm.[100] It would definitely be a good thing to prevent numerous kids of going through these harmful situations. On the other hand, it is questionable if we as humans should want to manipulate feelings that are brought by nature and are just part of human life. If the situation of love is dangerous for an individual, for example the spouse that refuses to leave their abusive partner, I think it would be acceptable as it could possibly save someone's life. Though, with a situation of troubled love that does not put someone or people around someone in direct danger, being able to manipulating love would be a mean of luxury. Furthermore, enabling love-manipulating drugs to the public could enhance differences between rich and less wealthy people. It is likely these kind of medicine will not be very cheap. Then what would happen is that saving a relationship with drugs becomes only available to the elite. People with less money cannot afford drugs to manage their relationship. Possibly this could lead to overall lower quality of life in the population with low incomes, as their overall satisfaction in relationships is also lower. Overall, this is a discussion that hears pro and con arguments that are both reasonable. I believe that in the end, experience will show how far drugs for love-manipulation will go and which rules will be made to control the use of this drugs.

9. Conclusion

In general, love in humans is seen as a very romantic, poetic phenomenon. In this thesis I tried to explain love from a more biological perspective. Biologically seen, love can probably best be described as a series of behaviors that lead to the formation of a long-term bond between two partners. Most likely, this is an evolutionary mechanism to promote reproduction, survival and support in species where bi-parenting is beneficial. Behaviors of love can be divided in three different sub-motivation systems: Lust, attraction and attachment. Even though all motivation-systems can act separately, they also cooperate, which is actually essential for the development of the concept 'love' as we know it. These motivation systems all have their own underlying neurobiology. 'Lust' is the initiator of love, as it creates sexual attraction to a person. Someone's lust, or sex-drive, is mainly regulated by the gonadal hormones testosterone and estrogen. Testosterone levels are associated with the sex drive in men and women. Males appear to have higher levels of testosterone, which might explain the overall higher urge for sex in men than in women. In the initial stage of love, women show an increase in testosterone. Men, however, show a decrease of their testosterone. This remarkable event is not yet understood. However, some suggest females have to become more man-like and males have to become more woman-like in the initial phase of love, yet the reason why stays unclear. Possibly, somehow this makes them more appealing to the other. Estrogen mainly influences sex drive in women. The high levels of estrogen during the ovulatory phase of a woman's menstruation cycle is associated with higher response to sexual stimuli. Fascinating enough, estrogen also seems to influence the type of man a woman feels attracted to. The main players in the attraction-system are dopamine and serotonin. Dopamine is part of the brain's reward system. Dopamine is released during sex, and probably during other positive interactions with the partner, causing activation of the reward-system when this happens. In short-term and long-term relationships, showing someone a picture of their loved one also evoked an activation of the dopamine reward-system. This indicates that through the reward signals received by sex and spending time together, the reward-impulse evolved to not only being activated by being together but also by thoughts of the partner alone. Serotonin is responsible for the obsessive thoughts about the loved one that occur during the initial intense phase of love. Remarkably, the reduction of serotonin when falling in love shows similarities to a drop in serotonin in patients suffering from obsessive compulsive disorder. Lastly, the neuropeptides oxytocin and vasopressin are shown to be responsible for the attachment-system. The attachment system underlies the process of pair-bonding that is necessary to form a long-term relationship. Oxytocin is involved in pregnancy and forming a bond between mother and child, but is also released during sex, orgasm and skin-to-skin contact. The role of oxytocin and vasopressin in pair-bonding and monogamy was largely discovered in different vole-species. The prairie vole is a monogamous animal, where montane voles do not show this monogamous behavior. Blocking of oxytocin and vasopressin resulted in the loss of monogamy in prairie voles.

In this thesis I also tried to discover a biological explanation for why humans cheat in their relationships. Infidelity can bring a lot of emotional harm to the persons that are cheated on. Overall, some of the highest risk-factors for why people involved in infidelity were low satisfaction in the relationship and low commitment to the relationship. When approached more biological, cheating individuals often show avoidant attachment, which is associated with mental disorders that involve deviant signaling in dopamine pathways. The theory of defective dopamine signaling causing infidelity is, however, rather speculative. More grounded is the theory of Sue Carter, that claims monogamy does not include sexual exclusivity. That is, in most non-human animals that show monogamous behavior, it is rare to observe total sexual exclusivity. That could mean that total sexual exclusive monogamy in humans is more of a forced behavior than instinct. Interestingly, current

literature provides several biological occurrences that can make an individual more prone to cheating. Increased testosterone levels in men, for example, is a predictor of infidelity. Furthermore, two gene-polymorphisms appear to form a risk for extra-dyadic behavior. Men expressing the 7+-allele of the D4 dopamine receptor and the 334-allele of the AVPR1A vasopressin receptor gene show an increased risk of infidelity. It appears that all risk factors for cheating point to a specific type that would involve in extra-dyadic activities more easily. Namely, the thrill-seeking "alpha-male". However, even though most of the risk factors can be associated with specific 'manly' behaviors, it are all separate risk factors that most likely do not occur in one person all at once. On top of that, these risk factors only enhance the chance of someone cheating. Having one of previous risk factors does not guarantee someone will cheat. The absence of the risk factors, similarly, does not guarantee someone will not cheat. Infidelity is most likely caused by a combination of environmental risk factors either enhanced or not by biological risk factors.

This thesis, likewise, tried to discover a biological profile for individuals that refuse to leave a relationship with an abusive partner. As domestic violence causes mental and physical health problems, figuring out a biological explanation for why victims staying in an abusive relationship, could possibly help them. Current literature is, however, not very focused on the underlying biology of this situation. Therefore, I tried to argue this behavior by the neurobiology of love I described earlier. It is likely that the dopamine reward-system and the attachment-system keeps the victims bound to their abusive spouse. The reward-system that is probably triggered when the abusive spouse makes up for their deeds, feeds the feeling of the abused partner to still be in love with the aggressor. At the same time, if the oxytocin/vasopressin system is still triggered, this feeds the attachment of the victim to the abusive partner. Possibly victims that refuse to leave the relationship have an extra strong attachment-system, that causes feelings of attachment despite the violence they are confronted with. This all, however, is largely speculation as there are very little studies covering the neurobiology of domestic violence victims. A higher risk of falling victim to domestic violence has been found for women exposed to domestic violence in their youth. Perhaps there is no underlying biological reason for this behavior at all, however it requires scientific research to clear this up. Future research on this topic could therefore be helpful to all the victims of domestic violence.

Some people are unable to feel love at all. This can be especially harmful for the people surrounding these individuals. Currently, it has been found that psychopaths, which characteristically do not feel love, show less activity in brain areas that involve emotional processing and social decision making. However, there are no studies yet that describe a specific neurobiological profile for all people that claim are unable to feel love. When taking the neurobiology of love into consideration, it could be likely that, similar to the not-monogamous montane voles, they show lower densities of the neuropeptides oxytocin and vasopressin. Those are essential for the feelings of attachment, that people who cannot feel love seem to lack. Similar to the victims of domestic violence, more specific research on a biological profile of people that do not feel love could give us more understanding about this problem.

Finally, this thesis addressed the interesting question if love can be manipulated artificially. If love is regulated on a neurobiological level, it seems likely that manipulating these pathways would also influence the feelings of love. The answer appeared to be just as interesting as the question. Currently a lot of different substances are shown to be capable of manipulating at least a part of love. For example, a diminished sex-drive is an unwanted side effect of drugs that are used for other purposes. SSRI's that are normally used by patients with OCD cause concomitant decrease of one's sex drive. Some anti-androgens are used already to deliberately eliminate the sex drive of individuals showing

paraphilic behaviors. These substances however, often cause an undifferentiated loss of the sex drive. Furthermore, researchers have shown that attachment in prairie voles can be counteracted by blocking oxytocin and vasopressin, where injecting oxytocin caused spontaneous pair-bonding. Likewise, they showed more promiscuity in prairie voles when dopamine receptors in the nucleus accumbens were blocked. This effect on attachment is, however, never tested in humans so far. So, current love manipulating strategies obviously have their shortcomings. Probably, we are still far away from actual “love-drugs”, as it requires further research in humans and fine-tuning so that the separate motivation systems of love can be targeted selectively. The existence of “love-drugs” goes hand in hand, however, with an ethical discussion. Do you interfere with something natural as love, or does that go too far? You could argue that love is just a part of life, including all its difficulties, and does not needs to be manipulated by humans. On the other hand, it could be a genuine solution for preventing for example pedophilia, helping someone to leave a violent relationship or maybe helping someone to actually feel love. With all its pros and cons, I believe this is a very interesting discussion that will only be closed when it is actually possible to produce love-manipulating drugs for humans.

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