universität wien

MASTERARBEIT / MASTER'S THESIS

Titel der Masterarbeit / Title of the Master's Thesis

"The role of endogenous opioids in wanting and liking of social touch"

verfasst von / submitted by

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angestrebter akademischer Grad / in partial fulfilment of the requirements for the degree of

Master of Science (MSc)

Wien, 2020 / Vienna 2020

Studienkennzahl lt. Studienblatt / degree programme code as it appears on the student record sheet:	UA 066 840
Studienrichtung lt. Studienblatt / degree programme as it appears on the student record sheet:	Masterstudium Psychologie UG2002
Betreut von / Supervisor:	Giorgia Silani, Privatdoz. PhD

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Introduction

This study proposes to conduct a systematic, multi-methods and multi-level investigation of two crucial aspects of social reward in humans: wanting and liking. While in animal research these two different neurobiological components of primary reward (e.g. eating) have clearly emerged (Berridge, 1996; Berridge & Robinson, 1998), comparative studies on humans have been controversial (Pool, Sennwald, Delplanque, Brosch & Sander, 2016; Finlayson & Dalton, 2012; Havermans, 2011). It is questionable whether the distinction between wanting and liking applies to humans at all, but the ambiguous results could also be due to a lack of comparability in operationalisations, especially regarding the expected pleasure (Pool et al., 2016). Expected pleasure is deeply connected with the experience one gains throughout their life and can therefore change the "taste" of an acquired rewarding stimulus.

Notably, in the domain of social reward a distinction of wanting and liking has not been established yet. This would be important and useful since behavioural disorders like autism, schizophrenia, anorexia nervosa and depression could be affected by "impaired wanting" rather than "impaired liking". On the contrary, in addiction (e.g. drug abuse or gambling), the imbalance behaves exactly the other way around ("excessive wanting" vs. "impaired liking"). Well-known TV stations such as arte, a German-French collaboration with 1.1 % percent audience share in Germany (Weidenbach, 2020), even advertise using titles such as "Addicted to dopamine", a documentary series in which they want to raise awareness about how apps and social media platforms are designed to get us addicted, so to speak, or how they affect our dopamine release. In the past, dopamine has been seen as the main neurotransmitter in the reward system, but if we turn to more recent research, this is a strongly reductionist view. Other neurotransmitters such as opioids are considered to have a far greater influence on pleasure than dopamine. There is strong evidence that dopamine is only involved in the motivational component and that pleasure perception is mainly regulated and influenced by opioids and opioid-like signals (Berridge, 1996; Berridge & Robinson, 1998).

Since there is an endless number of things that can be rewarding, and research has focused mainly on food (Pool et al., 2016) and monetary rewards (Grabenhorst, D'Souza, Parris, Rolls, & Passingham, 2010), there is a large research gap in the study of social rewards. In this study, we want to get to the bottom of this knowledge gap by using behavioural paradigms and employing psychopharmacological methods combined with electromyography to differentially target wanting and liking for social reward. The long-term goal is to understand whether deficits in social cognition might be rooted in an altered reward

system. The present master thesis, the data of which were collected within the framework of a large-scale study, will focus in particular on the role and function of endogenous opioids in social touch rewards.

Reward

First of all, it is essential to precisely define what we refer to when we speak of rewards in science. In the colloquial context of our everyday lives, reward is generally understood as something given in recognition for an outstanding performance or an effort that has been made. This understanding has evolved as rewards originally functioned as positive behavioural reinforcers which influence the frequency of behavioural responses (Thorndike, 1927; Cameron & Pierce, 1994). From a behavioural perspective, rewards and punishment seem to impact learning through an adjustment of expectations about future events (Schultz, Dayan, & Montague, 1997), also known as operant conditioning (Thorndike's law of effect (1927)). Furthermore, a rewarding stimulus can be paired with a neutral stimulus or behaviour (classic Pavlovian conditioning), which then becomes a conditioned stimulus through associative learning (Pavlov, 1927); this is how many of our habits come about. In this way, a non-rewarding stimulus can be associated with a rewarding stimulus and then becomes rewarding itself. The conditioned stimuli are called higher-order or non-primary rewards, e.g. monetary, artistic, musical, altruistic, transcendent pleasures (Berridge & Kringelbach, 2015).

When speaking of reward in neuroscience, we don't refer to the stimulus itself, but to the positive value or emotional state that living beings attribute to an object, a behavioural act, or an internal physical state, particularly ones which involve pleasure (Schultz, Dayan, & Montague, 1997). Consequentially the reward value is not a static, intrinsic property of a stimulus. As it is strongly connected with the current internal state (e.g. the attractiveness of a stimulus usually increases after deprivation) and former experiences of the individual, "any stimulus, object, event, activity, or situation that has the potential to make us approach and consume it is by definition a reward" (Schultz, 2015).

A main function of our underlying reward system (a group of neural structures which will be described later) is to naturally influence our behaviour in a way that ensures the survival of our species (Rolls, 2000; Schultz, 2015). Thus, the so-called primary rewards refer to our basic needs, such as finding nutrients for survival, maintaining a homeostatic balance, as well as a successful reproduction. The ultimate reward function is fitness and gene propagation of one's self and offspring (Schultz, 2015; Zarrindast, Izadi, Nasehi, Paktinat, & Hoseinpourfard, 2015). This is obviously a quite evolutionary-focused definition of reward,

but since this master thesis is focusing on a specific neurotransmitter (the opioid) system and therefore investigating the functional evolvement of our brain structure, we will use this definition here. Beside learning (in the sense of predicting future rewards), the construct of reward consists of two other key components, namely wanting (the motivational component) and liking (the affective reaction) (Berridge & Kringelbach, 2008; Berridge, Robinson & Aldridge 2009). Since we concentrated on the neuroscientific perspective in the experimental design of the study, we will only consider wanting and liking in the following; there is no evidence to suspect a neurological dissociation of learning, as this process is more likely to run parallel to the other two.

Wanting and liking

Liking refers to the pleasure component and hedonic value of a rewarding stimulus and is defined as the objective affective reaction to a stimulus (Berridge & Robinson, 2003). Pleasure can be distinguished into the fundamental unconscious liking reactions as well as the conscious attributions resulting from the awareness of the actual liking reaction (Berridge & Kringelbach, 2008). Wanting on the other hand is defined as the "attribution of incentive salience to a percept or other representation" (Berridge & Robinson, 2003) and concerns the motivation or drive to seek for rewards. Wanting also includes both, unconscious wanting processes and conscious desires to receive a rewarding stimulus (Berridge & Kringelbach, 2008). To sum up the key points, rewards influence our behaviour even when we are not consciously aware of their presence. Thus, wanting and liking both have a lot in common, but focusing on the differentiation might help us to become aware of what we want and what we actually like. Most people will realize that these two are not always in line, which to a certain degree is totally normal. As with any psychological pathology it is a matter of peculiarity and degree of severity on the dimension, or in this case the size of the gap of these two possibly dissociable variables.

The process of wanting takes place during the phase of anticipation of a stimulus, while liking is rather being assigned to the consumption phase or even after that. The subdivision of these two phases goes back to Ivan Pavlov (1927), who in his conditioning experiments noticed that dogs began to salivate in anticipation of a desired stimulus. In animal studies this subdivision was also confirmed by neurobiological correlates, since different brain areas were active during the two phases (Schultz et al., 2000), therefore we have decided to split the experimental data collection into these two sections.

The two corresponding transmitter systems regarding the neurochemical dissociation of wanting and liking are mainly the dopamine (DA) and the opioid (OI) system. We will go into this point in more detail in the neurotransmitter section.

Social reward

As described above, there are already animal studies that indicate a clear distinction between wanting and liking in primary reward stimuli (Berridge, Robinson & Aldridge 2009). Nevertheless, no comparable studies on humans exist and social reward stimuli have been neglected or not clearly distinguished from primary rewards in previous research.

For social reward, which is a relatively unexplored domain in neuroscience (Purves et al., 2008), no distinction of wanting and liking has been established yet. Such a distinction could be useful for treating clinical disorders of mood and motivation (see Clinical Significance). When it comes to the definition of social reward, theory becomes even more complicated. Albert Einstein stated in his famous work *Why socialism?* (1949): "The dependence of the individual upon society is a fact of nature which cannot be abolished". As we regard it as non-nutrient and non-sexual reward, social reward may arise from a fundamental need for maternal care (Schultz, 2015) and later on the need for belongingness (Baumeister & Leary, 1995; Ferguson, 2010; Lavigne, Vallerand & Crevier-Braud, 2011). Sexual reward is certainly also a social reward, but the reverse is not necessarily true, so the two should be distinguished as carefully as possible (Korb et al., 2020).

In contrast to primary reward, social reward in humans is defined as a pleasurable experience requiring an interaction with another living being, regardless whether it is actually encountered, memorized or simply an imagination. Undoubtedly human behaviour and experience at any given time strongly depend on the presence of others or often only imagined judgement by others, e.g. concern for reputation (Izuma, 2012). But since this need for acknowledgement by others only emerges in the course of development, this appears to be a conditioned higher-order reward. What are – beyond social reputation – deeply rooted social human needs that we can already observe in babies? Unfortunately, a lot of research on mother-child bonding is based on animal studies (Atzil et al., 2017), but the main results are outlined below.

The psychologist Harry Harlow (1958) is well-known for his experiments on baby rhesus monkeys using surrogate mothers. He found out that the little monkeys, which got separated from their mother, preferred a cosy figure that acted as a surrogate mother to a metal framework that only gave them food. When we look at parental attachment to their

babies and vice versa, we can observe the same bonding mechanism in humans (Karen, 1994). This indicates that social reward plays a crucial role from the very beginning of our lives. There are a number of animal experiments that show that social rewards can even be preferred to food rewards, even in a hungry (Mason, Saxon, & Sharpe, 1963) or thirsty (Deaner, Khera, & Platt, 2005) state. Social play (Trezza, Baarendse, & Vanderschuren, 2010) and social touch (Spitz, 1945) is not only pleasant and stress-reducing for all mammals, but even essential for healthy development and to not undergo physical, cognitive, emotional or psychological disturbances (Feldman, 2007). When diagnosing ASD in young children, impoverished social play is therefore considered a major symptom and confluence of the disorder (Jordan, 2003).

However, there is a controversy about whether social reward can be seen as a completely distinct concept from other rewards, like primary reward. Taking a look at Maslow's hierarchy of needs, we can observe that – according to his theory – the basic needs only include physiological and safety needs. After Maslow's theory (Maslow & Lewis, 1987), social needs like belongingness and love, are only taken into account when the basic needs are already satisfied. Maslow's pyramid model has often been criticized as there is clear evidence that it should be argued that social needs are also basic needs (Steverink & Lindenberg, 2006), but the model is still taught as a core important model of needs. The model also stands in contrast to Harlow's observations and that primates sometimes prefer social stimuli over primary ones (Deaner, Khera, & Platt, 2005). Other researchers observed that monkeys preferred to watch images of other monkeys in a live or non-live setting (Anderson, 1998), especially faces of higher ranked monkeys (Tremblay, Sharika & Platt, 2017), over receiving primary rewards. Still, it remains unclear if social rewards are perceived as rewarding as non-social ones. Some researchers (Fareri & Delgado, 2014) used the term social reward but are actually referring to a non-social reward that is embedded in a social situation. Early mother-infant bonding is also very much influenced and shaped by breastfeeding, another primary reward embedded in a social context (Else-Quest, Hyde & Clark, 2003). It is hard to tell if social stimuli are naturally rewarding or if they are simply linked to one's chances to obtain other pleasures (e.g. primary rewards) in the future. Like Mendoza and Schultz stated (2012): "Social interactions provide agents with the opportunity to earn higher benefits than when acting alone and contribute to evolutionary stable strategies". Furthermore, considering "social relationships and mortality risk"-studies in human adults, there is clear evidence that subjective loneliness is the crucial risk factor for morbidity and mortality with much higher effect sizes compared to other predictors like smoking or obesity (Cacioppo, Cacioppo,

Capitanio, & Cole, 2015; Atzil et al., 2017). Accordingly, seeking for social interactions might also strengthen our fitness and therefore again subserves the passing on of our genes.

To conclude it can be noted, considering that social interactions are so critical to our longevity, there might be a reason – evolutionary-wise – why socials behaviours evolved; sometimes even behaviours that put the individual in danger for the benefit of the larger group. For instance, with squirrels, it is the case that in the event of a threat they produce an alarm call which warns their conspecifics of the presence of predator but at the same time puts them in danger (Hare, 1998). Examples of similar behaviours in humans are the firefighters of 9/11 or the people who hid Jews during the National Socialist era (Batson, Van Lange, Ahmad, & Lishner, 2003), although this put their lives at risk without any great chance of gaining something out of it – besides great social recognition beyond their death. As was already exclaimed by Cassio in Shakespeare's famous work Othello (1883): *"Reputation, reputation, reputation! O, I have lost my reputation! I have lost the immortal part of myself."*

The present thesis thus starts from a theory that nature implemented a social reward mechanism in the brain to ensure the survival of the social group and perhaps also the fear of being forgotten and to overcome one's own insignificance.

A number of different stimuli have already been used in research on social rewards in humans (Bhanji & Delgado, 2014; Izuma, 2012), to name just a few: social touch (Gazzola et al., 2012; Nummenmaa et al., 2016; Mohr, Kirsch & Fotopoulou, 2017), joint attention, eye contact (Kampe, Frith, Dolan, & Frith, 2001), pair bonding, giving good advice to others (Mobbs et al., 2015), facial expressions or even just seeing an attractive face (Bray & O'Doherty, 2007). The perception of attractive faces even involves the same brain regions as those involved in primary reward processing (e.g. the orbitofrontal cortex and ventral striatum) (Bray & O'Doherty, 2007). Grabenhorst et al. (2010) used functional Magnetic Resonance Imaging (MRI) to investigate the subjective liking of different rewards: taste in the mouth and warmth on the hand. They found activity in the ventral prefrontal cortex that correlated with both rewards. All this seems to support the common currency hypothesis that different types of rewarding stimuli are based on similar neurotransmitters circles (Kobayashi & Hsu, 2019). However, the inconsistent definitions and standardisations make it difficult to interpret and fully understand the neurological functioning of social rewards and to distinguish it from primary rewards. In this project, we have chosen to use social touch stimuli for the experimental investigation because they play a major role for all mammals for the reasons mentioned above and below.

Social touch

In summary, there is evidence that touch has a variety of positive effects on the immune system, non-aggressive behaviour, heart rate, blood pressure, brain formation and generally a healthy development of human beings. Some researchers might even say that increasing touch could result in the prevention of some diseases (Barnett, 2005). The assumption that social touch – due to its multiple positive effects – activates our social reward system is in line with our initial theory that the social reward system naturally serves to steer our behaviour in a direction that ensures fitness and survival (of one's own and that of the species). Clearly social touch is essential for physical and emotional well-being: Deprivation of touch at an early age has severe emotional and developmental consequences (Spitz, 1945; Harlow, 1958) and even causes a decrease in the infant's metabolism (Schanberg et al., 1995; Schanberg, 2014). Interestingly this impact on the emotional, cognitive and physical development could be treated and reversed by massage therapy or touching and caressing of a caregiver (Field et al., 1986; Daga et al., 1998). In addition, touching promotes social bonding mechanisms, which in turn influences stress and emotional regulation, as well as the social and emotional development, communication and relationship development (Ainsworth, 1970). Hertenstein et al (2006) found that in couples the quality and quantity of social touch correlates positively with relationship satisfaction. Furthermore, many researchers (James Prescott, 1975; Field et al., 1986; Daga et al., 1998; Steven Suomi, 2014; Barnett, 2005) hypothesize that touch has a conducive effect on the immune system and the resistance to disease. Suomi (2014) described how only one month of massage therapy increased the number of natural killer cells in HIV-positive men. Some observers would even go so far as to say, that touching promotes not only growth and communication but also peacefulness and that a lack of touch can lead to aggression and even war (Ashley Montague, 1995, as cited in Barnett, 2005; James Prescott, 1975). The study of the Fore people who live in the highlands of New Guinea, conducted by the anthropologist Richard Sorensen (1976), confirmed that physical contact promotes 'confidence, a realistic self-reliance and an inquisitive experimentalism in children leading to non-aggressive, co-operative adults' (as cited in Barnett, 2005).

In adulthood however, the implication of social touch seems to be more complicated and less well understood. Due to many factors, different meanings can be attributed to social interactions involving touch (Jourard, 1966). Those attributions are of great importance since they lead to different reactions to the touching which can be either positive or negative. On

the one hand, social touch is considered calming and highly rewarding but on the other hand it can generate feelings like anxiety or shame. The different reactions are very personal and shaped by the unique experiences individuals make during their lifetime. Wilhelm, Kochar, Rot and Gross (2001) compared socially high-anxious women to socially low-anxious women and found that the high-anxious individuals reported greater anxiety to a variety of social situations involving touch. Accordingly, the high-anxious individuals also reported an increase of anxiety, self-consciousness and embarrassment after being touched by a male experimenter. Thus, the consequences elicited by social touch can be either likeable or anxiety provoking. This depends on whether the touching is perceived as appropriate or inappropriate (Wilhelm et al., 2001). However, which form of touching is perceived as appropriate and which is not, is shaped by the behaviour of people we observe in our environment. After the social influence theory (Kelman, 1958) not only insecure and socially-anxious individuals, but all people adapt their attitudes, beliefs and subsequent behaviour depending on referent others. Those referent others serve as examples or role models and cause - both intentionally or unintentionally - a change in our behaviour and self-perception in relation to other people and society (Kelman, 1958). Therefore, it can be presumed that some inter-individual differences in the perception and attribution to social touch might be rooted in the (cultural) environment. Studying the perception of social touch and its emotional consequences is complex since the use of touch can have different implications depending on the context and touch-giver. It can be used for calming and consolation (Burkett et al., 2016) but also as an expression of superiority. Touch as a fundamental form of communication can emphasize or even change the meaning of something that is being said. On the contrary, uninvited touch by a stranger is mostly experienced as offensive, intrusive or threatening (Sussman and Rosenfeld, 1978). In brief, social touch underlies a set of implicit rules that define who is supposed to touch whom how and where in which situations (Jourard, 1966).

Social touch paradigm

As has just been explained, social rewards, such as social touch, have a major impact on mammalian development and well-being, but what do we know about the mechanism of action that underlie touching and especially human development? Basic sensory research shows why the skin in particular is suitable as an organ for transmitting pleasant, soothing stimuli. For example, it has been shown that by stimulating free nerve endings, the CT afferents, areas of the limbic system can be directly stimulated, as well as the release of oxytocin – which is often colloquially referred to as the “cuddling hormone” – can be induced

by stimulating these afferents (Morrison et al., 2011). CT afferents in hairy skin are specific mechanoreceptors that are supposed to transmit pleasant touching experiences to the brain; the non-myelinated CT afferents react optimally to slow, gentle stroking movements (1-10 cm/s) at normal skin temperature compared to more myelinated fibres (McGone et al., 2014). It is assumed that their function is to provide pleasant skin contact between people in order to promote touch and bonding or to reduce feelings of ostracism and social stress (McGlone et al., 2014; Mohr, Kirsch & Fotopoulou, 2017).

Self-touching also seems to have an emotion-regulating effect: Grunwald, Weiss, Mueller and Rall (2014) found out by means of an EEG study that spontaneous self-touching, as we do on average 400-800 times per day, reduces emotional dysregulation and concentration difficulties, which was shown by an increase in Theta and Gamma waves. Studies on spontaneous self-touching (de Vries & Fong, 2006; Reissland, Francis, Kumarendran & Mason, 2015) show that we humans make use of this mechanism even before being born: For example, foetuses already touch themselves in utero particularly frequently on the face when the mother is stressed, resulting in physiological self-regulation, which is expressed by a decrease in the foetus' heart rate. However, further neuroscientific studies are needed to understand the molecular mechanisms of touching in more detail.

Facial muscles as an indicator of touch-induced pleasure

Since animals and babies cannot simply be asked whether they experience something as pleasant or not, other ways of measuring had to be found (however, this should also be taken into consideration for adults, as thoughts or statements are often not in alignment with genuine feelings). For this purpose, the examination of facial muscles is useful and has been cited many times in reward literature, e.g. positive food rewards triggered strong facial reactions in human new-borns, juvenile monkeys and adult rats (Berridge, 2000). In adult humans who have undergone an adaptation of their facial expressions in social development, the results of facial data are more difficult to interpret. With them, relaxation rather than activation of facial muscles seems to play a major role and indicator of pleasure (Zeinstra, Koelen, Colindres, Kok, & de Graaf, 2009). Paul Ekman (1988), the best-known researcher on facial muscle examination and emotional interpretation, explains the high variance and sometimes weak significance of empirical findings with the cultural imprinting of expression by social norms as well as culture-related decoding rules.

Nevertheless, EMG research in human children and adults showed that with positive food or odour rewards, the classic frowning muscle Corrugator Supercilii (CS) showed

spontaneous relaxation, while the classic laughing muscle Zygomaticus Major (ZM) tended to go more in the direction of activation (Gilbert, Fridlund, & Sabini, 1987; Hu et al., 1999; Zeinstra et al., 2009). This negative correlation of the two muscles could also be observed when examining spontaneous facial reactions, for example when looking at happy faces (Korb et al., 2015).

Researchers also observed that gentle stroking on the forearm was directly associated with increased activation of the ZM muscle (Pawling, Cannon, McGlone, & Walker, 2017) and with significant relaxation of the CS. By contrast, less preferred social contacts were associated with increased activation of the CS muscle (Mayo, Lindé, Olausson & Heilig, 2018). These results lead to the assumption that stroking the forearm triggers a positive sensation that can be implicitly measured by facial electromyography (EMG) – an instrument that measures facial muscle activity.

Neurobiology of the dissociation of wanting and liking

As a preliminary, it could be summarized that the pleasure reaction (liking) is strongly dependent on the activity of a limited number of hedonic hotspots which are located within the limbic system, whereas wanting seems to be more subject to a widely scattered network of distinct dopamine (DA) pathways which modulate several target regions of the brain (Berridge & Kringelbach, 2015). The example of drug addiction can be used to illustrate very clearly which consequences the neurological dissociation of wanting and liking and in particular an imbalance between the two have in real life: Addicted subjects react with an even stronger DA increase in striatum towards drug-associated cues (e.g. the craving) than towards the drug itself (e.g. the hedonic response) (Volkow, Wang, Fowler, Thomas, & Telangb, 2011). Therefore, compulsive consumption behaviour may arise from a desire to compensate this discrepancy between wanting and actual liking whereby subjects repeatedly attempt to receive the expected rewarding effects and thereby initiate an ever-increasing vicious circle. Astonishingly, another study has shown that administrating dopamine blockades does not affect the liking reaction to tasteful stimuli which supports the theory of DA being involved in the motivational component rather than in the hedonic response (Pecina & Berridge, 2005). The hedonic response seems to depend on (an)other neurotransmitter system(s) which has been comparatively neglected in reward research, therefore this master thesis will particularly focus on the opioid (OI) system (see section after next).

Brain regions of reward-circuitry

To date, conclusions about pleasure causation have only been drawn for a few subcortical brain regions or so-called hedonic hotspots, which can be found in the nucleus accumbens (NAcc), in the posterior half of the ventral pallidum and brainstem parabrachial nucleus (Berridge & Kringelbach, 2015). There are several hedonic opioid hotspots for the enhancement of sensory pleasure, e.g. the administration of an opioid agonist within these hotspots amplifies the core liking reactions elicited by sucrose taste whereas, interestingly, the same substance causes contrary effects outside of the hotspot, so-called coldspots (Berridge, Robinson & Aldridge, 2009).

However, animal studies have shown that these subcortical regions interact with cortical regions such as the orbitofrontal cortex, the insular and the anterior cingulate cortex (Schoenbaum, Roesch & Stalnaker, 2006; Wallis, 2007). Nevertheless, the hypothesis that the cortex is involved in pleasure causation is controversial and lacks empirical studies. Since it is generally assumed that the reward system evolved very early in the evolution of mammals, it is likely that the basic mechanisms and instinctive or affective reactions are more deeply anchored in the brain and that the cortical regions are associated with cognitive processes that go along with pleasure (Damasio & Carvalho, 2013), which makes sense evolutionary-wise, since the mammalian brain has formed from the inside out (Sapolsky, 2017).

Using Magnetoencephalography (MEG) in humans, it was found that direct stimulation of the brain stem (a very deep and early evolved brain structure) was associated with release of endogenous opioids and pain relief and also led to activation of the mid-anterior orbitofrontal cortex (Kringelbach et al., 2007), which appears to be associated with the coding mechanism for subjective pleasure experience in the cortex (Kringelbach, 2005). In addition, Mendoza and Schultz (2013) found out that the striatum plays an important role in the coding of reward during social behaviour, especially in pair-bond formation. Although it could be shown that the striatum is activated during reward stimuli in social situations (Mendoza & Schultz, 2013), it is not quite clear whether the social situation is the reward itself or only the context in which it was anticipated. Furthermore, it remains controversial which rewards truly are fundamental social rewards and which ones society has induced in us (secondary social rewards).

However, there are data that show that the striatum is responsible for linking one's own reward with the behaviour of others (Mendoza, Harris, & Schultz, 2012). These results could serve as a basis for clarifying the question concerning whose action was ultimately responsible for the reward (agency-credit assignment problem). At any rate, social contacts

and rearing conditions have major effects on the striatal anatomy and physiology, both in rodents and primates, as the striatum seems to play a crucial role in integrating social information into coding of social action and reward (Mendoza & Schultz, 2013). Saxo and Haushofer (2008) investigating monetary and social reward, found that these two kinds of reward involved overlapping anatomical substrates and brain regions, such as the striatum and the ventromedial prefrontal cortex. Berridge and Kringelbach (2015) provide several findings supporting this theory in their literature review, claiming that very different types of pleasure activate a surprisingly similar neuronal pathway. Building on this, they propose a common neural currency shared by all (Bhanji & Delgado, 2014; Izuma, Saito & Sadato, 2008; Ruff & Fehr, 2014). By contrast, Rademacher et al. (2010) found reward-independent activation of the limbic system during the anticipation phase, however, different reward patterns for money versus social recognition were found for the consumption phase: Social stimuli were mainly associated with amygdala activation, whereas the thalamus was more strongly activated by monetary rewards. To demonstrate a possible neuronal dissociation of the anticipation and consumption of rewards, further studies are needed. However, previous studies imply that the neural mechanisms underlying reward consumption are more modality-specific than those for reward anticipation, and that they are influenced by the subjective value of a particular reward type. This theory is also supported by Spreckelmeyer et al. (2009) who discovered gender-specific differences in the reward-related activation of brain areas: Men reacted with stronger activation to monetary reward stimuli, whereas women reacted to monetary and social stimuli in the same way. Another study by Gazzola et al. (2011) addressed the question to what extent the assumed gender of touch givers playing a role in the perceived pleasantness of touch. The results suggest that the primary somatosensory cortices (SIs) may be more involved in affective processing than has been assumed so far, since the response of the SIs to a sensory touch is modulated by the perceived gender of the caressing person.

The Opioid (OI) System

OIs and other neurotransmitter systems (such as endocannabinoids or GABA-benzodiazepines) are responsible for generating the pleasurable reactions in our brain (Berridge, Robinson & Aldridge, 2009). Especially for social factors such as social connection, social affiliation, social bonding, attachment and social reward, a strong connection with endogenous OIs was found (Ignaki, 2018). This theory is supported as OI antagonists (e.g. Naltrexone) can greatly reduce feelings of social connectivity and affiliation (Ignaki et al., 2016). Furthermore, social exclusion, loss or separation leads to a reduction of

endogenous OI activity and thereby elicits feelings of disconnection or separation distress (Panksepp et al., 1978). Moreover, regarding social reward, there was found a strong link between OI activity in the Nucleus accumbens (NAcc) and positive feedback and attribution to social interaction in humans (Meier et al., 2016). Furthermore, according to the OI theory of social attachment, endogenous opioids are released especially during bonding experiences and inhibit separation distress (Panksepp, Herman, Conner, Bishop, & Scott, 1978). Opioid antagonists have been shown to increase social care in non-human primates (Graves, Wallen, & Maestripieri, 2002), hence the hypothesis that low endogenous opioid levels are associated with affiliate behaviour and social bonding. Nummenmaa et al. (2016) found that social touch in humans triggered feelings of pleasure and thereby increased the availability of μ opioid receptors (MOR) in the thalamus, striatum and frontal, cingulate and insular cortices. Changing the activity of the opioid system through social touch may therefore represent a neurochemical mechanism that strengthens social bonds between people. Ultimately, however, synthetic opioids – which are mostly used as pain killers – are often associated with the development of addictive behaviour (Lutz & Kieffer, 2013).

Neurochemical features of OIs

Endogenous OIs are peptides that can act as neurotransmitters, neurohormones or as moderators of other neurotransmitters. A distinction is made between three different endogenous OIs: encephalin, dynorphin (both ubiquitously present in the central nervous system) and endorphin (which occurs particularly in regions where pain occurs). Endogenous OIs bind to receptors found especially in the thalamus and limbic system (Horn, 2009). To date, three different types of receptors have been identified: The μ-receptor (great affinity for β-endorphins and enkephalins), the κ-receptor (great affinity for dynorphins) and the δ-receptor (great affinity for enkephalins). B-endorphins and a range of exogenous opioid agonists and antagonists bind in particular to MORs and the endogenous mesolimbic opioid system is associated with the rewarding effects of primary rewards (e.g. food or drugs) (Henriksen & Willoch, 2008), but also with several kinds of social rewards (Trezza, Damsteegt, Achterberg, & Vanderschuren, 2011; Nummenmaa et al., 2016). Clinically used OIs often act selectively via the μ-receptor or at least have a high affinity for it, e.g. Naltrexone (Horn, 2009). It is assumed that OIs are mainly found in areas of the central nervous system associated with pain perception, modulation of affective behaviour and neuroendocrine functions.

Clinical and Societal Significance

The distinction of wanting and liking has high clinical relevance, since widespread inheritable clinical disorders like autism (ASD), schizophrenia, anorexia nervosa and depression could be affected by “impaired wanting” rather than “impaired liking” (Barch, Treadway, & Schoen, 2014; Treadway & Zald, 2011).

ASD was first defined in 1943 as "profound lack of interest in others" (Leo Kanner, 1943, as cited in Blacher & Christensen, 2011). By contrast, modern theories regarding ASD propose that it could be affected by a disruption of social motivational mechanisms whereas liking of social engagements seems not to be impaired in people with ASD (Chevallier, Kohls, Troiani, Brodkin & Schultz, 2012). Hence, deficits in social cognition (e.g. theory of mind, mentalization) might not be the cause but the consequence of disrupted social interest. Empirical support for those theories would have a major impact on treating methods and possibilities of ASD. In order to understand whether people with ASD do not find social interactions rewarding or whether they simply lack motivation to engage them, it is essential to understand how the brain encodes social interactions and social rewards.

On the other hand, in addiction cases the sensitization of the mesolimbic system may cause compulsive pursuits of the rewards, which is linked to an excessive increase of wanting but rather a decrease of liking by the habituation effect (Berridge, Robinson & Aldridge 2009; Robinson & Berridge, 2008). Although humans naturally have various predispositions, neurobiological and neurochemical constitutions, substance abuse has a great impact on the formation of our brain and changes the constitution of receptors and the natural availability of endogenous neurotransmitters after frequent use.

Another example regarding addiction (without the intake of any substances) is social media. When taking a closer look at this topic, it can be observed that many people have a strong urge to be online and “socially networking” at all times, but at the same time cannot enjoy it as much. Many even suffer from concentration restrictions or depression as a result (WHO, 2011). All this leads to the assumption that our reward system (which is actually supposed to steer our behaviour in a positive species-preserving direction) can be changed in a way that causes damage and disappointment. That is, when wanting and liking of rewards are off-balance.

Perceived social isolation is very harmful to humans and causes high mortality risk rates (Cacioppo, Cacioppo, Capitanio, & Cole, 2015) which is another argument that social media and the context of rapid digitisation play an important role. Although we are connected online at all times, we often feel lonely, as deep and fulfilling relationships (which is the

crucial factor for human health and well-being) gradually diminish. Economic and socio-political actors yet take advantage of the vulnerability of the human reward system and its weakness in manipulation, e.g. by developing software that is addictive in a way that we constantly have the urge to use them.

At this point it is important to mention, that through linguistic abstraction ability, human beings have the possibility of drawing rewards from very different, sometimes purely psychological or intellectual processes. For example, we can experience social rewards in daydreaming by imagining a pleasant social interaction or by virtually connecting with people, often not even real ones, e.g. virtual character figures or simulation robots (Frederiks, Kröse & Huisman, 2016). How can such moments (of pleasure) be differentiated from "genuine" social interactions? Given that the ability of linguistic abstraction changes the object itself, we must take into account once again that we cannot simply transfer animal studies to humans, but must carefully weigh and interpret the results.

In many societies, social behaviour is already a criterion for obtaining privileges or access to higher-class-institutions (Izuma, 2012). Social behaviour and incentives have thus already become instruments in the public context and in this way, exert an influence on our reward system. Since the adaptation of our biology and genetics is slower than that of the environment, further discrepancies and risks of maladaptation arise. If we look at the current “social credit system” in China (Creemers, 2018), it is hardly possible to investigate whether social behaviour is intrinsically or extrinsically motivated, although a meta-study on reinforcement through reward revealed, that there was no negative impact found unless a positive reinforcer was taken away (Cameron & Pierce, 1994). Recent developments underline once again the importance of handling science and study results in an ethical and confidential manner: not all stakeholders put the well-being of people first.

However, if we take a look at social-man theory from industrial psychology, it can be noted that social reward (interactions, recognition, etc.) is essential to stay healthy and work effectively at the same time (Dingley, 1997). Thus a few reinforcers and psychological nudges in that direction can't hurt. Furthermore, Meier and Stutzer (2007) propose a strong correlation between intrinsic pro-social behaviour like volunteering and life-satisfaction.

In order to implement strategies to restore or treat maladaptations and manipulations of the reward system, we propose to gain a deeper understanding of the neurological dissociation of wanting and liking and the corresponding neurotransmitter systems in humans.

Aim of the study

For reasons that have just been explained, there is an urgent need for research that examines whether wanting and liking really differ regarding underlying neural circuits and neurotransmitters involved for human subjects. Thus, the aim of this study is to investigate the role of endogenous opioids in wanting and liking of social reward with a psychopharmacological study in a healthy sample.

Research question

It should be emphasized again that this master thesis was only part of a large-scale study, which includes both, primary and social reward. In the whole project, the focus does not only lie on the opioid system, but also the dopamine system, which seems to be the crucial neurotransmitter for wanting (e.g. the motivation or drive to get a wanted stimulus). Participants who have been administrated the dopamine antagonist amisulpride were expected to have lower scores in wanting (in terms of ratings and force) but remain at the same level of liking (in terms of ratings and muscle response) as participants of the control group. Participants who have been administrated the opioid antagonist naltrexone were expected to have lower scores in liking and wanting social rewards than participants of the control group, but based on current data, exert a stronger influence on liking. Thus, the ultimate research question for this master thesis is: "Which role do endogenous opioids play in wanting and liking of social rewards?". We will explore the five individual research questions derived from it in the next section and elaborate each of the hypotheses to be tested.

In the following I have developed two basic questions (Question 1 and 2) respectively initial hypotheses (H1 and H2), while Questions 3-5 represent the aspects of the research question that are actually of interest.

1. Do participants exhibit higher ratings of objective and subjective wanting in response to their preferred social rewards?
2. Do participants show higher ratings of objective and subjective liking in response to their preferred social rewards?
3. Does naltrexone (opioid antagonist) influence subjective and objective liking of social reward?
4. Does naltrexone (opioid antagonist) influence subjective and objective wanting of social reward?
5. Is the effect on liking stronger under the influence of naltrexone than the effect on wanting?

Hypotheses

In summary, the hypotheses to be tested for this study are as follows:

H1: There are changes in objective and subjective wanting in response to different types of social rewards.

1a. Participants indicate higher ratings of wanting for high-reward versus low-reward stimuli.

1b. Participants exhibit higher force for high-reward versus low-reward stimuli.

H2: There are changes in objective and subjective liking in response to different types of rewards.

2a. Participants indicate higher ratings of liking for high-reward versus low-reward versus very low-reward stimuli.

2b. Participants demonstrate higher ZM activity for high-reward versus low-reward versus very low-reward stimuli.

2c. Participants exhibit lower CS activity for high-reward versus low-reward versus very low-reward stimuli during consumption.

H3: Naltrexone influences objective and subjective liking for different types of social rewards.

3a. Naltrexone influences the ratings of liking for high-reward versus low-reward versus very low-reward trials.

3b. Naltrexone influences CS activity for high-reward versus low-reward versus very low-reward trials compared to a placebo during consumption.

3c. Naltrexone influences ZM activity for high-reward versus low-reward versus very low-reward trials compared to a placebo during consumption.

H4: Naltrexone influences objective and subjective wanting for different types of rewards.

4a. Naltrexone reduces the ratings of wanting for high- versus low-reward trials.

4b. Naltrexone reduces the force exerted for high-reward versus low-reward trials.

H5: The effect on liking is expected to be higher under the influence of Naltrexone than the effect on wanting.

Methods

Sample

The present sample consists a total of 43 voluntary participants – 12 male and 31 female subjects with a mean age of 23.0 (*SD* = 3.8), ranging between 18 and 35 years. The average Body Mass Index (BMI) was 22.27 (*SD* = 2.59), ranging between 17.72 and 27.58 kg/(cm/100)^2. All participants had regular blood panel and electrocardiogram (ECG) measurements, reported being right-handed, to smoke less than five cigarettes daily, not to suffer from lesions or skin disease on the left forearm, and to be free of psychiatric or neurological disorders. Another requirement was to have fluent German language skills. Psychology Students were excluded because they could be familiar with the content of the study. Moreover, to rule out any possible confounding factors, participants could not have any impairments in sight or hearing. In order to avoid any sexual or romantic attributions to the touching – which was provided by a same-sex experimenter – homosexuals and bisexuals were excluded. Each participant had to sign an informed consent before the testing and received monetary compensation (at least 90 €).

The study was approved by the Ethics Committee of the Medical University of Vienna and followed the regulations of the Declaration of Helsinki (World Medical Association, 2013).

Description of stimuli

To examine social reward three different touch stimuli were given to the participants. To obtain three comparable and differently pleasant stimuli, there should be no difference in the quality of the touching between and within the experimenters. The three standardized touch stimuli were administered during six seconds on a previously marked 9 cm area on the forearm, starting from the radial bone. The same-sex experimenter, who administered the touches, received the respective signals for the pace through headphones, which set the rhythm of the movement (6 cm/s, 21 cm/s and 27 cm/s). The touch was performed with only two fingertips (Index and middle fingers) and the applied pressure was maintained at a constant level.

Corn starch powder was applied in order to balance the skin's moisture to ensure that the touching was smooth and pleasant. The selection of the stimuli and procedure were based on the social touch paradigm and pilot testing.

Study Procedure

The present thesis is part of a larger project encompassing both primary and social reward (Taste & Touch) and will focus in particular on the role and function of endogenous opioids in social reward. The Taste & Touch Study proposes to conduct a systematic, multi-methods and multi-level investigation of two crucial aspects of social reward in humans: wanting and liking. Therefore, the role of endogenous dopamine and opioids were investigated by manipulating the two different neurotransmitter systems by administrating in a single pill either 50 mg of the opioid antagonist naltrexone (brand name Dependex) or 400 mg of the dopamine antagonist amisulpride (brand name Solian) to the two experimental groups. The control group received a placebo pill. The study took place in the University Clinic for Psychiatry and Psychotherapy (Allgemeines Krankenhaus der Stadt Wien – AKH) and was divided into two phases on two days. The data for this paper was collected in a 6-months period from February until July 2018.

As the present thesis only examined the effect of endogenous opioids and their receptors, other parts of the study (e.g. the experimental dopamine group) will be excluded in the following description of the methods.

The naltrexone group comprised 22 participants and the control group 21 participants. The allocation to the two experimental conditions was randomized. The setting was standardized, i.e. environmental conditions were kept as constant as possible (screen distance, fixation cross, room lighting, room temperature etc.). A blood sample was taken again from the test person after the main experiment (about five hours after taking the pill).

Naltrexone as an Opioid antagonist (drug condition)

Naltrexone is a pure opioid antagonist (inhibition of all opioid receptors, but with highest affinity for μ-receptors) with no intrinsic activity (Lee, Wagner, Tanada, Frost, Bice, & Dannals, 1988). However, compared to other opioid antagonists (e.g. naloxone), naltrexone has the advantage of a longer half-life (up to 24 h) and the possibility of oral administration (Karow & Lang-Roth, 2009). In medicine, naltrexone is mainly used to prevent opioid-induced respiratory depression or in withdrawal therapy for opiate or alcohol dependence (Minozzi et al., 2011). Naltrexone should not be administered to patients with opioid dependence or to patients with heart disease; in other people, the drug has proven to be very low-risk in the prescribed dosage (Karow & Lang-Roth, 2009).

Facial Electromyography (EMG)

By means of current facial EMG technology it is possible to monitor two major muscle groups: the CS and ZM muscle groups. The former is being associated with frowning, the latter with smiling. Electrodes are attached to the cheek and on the inside of one eyebrow to measure the electrical impulses associated with movements of these muscles. Data captured from the electrodes are then processed and analysed to draw conclusions about the emotional state of a person. Compared to a simple observation of facial expressions, EMG offers an exact measurement of barely noticeable and even (unconsciously) suppressed muscle movements. Despite the positive results and comparatively simple application, facial EMG was rarely used to investigate implicit sensations of pleasure (Pool et al., 2016).

Selection of participants

Prior to laboratory testing, participants had to pass an online screening questionnaire and answer standard questions on the phone. Among other requirements, the Social Touch Questionnaire (STQ) by Wilhelm et al. (2001) was given to ensure that none of the test persons had an aversion to being touched. Eligible subjects were invited to another screening procedure in the laboratory (T0). After signing the informed consent, they were given *Mini-International Neuropsychiatric Interview* (M.I.N.I.) – a questionnaire about clinical and personality traits (Sheehan et al., 1998). Moreover, a doctor took a blood sample from each participant and tested their general health condition by means of an EKG. If no exclusion criteria were found and the subjects had qualified to participate in our study after T0's tests and preliminary investigations, they were invited to the main testing (T1) which had to take place up to a maximum of 60 days after the first lab visit.

Preparation time

On the day of the main testing, participants were not allowed to have eaten for the last 6 hours before arriving at the AKH. The doctor first took a urine sample to ensure that participants had not consumed drugs and also to rule out pregnancy, as some of the drugs administered could have been potentially harmful in such a case. If the urine test was negative, the study doctor gave them a pill containing either 50 mg Dependex (naltrexone) or a placebo pill containing mannitol (i.e. sugar); the pill was administered randomized, double blind and counter balanced. Since there was a low but not insignificant risk of undesirable side effects (some subjects felt a little dizzy or tired), the study doctor was always available during and after the testing. Right after the pill was taken, participants received their first

snack (an oat energy bar) and got offered another one later on. In this way, we ensured that the drugs had approximately the same blood concentration at the time of the different tests and experiments. The Taste & Touch experiment started approximately 3 hours after pill administration for the effect of the drug to unfold. During the waiting period, the participants were allowed to read neutral magazines provided to them. However, they were not allowed to read their own books and especially not to use a smartphone or laptop. They were also asked to do several independent computer tests and questionnaires. About 180 and 300 minutes after taking the pill, the doctor checked the participant's condition and potential side effects.

Dependent Measurements

Stimuli Rating

Participants were asked to sit at a table with a screen on it and put their left forearm comfortably on a pillow. They were firstly exposed to the three different touching stimuli in order to give subjective ratings on them. For the administration of the touch stimuli, a curtain blocked the participants' view of the experimenter so that they were not biased by any experimenter preference and could concentrate fully on the sensation of touch. Both experimenters were present during the whole experiment: one experimenter administered the touch stimuli while the second one was responsible for the instructions. While receiving the touches on the left forearm, participants were sitting in front of the computer screen on which different icons for each of the 3 stimuli were announcing the respective stimuli. After receiving one stimulus after another they were asked to rank the stimuli from least pleasant to most pleasant. All ratings were conducted on a continuous visual analogue scale (VAS) ranging from -10 to +10). A photo of the experimental setup is provided in the appendix.

Behavioural assessment of touch-induced wanting and liking

Dynamometer

The motivation to receive a certain stimulus (the 'wanting' component) was recorded by the collection of data from a Dynamometer (HD-BTA, Vernier Software & Technology, USA). After having rated the stimuli, participants should press the Dynamometer as strongly as they could in order to measure their maximum voluntary contraction (MVC). For the final MCV estimation, the maximum value of three trials was taken.

Facial EMG procedure

After MVC and the explicit 'liking' preferences had been collected and averaged, the preparations for the electromyogram (EMG) began. For this, a total of six electrodes with gel and adhesive stickers were attached to the participant's left side of the face. Before sticking the electrodes, the face was thoroughly cleaned with alcohol, face scrub and water so that the signal was not reduced by any deposits on the skin (such as cream or skin flakes). The EMG was used to measure facial muscle activity during the experiment in order to assess how the participant unconsciously reacted to the given stimuli, apart from the ratings. For positive sensations, the activity of the Zygomaticus Major was used and for adverse sensations the activity of the Corrugator Superciliis. Two Ag/AgCl electrodes with 4 mm inner diameter per muscle, as well as a reference and ground electrode were attached (Fridlund & Cacioppo, 1986). EMG was acquired with a sampling rate of 1200 Hz using a g.USBamp amplifier (g.tec medical engineering GmbH, Austria), and the Matlab software (the Mathworks, Inc.).

EMG data were preprocessed in Matlab R2014b (www.themathworks.com), partly using the EEGLAB toolbox (Delorme & Makeig, 2004). A 20 to 400 Hz bandpass filter was used, then data were corrected and smoothed with a 40 Hz low-pass filter. Phases were then extracted that corresponded to periods of reward anticipation and consumption.

Main experiment

First of all, it had to be ensured that the participant was in a comfortable position to hold this position for an hour and a half, as any motion could distort the EMG recording. The participant received a standardized instruction and conducted four practice trials under the guidance of one experimenter. The experiment was divided into four blocks, two social reward and two primary reward blocks encompassing 20 trials each. The blocks were counterbalanced in order across different participants to prevent serial effects, but social and primary reward blocks were always alternating.

Each social reward trial contained the following steps: One touch stimulus (either the most or the second preferred) was presented on the screen by its icon. It was explained beforehand that they would either receive the presented stimulus (Option A) or the least preferred stimulus (Option B), depending on the effort invested. The participants had to indicate how much they wanted the presented stimulus on a VAS (not at all – a lot). The participants were then asked to press the dynamometer to obtain their desired stimulus. The probability to receive the announced stimulus over the least preferred stimulus was linearly determined by the exertion of force. If participants accomplished 90 % of their maximal

strength, the probability to receive option A was 90 % and thus the probability for option B was 10 %. For four seconds, participants received a visual feedback of their force in form of a rising bar. Afterwards another icon appeared to show them which stimulus they would receive. After having received the according stimulus, there was a short relaxation phase before the participants were asked to rate how much they liked the stimulus on a VAS (not at all – a lot). There were also several trials per block without pressing to ensure that each participant received all the stimuli to avoid missing data for statistical analysis, as shown in Figure 1(Korb et al., 2020).

After each block, the participants were allowed a short break and the experimenter looked behind the curtain to check on the participant.

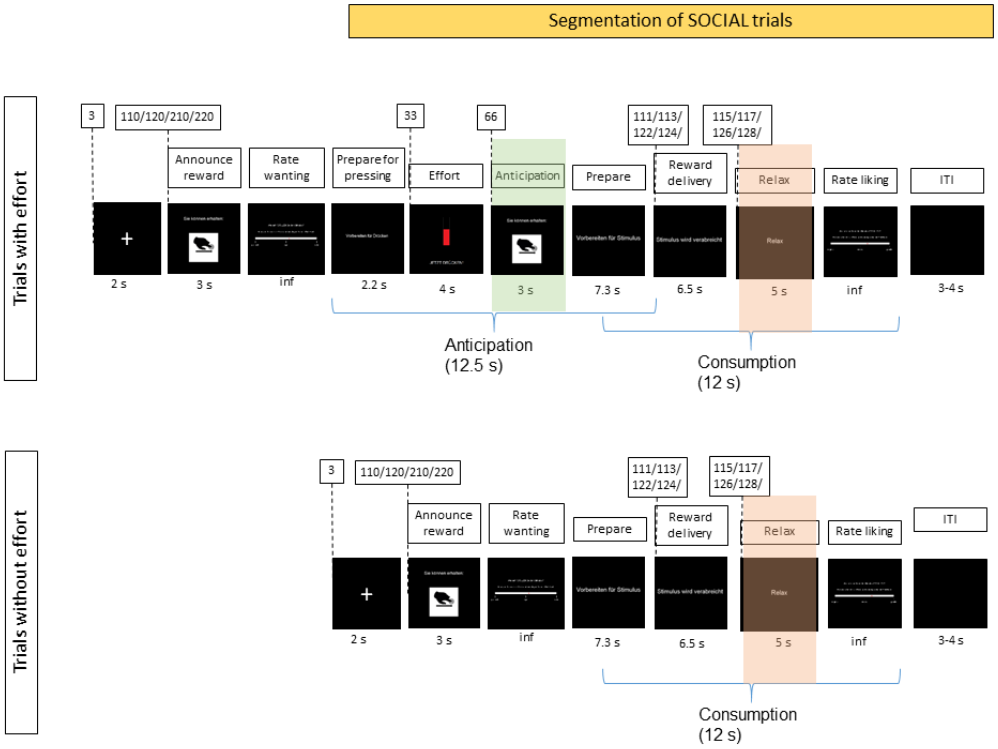


Figure 1. Step-by-step description of each trial of the experiment

Statistical Analysis

Descriptive and inferential statistical analyses were performed using IBM SPSS® 26 for Mac OSX statistical software. The significance level was defined in advance as $\alpha = 5\%$, so a result of $p \leq .05$ in inferential statistics is considered significant. To evaluate the practical relevance of the results, the standardized effect sizes η^2_p with classification thresholds ≥ .01 for small, ≥ .06 for medium and ≥ .14 for large effects, and *d* with classification thresholds ≥ 0.20 for small, ≥ 0.50 for medium and ≥ 0.80 for large effects, were taken into account (Cohen, 2013). The descriptive statistical representation of characteristic values of metric

parameters were based on the mean value (*M*), standard deviation (*SD*) of the measured values as well as the percentages of the EMG values and intensities of the exerted force measured in the dynamometer.

The inferential statistical analyses were carried out using variance analyses (ANOVA GLM), taking into account both between-subject-factor (drug – placebo vs naltrexone) and within-subject-factor (the dependent variable in the stages of the repeated measurement – 2 stages for wanting and 3 stages for liking). For the within-subject-factors the sphericity, tested by Mauchly's test, had to be taken into account. In case of a correction, the factor ε was used for correction. The variance homogeneity was tested by Levene's test. Welch's t-test was used to test the group differences following variance analyses (follow-up), since it is known to be robust to procedural constraints (Kubinger, Rasch & Moder, 2009).

Results

First of all, the prerequisites of our analysis have been examined. For this we had to investigate by means of a within-subject design whether our test persons really differed with regard to the liking of different touch stimuli and also whether their motivation to receive a certain stimulus was also in line with their stated preference. Subsequently, the two experimental groups (drug vs. placebo) were investigated using a between-subject design.

Explicit Measures of Wanting and Liking

Analysis of explicit wanting (Rating on a VAS)

Using 2-way (2x2) mixed rmANOVA, the differences between the two experimental groups (between-subject-factor drug with the levels naltrexone vs. placebo) and changes in ratings of wanting with respect to the two reward types (within-subject-factor, high vs. low) were examined. The interaction effect of wanting*drug condition was not significant with $F(1, 41) = 0.216$, $p = .645$. Therefore, the main effects could be interpreted without restriction. The difference between the two conditions was not significant with $F(1, 41) = 0.011$, $p = .915$, whereas the within-subjects factor was significant with $F(1, 41) = 29.871$, $p < .001$, $\eta^2_p = .53$). Figure 2 shows the ratings of explicit wanting regarding the two reward types.

Concluding, there is a significant decrease of subjective wanting within the two reward types (high, low), but there was no significant difference between the experimental groups.

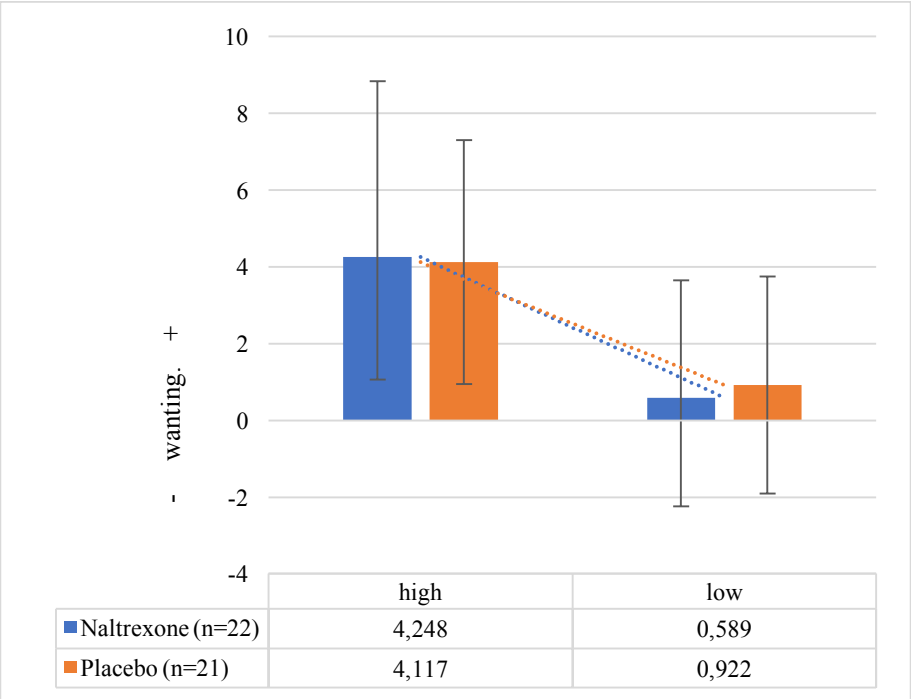


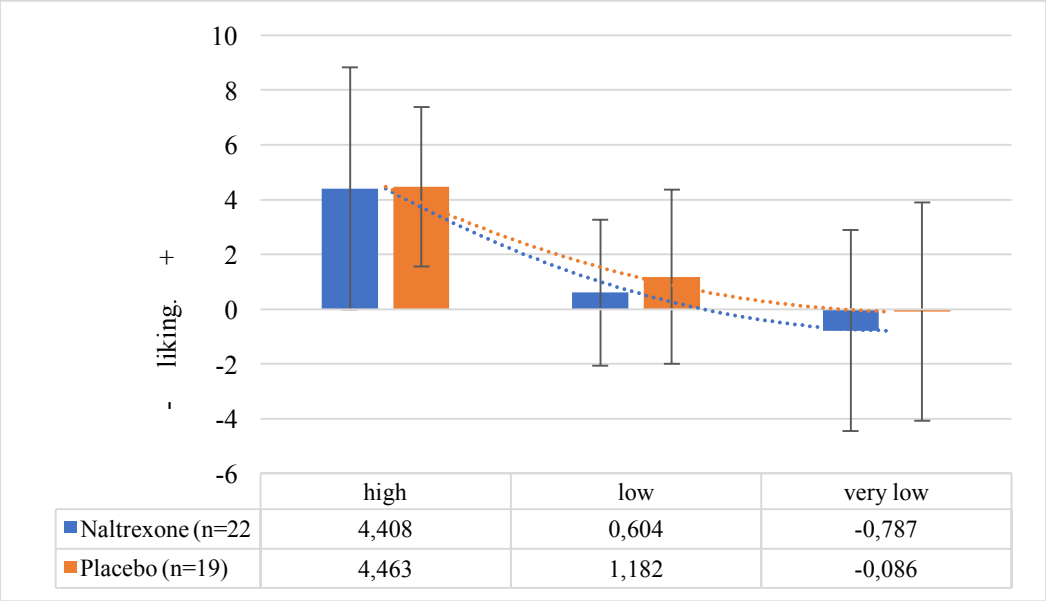
Figure 2. Extent of subjective wanting, depending on drug condition and reward types

Analysis of explicit liking (Rating on a VAS)

Using 2-way (2x3) mixed repeated measures ANOVA (rmANOVA), the differences between the two experimental conditions (between-subject-factor) and changes in ratings of liking with respect to the three reward types (within-subject-factor) were examined. Sphericity could not be assumed (Mauchly's test with p = .001 was significant), correction according to Huynh-Feldt (ε = .81) was necessary. The interaction effect of liking*drug condition was not significant with $F(1.61, 62.92) = 0.138$, p = .827. Therefore, the main effects could be interpreted without restriction: The difference in liking between the two conditions was not significant with $F(1, 39) = 0.299$, p = .588, whereas the main effect of the within-subjects factor reward types was significant ($F(1.61, 62.92) = 29.871$, $p < .001$, η^2_p = .43). Figure 3 shows the ratings of explicit liking regarding the three different reward types.

Pairwise post-hoc comparisons with Bonferroni correction showed a significant difference of liking between high vs. low ($p < .001$) and high vs. very low ($p < .001$), however the difference between low vs. very low remains marginal (p = .086).

Concluding, there is a significant decrease of subjective liking within the three reward types (high, low, very low), but there was no difference observed between the experimental groups.



	high	low	very low
Naltrexone (n=22	4,408	0,604	-0,787
Placebo (n=19)	4,463	1,182	-0,086

Figure 3. Extent of explicit liking, depending on drug condition and reward types

Implicit Measures of Wanting and Liking: Effort and Facial EMG

Analysis of implicit liking (Facial EMG)

For the following analyses cases with z-values *SD* > 3 above the mean in the dependent variable within the own group were excluded. The outliers were considered separately for each analysis.

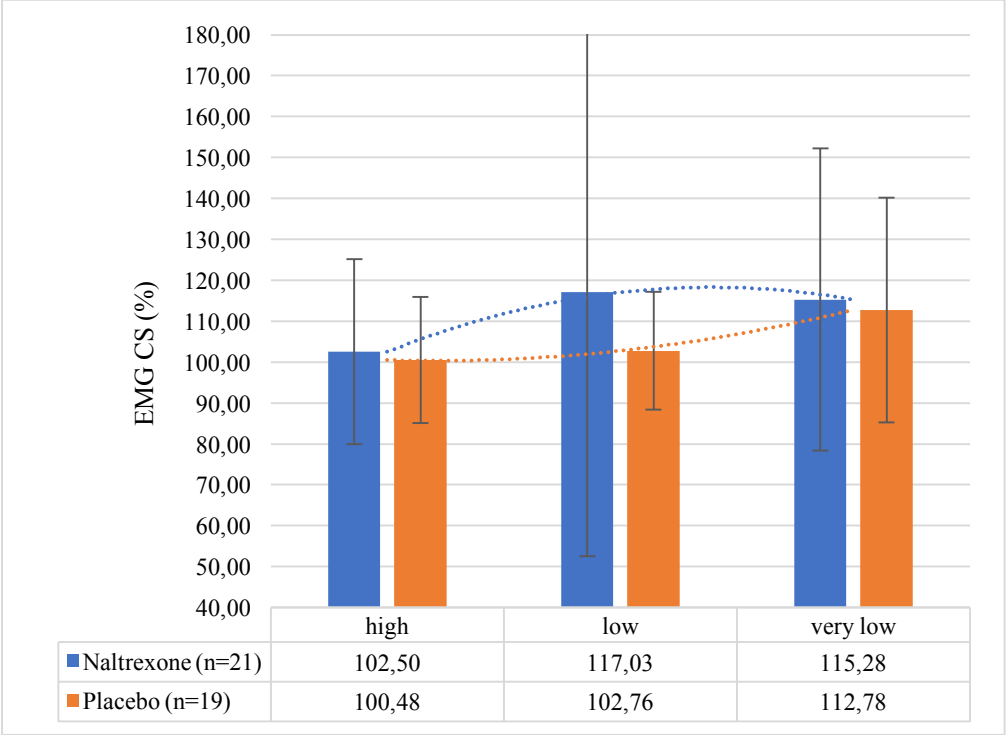
Consumption Phase (T1 – T5)

Corrugator Supercilii

Using 2-way (2x3) mixed rmANOVA, the differences between the two experimental conditions (between-subject-factor) and changes in EMG CS with respect to the three reward types (within-subject-factor) were examined. Sphericity could not be assumed (Mauchly's test with p=.001 was significant), correction according to Huynh-Feldt with ε = .81 was adequate. The variance homogeneity, tested by Levene's test, was given with p = .143 for the reward type high, for reward type low with p = .122 and for very low with p = .179. The interaction from reward type*drug condition was not significant with $F(1.62, 61.42) = 0.536$, p = .550. Accordingly, the main effects reward and condition could be interpreted without restriction.

For the main reward type effect, a non-significant difference of the EMG values between the different reward types (high, low, very low) could be found under the correction of Huynh-Feldt with $F(1.62, 61.42) = 1.820$, p = .177. Between the two groups, $F(1, 38)$ = 0.601, p = .443 a non-significant small effect (η^2_p = .02) was found.

Furthermore, follow-up Welch-t-tests were performed for independent group comparisons for the reward types. For the reward type high a non-significant difference of the EMG values were observed with $t(35.39) = 0.334$, $p = .740$ (two-tailed), as well as for the reward type low with $t(22.20) = 0.987$, $p = .334$ (two-tailed) and for very low with $t(36.67) = 0.244$, $p = .809$ (two-tailed). Figure 4 shows the extent of implicit disliking (CS) regarding the three reward types.



	high	low	very low
Naltrexone (n=21)	102,50	117,03	115,28
Placebo (n=19)	100,48	102,76	112,78

Figure 4. Extent of EMG in % (CS), depending on condition and reward types

Zygomaticus Mayor

Using 2-way (2x3) mixed rmANOVA, the differences between the two experimental conditions and changes in ZM with respect to the three reward types were also examined. Sphericity could not be assumed calculating Mauchly's test with $p = .003$; the correction according to Huynh-Feldt ($\varepsilon = .83$) was suitable. The variance homogeneity, tested by Levene's test, could be assumed for the reward type high with $p = .698$ and for very low with $p = .480$. For reward type low, homogeneity was restricted with $p < .001$, but ANOVA is robust due to the similar cell population (Backhaus et al., 2006). For the interaction of reward type*drug condition a significant result could be observed with $F(1.65, 59.50) = 3.443$, $p = .047$ ($\eta^2_p = .09$). Accordingly, the main effects reward and condition had to be interpreted with caution.

For the main effect of reward type, a non-significant difference of the EMG values between the different reward types (high, low, very low) could be found under the correction of Huynh-Feldt with $F(1.65, 59.50) = 2.960$, $p = .069$ ($\eta^2_p = .08$). Between the two groups, $F(1, 36) = 3.364$, $p = .075$ (two-tailed) a medium effect ($\eta^2_p = .09$) was found for tendentially higher EMG values of the naltrexone group. Furthermore, follow-up Welch-t-tests were performed for independent group comparisons for the reward types. For the reward type high a non-significant difference of the EMG values were observed with $t(34.90) = 0.318$, $p = .752$ and for very low with $t(35.99) = 0.384$, $p = .703$. However, for the reward type low a significant difference was observed with $t(19.89) = 2.248$, $p = .036$ (two-tailed), representing a medium effect ($d = 0.73$), as shown in Figure 5.

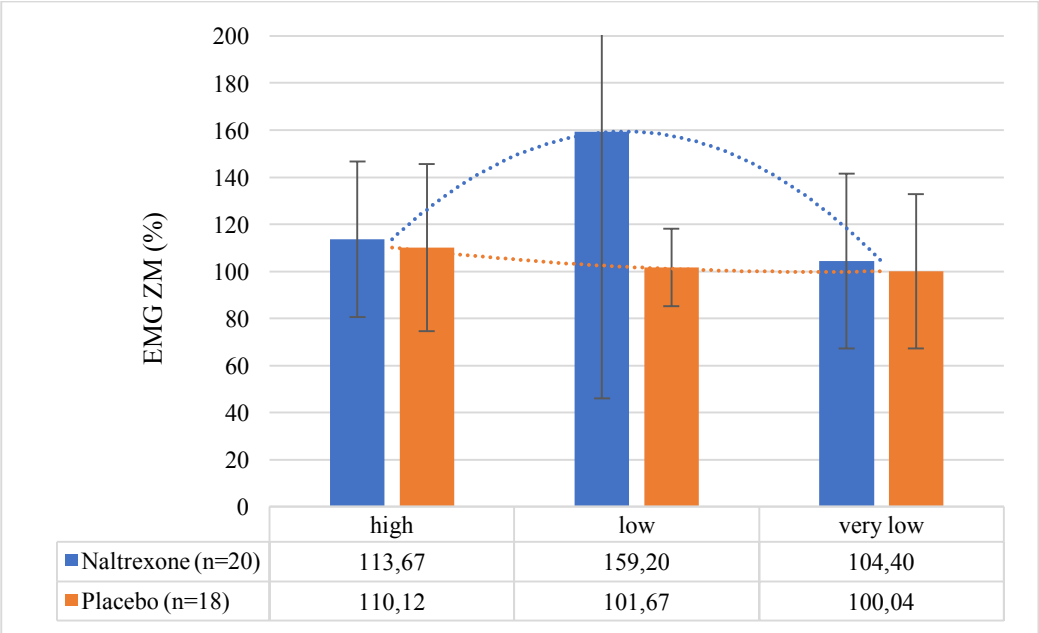


Figure 5. EMG of the ZM in % of baseline, depending on drug condition and reward type

Relax Phase (T6 – T10)

Corrugator Supercilii

Using 2-way (2x3) mixed RMM-ANOVA, the differences between the two experimental conditions (between-subject-factor) and changes in EMG CS with respect to the three reward types (within-subject-factor) were examined. Sphericity was given by the Mauchly's test with $p = .204$. The variance homogeneity, tested by Levene's test, was given with $p = .135$ for the reward type high. For reward type low and very low the homogeneity was restricted with $p < .05$, but the ANOVA is robust against this condition violation due to the approximately equal cell population (Backhaus, Erichson, Plinke, & Weiber, 2006). A

trend for a significant reward type*drug condition interaction was found ($F(2, 76) = 2.760$, $p = .070$). Accordingly, the main effects reward and condition had to be interpreted separately.

For the main effect of reward, the difference between the different reward types (high, low, very low) was not significant in the naltrexone condition by means of one-way-RMM_ANOVA (with correction according to Huynh-Feldt = .81) with $F(1.63, 32.53) = 2.509$, $p = .106$ regarding the reward types (high, low, very low). For the placebo condition (sphericity could be assumed) a global effect ($\eta^2_p = .16$) for differences between the reward types was found with $F(2, 36) = 3.381$, $p = .045$. However, the post hoc pairwise comparisons according to Bonferroni did not show significant differences (p's > .05).

Likewise, follow-up Welch-t-tests for independent group comparisons (the homogeneity of the variances could not be assumed) for the reward types were performed. For the reward type high a non-significant difference of the EMG expressions could be found with $t(35.38) = 0.235$, $p = .816$ (two-tailed), as well as for the reward type low with $t(29.65) = 1.155$, $p = .257$ (two-tailed). In contrast, for very low with $t(28.02) = -1{,}800$, $p = .083$ (two-tailed) a tendency for a higher EMG of the placebo group (117.91, $SD = 30.21$) compared to the naltrexone group (103.71, $SD = 17.27$) was observed, Figure 6.

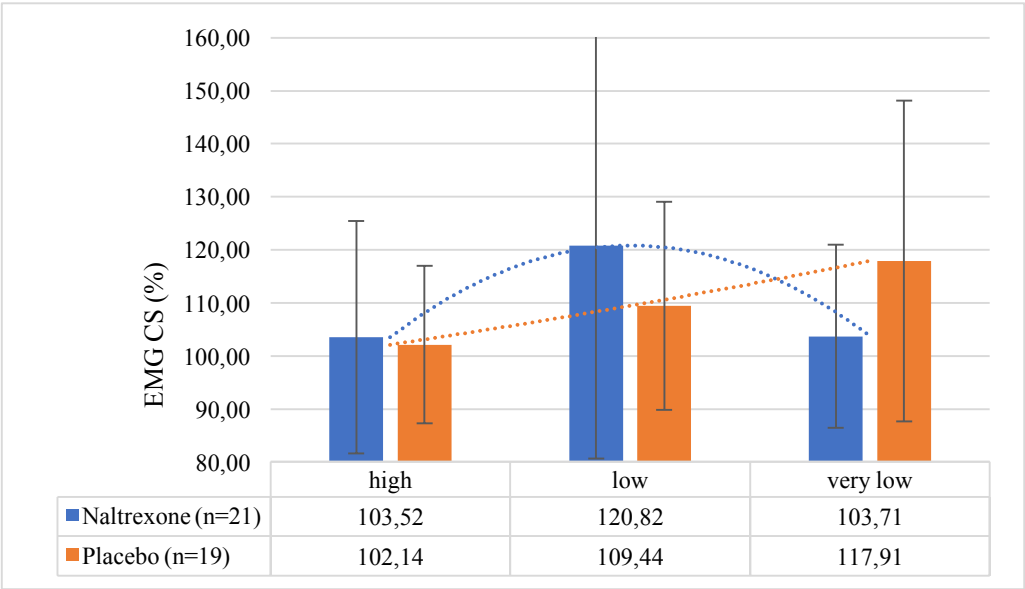


Figure 6 . Extent of EMG in % (CS), depending on drug condition and reward type

Zygomaticus Mayor

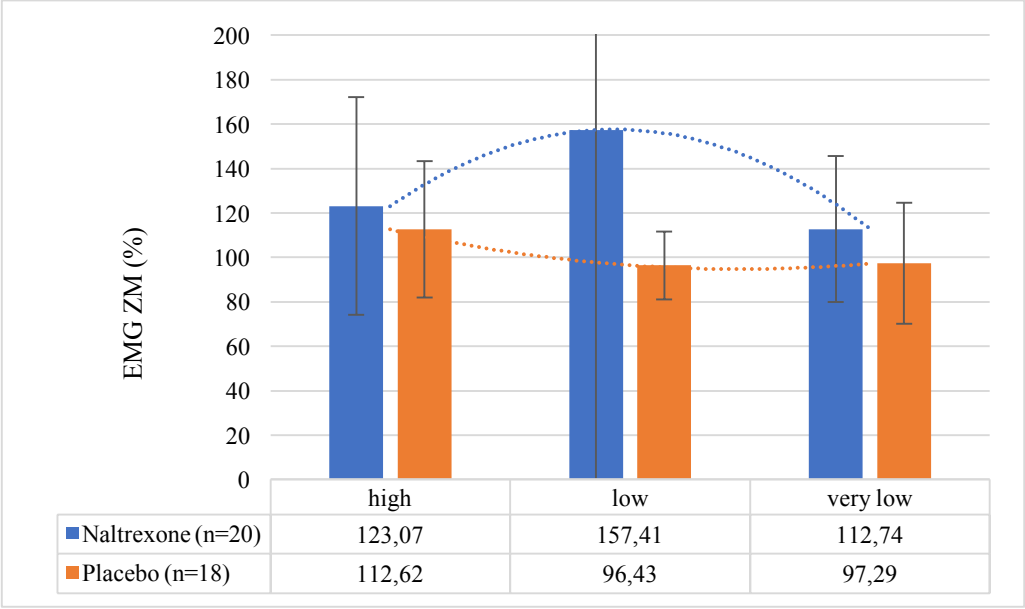
Using 2-way (2x3) mixed RMM-ANOVA, the differences between the two experimental conditions and changes in EMG ZM with respect to the three reward types were

also examined. The condition of sphericity could not be assumed on the basis of Mauchly's test with p < .001; the correction according to Greenhouse-Geisser with = .65 was necessary. The variance homogeneity, tested by Levene's test, could be assumed for the reward type high with p = .226 and for very low with p = .243. For reward type low, homogeneity was limited with

p = .029, but ANOVA is robust due to the similar cell population (Backhaus et al., 2006). For the interaction from reward x condition a non-significant result could be observed with $F(1.30, 46.75) = 1.499$, p = .232. Accordingly, the main effects reward and condition could be interpreted without restriction.

For the main reward effect, an non-significant difference of the EMG values between the different reward types (high, low, very low) could be found under the correction of Greenhouse-Geisser with $F(1.30, 46.75) = 0.937$, p = .362. Between the two groups, $F(1, 36) = 3.545$, p = .068 a medium effect (η^2_p = .09) was found for higher EMG values of the naltrexone group.

Furthermore, follow-up Welch-t-tests were performed for independent group comparisons (the homogeneity of the variances could not be assumed) for the reward types. For the reward type high an non-significant difference of the EMG values could be found with $t(32.37) = 0.794$, p = .433, as well as for the reward type low with $t(19.38) = 1.679$, p = .109 and for very low with $t(35.77) = 1.586$, p = .121, Figure 7.



	high	low	very low
Naltrexone (n=20)	123,07	157,41	112,74
Placebo (n=18)	112,62	96,43	97,29

Figure 7 Extent of EMG in % (ZM), depending on drug condition and reward type

Analysis of implicit wanting (Dynanometer)

Using 2-way (2x2) mixed RMM-ANOVA, the differences between the two experimental conditions (between-subject-factor, naltrexone vs. placebo) and changes in implicit measurements of wanting (% from Dynanometer baseline) with respect to the two reward types (within-subject-factor, high vs. low) were examined. The interaction effect of wanting x condition was significant with $F(1, 41) = 4.257$, $p = .045$. Therefore, the main effects had to be interpreted with caution. Follow-up t-Tests for independent samples showed no significant difference between the two groups for high rewards ($t(40.99) = -0.906$, $p=.370$), however a significant difference for low rewards could be observed ($t(39.90) = -2.235$, $p = .031$, $d = - 0.68$). This indicates a medium difference for the low reward type between the two groups

In summary, there is a significant decrease of implicit wanting ($F(1,41) = 35.566$, $p < .001$, ($\eta^2_p = .045$) within the two reward types (high, low). Using dependent t-tests, the main effect was examined separately for the two conditions (naltrexone, $t(21) = 5.020$, $p < .001$, $d = 1.07$ vs. placebo, $t(20) = 3.317$, $p = .003$, $d = 0.72$), thus naltrexone showed as greater decrease from the high reward condition to low reward condition than the placebo group, Figure 8.

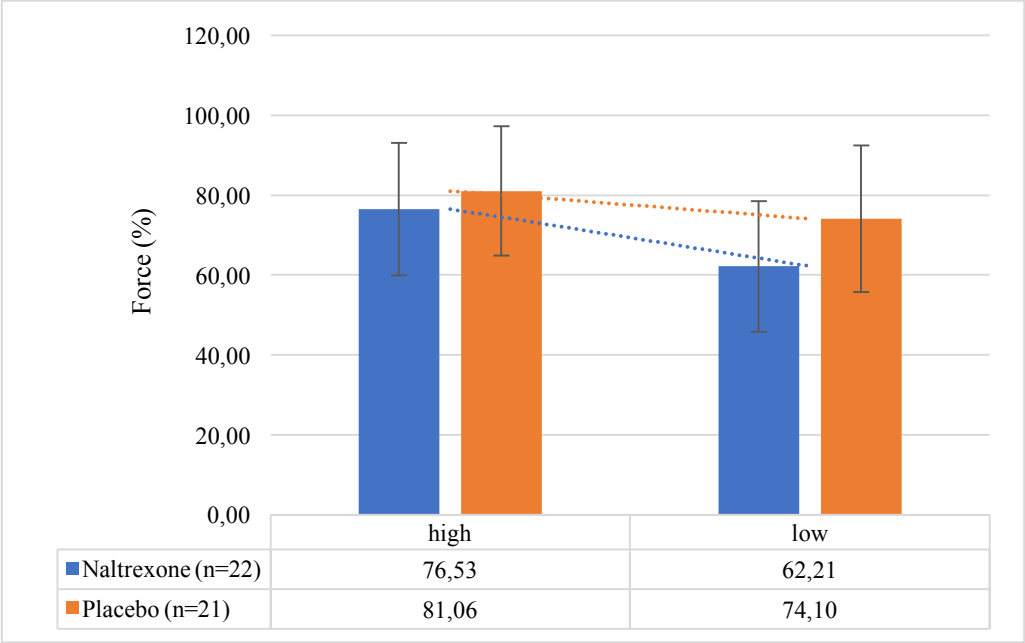


Figure 8. Extent of force in % of baseline, depending on drug condition and reward type

Discussion

The aim of the present research was to investigate the role of endogenous opioids in the context of different types of social touch rewards in order to close the research gap on social rewards. Building on the literature from animal studies which show a neurological dissociation of wanting and liking, there is considerable evidence that neurological mechanisms of action in humans may exhibit similar characteristics (Berridge & Kringelbach, 2008).

In this study, we have addressed that knowledge gap by using behavioural paradigms and psychopharmacological methods in combination with electromyography to address desire and pleasure for social rewards in a differentiated way. For this purpose, a sample of 43 healthy participants was tested in a randomized, double-blind, placebo-controlled experiment.

In particular, the role of endogenous opioids in the wanting and liking of different sensations of touch was tested and analysed. The responsible neurotransmitters are dopamine for wanting and opioids for liking (and also wanting, as both cannot be considered completely isolated from each other (Pool et al., 2015)). Throughout the study, both primary (food) and social rewards (touch) were investigated, but this thesis focused solely on social rewards associated with touch.

The present results must be viewed from different perspectives, since on the one hand opioids play a crucial role in the context of wanting and liking and on the other in the context of social touch and bonding (Nummenmaa et al., 2016) i.e. the effect of endogenous opioids is influenced by the experimental variable naltrexone as well as by the respective touch stimulus itself.

It was assumed that naltrexone reduces the levels of both components but exerts a stronger reductive effect on liking. In addition, the underlying experimental design, including the social touch paradigm, was examined to ensure that wanting and liking characteristics of three differently paced touch stimuli matched the preferences given at the beginning.

The results of explicit wanting and liking (ratings on VAS) showed no significant differences between the two experimental groups (naltrexone vs. placebo). However, there were found significant differences in the assessment of the different touch stimuli with respect to explicit wanting and liking, i.e. the self-reports were consistent with the preference given at the beginning. Looking at explicit liking, data of high rewards showed that the naltrexone group was relatively more heterogeneous than the placebo group (i.e., CI and SD were larger), which could suggest that the drug had a varying effect on different participants, especially

when exposed to a high reward. Reward type low and very low only showed marginal differences and also SD were comparable between the two groups.

For the implicit liking during the consumption phase, there were found tendentially higher EMG values in the naltrexone group, both for CS and ZM activation, which contradicts current literature (Gilbert, Fridlund, & Sabini, 1987; Horio, 2003; Hu et al., 1999; Korb et al.,2015) regarding the interpretation of EMG data from ZM and CS, which states that the two muscles correlate negatively. Regarding CS, there was found a non-significant small effect between the two groups. Looking at the bar charts we can observe a trend in the direction, that the naltrexone group had more activation throughout all the reward types, which is in line with the hypotheses, that functioning as an opioid antagonist, naltrexone should decrease liking which is expressed by more activation of the CS. For ZM, a medium effect for tendentiously higher EMG values in the naltrexone group was found in the comparison between the two groups. This result contradicts the initial hypothesis, that naltrexone as an opioid antagonist should decrease liking. Nevertheless literature (Zeinstra, Koelen, Colindres, Kok, & de Graaf, 2009) states that in adults the deactivation of CS is a better indicator of liking than, conversely, the activation of ZM, which is very susceptible to confounding. Possible reasons for this could be that the data set is too small or that there are many motion-related distortions. For example, many participants supported their chins with their palms because the experiment lasted for a very long time and we could not observe them behind the curtain.

Particularly notable were the characteristics of the reward type low: there was a significant medium group difference. This might suggest that under extreme conditions within the reward types, such as high and very low, the drug has no effect statistically, but it does have an effect with moderate reward stimuli.

However, the bar chart again shows that the naltrexone group has a much larger dispersion (larger CI and SD), which again indicates a divergent effect of the drug on the different participants. This could mean that individual factors within the sample play a far greater role than assumed. This result appears to be particularly important as it behaves systematic through different observations.

Furthermore, it was striking that no significant differences between the three different types of rewards for implicit liking could be observed, which is neither consistent with the data of explicit likings nor with the basic assumptions of the study design. This implies that the available results should be interpreted with utmost caution.

It is interesting to note that the results of implicit liking do not match those of the explicit ratings. Apart from distortions, the EMG data from the implicit survey should be more reliable than the ratings with respect to genuine emotions, which may not be consciously perceived. There is a possibility that explicit liking data may be distorted by the fact that the participants are primed through the design of the study and the instructions – especially, of course, the ranking of the stimuli from most pleasant to least pleasant at the beginning – in such a way that they assume that the different stimuli are pleasant or even different. This could explain why on an explicit level the touches were rated pleasant (an average of 4/10 on the scale), but on an implicit behavioural level the touch stimuli are perceived as rather neutral or rather unpleasant (increased CS above 100% of the baseline with naltrexone, with placebo only the very low reward types, ZM overall rather neutral around 100%, the outlier in the middle has a large CI and is therefore not interpreted here).

Perhaps the strange situation in the laboratory and the anonymous touch leads to the fact that the administered touches were not experienced as pleasantly as expected. Literature makes a clear connection between opioids and bonding (Ignaki, 2018; Panksepp, Herman, Conner, Bishop, & Scott, 1978). In this respect, the administration of natrexone could cause completely different effects when touched by people to whom one has a bond. Maybe the antagonist does not work in the expected way because there is no real relationship involved.

In the relaxation phase (the phase immediately after the caresses in the consumption phase), an interaction effect between reward type and group could be observed in CS. The naltrexone group showed no significant differences between the different types of rewards, which could be due to varying drug effects, or – as explained above – that in fact the touches were not perceived as being so differently pleasant. The placebo group behaved more homogeneously overall and showed a global effect with regard to the different reward types (although post-hoc tests under Bonferroni correction showed no significant differences). The group differences were contradictory at first glance: for the reward types high and low, the naltrexone group showed higher values than the placebo group (but not significant) and for the category very low, the placebo group tended to show higher values. This could be interpreted to indicate that while the administration of naltrexone has the expected effect (reduction of liking) on extremely liked stimuli, this effect does not exist or may even be reversed for less liked stimuli. Initially, this does not sound entirely plausible, but if we take a closer look at drugs (e.g. the other drug in the study: Solian) we find that the effect is strongly dependent on the dosage, which in turn is adapted to the occurring symptoms. Solian, for example, is prescribed for the disease schizophrenia in a low dose to treat negative symptoms

and in a much higher dose (four times as strong) for positive symptoms. In fact, there are a number of substances that have an activating effect in a low dose and a dissecting effect in a higher dose, especially with regard to substances binding to opioid receptors. Such a possibility should also be considered in the future regarding the investigation of opioid antagonists and agonists.

No significant differences in the relaxation phase could be found for ZM between the different reward types with regard to their EMG characteristics either. In a group comparison, a mean effect for higher EMG values was found in the naltrexone group. Again, the scatter of data was significantly greater in the naltrexone group than in the placebo group. Perhaps ZM is not a sufficient indicator of pleasure in adults after all. In the course of socialization, we change our facial expressions and the different facial muscles often take on a different function or are at least adapted, so that ZM in particular could be very susceptible to distortion. Laughter plays a major role in the social context and therefore it is used very often, even if we do not feel pleasure at all (e.g. cramped smiles), relaxation in turn is less easily falsified.

In summary and in general, the EMG results of the available data might indicate that the explicit data are not always reliable. However, this interpretation should be treated with caution due to the possible perturbations in EMG data and should be tested on a larger sample to obtain representative results.

The analysis for implicit wanting by pressing the dynamometer showed a significant difference between the two reward types, i.e. more force was exerted for the high reward types. No difference was found between the two groups for high rewards. For low rewards, however, a medium difference was found, and the bar graphs also show a trend towards a reduction in wanting under naltrexone. This is consistent with the hypothesis that opioid receptor blockade reduces wanting, and seems to have a stronger reductive effect, especially on less liked stimuli, i.e., the touches of reward type low are even less desirable under naltrexone. If something is really wanted, naltrexone has no antagonistic effect, just as EMG data in the high and very low condition show no effect, but with medium low stimuli the effect of the drug does exist.

Conclusion

In conclusion, the present study extends existing literature on the function of endogenous opioids with respect to slow vs. fast touch and partly confirms that naltrexone reduces the wanting and liking, especially when touch is not very pleasant from the

beginning. However, the present results show almost no significant differences between the two groups, possibly due to the high variability of data in the naltrexone group. The present results behave similarly to the ambivalent previous research results, e.g. it is not clear whether a pleasant touch lowers the endogenous opioid level (Nummenmaa et al., 2015) or increases it (Boecker et al., 2008; Koepp et al., 2009). Since in animals, low opioid levels are associated with social grooming (Keverne, et al., 1989; Meller, et al., 1980), it remains unclear how the reduced availability of endogenous opioids by naltrexone affects the perception of social touch in humans.

The results indicate the pleasant function of affective touches, in particular slow CT-fibre optimal tactile stimuli, but it remains unclear to what extent they are related to social bonding, as the experimenters were unknown to the participants and it was also not clear which of the two experimenters performed the touches. Harlow's experiments (1958) clearly show that touch in itself is something positive, even essential and existential. But what exactly is the nature of touch in humans, especially in adults who have already lived through a number of very different bonding experiences?

Future research is needed to further specify the neurophysiological mechanisms involved and to clarify the role of personal relationships in the function of touch.

Limitations

To the best of our knowledge, this is the first attempt to investigate the neurological dissociation of wanting and liking of social touch rewards in humans. However, the merits of the matter should be considered in light of study limitations and directions for future research. First, it was a mixed design, with a between-subjects' manipulation of the drug, thus the results may entail potential individual variability confounds in terms of responsibility to the drug. The main limitation of the study is therefore the small sample size, which prohibits generalization of the results. However, the basic investigation of opioids and social reward in humans is quite new, and the data collection in the whole course of studies still continues, thus final results will give more insight in regard to the role of opioids and dopamine in the primary and social reward system. Another limitation of experimental research is always the laboratory setting. The creation of a social reward situation in an artificial setting with people who are also unfamiliar to the test person significantly limits the ecological validity and the interpretation of the results; especially the transferability to daily life, must be treated with caution. Furthermore, despite the extensive training of the experimenters, there may have been inter-individual differences in the instruction as well as in the administration of the touch

stimuli. The respective attitudes towards social touch among the test subjects were assessed through the STQ (Wilhelm et al., 2012), which contains only 20 items. In order to be able to estimate the actually very individual and different attitudes of the participants towards being touched, it would have been necessary to collect more information about their biography and experiences in this respect to enable a more precise statement and comparability. Moreover, since participation in the experiment was reimbursed in monetary terms and most of the subjects were students who could well use the money, a "faking good" the answers to the questionnaires that served the inclusion procedure cannot be ruled out. For this reason, the question of whether a strict separation of purely social reward is possible must also be reconsidered and also the question whether a consistent separation from purely social rewards in an experimental setting is possible at all.

Future research

As aforementioned, this study should be repeated or continued with a larger sample. Due to the limitations mentioned above, it would be useful in the future to include a friend, partner or acquaintance as a toucher in the experiment, as touching in general and in our culture in particular is considered to be something very private and could be experienced as offensive, intrusive or threatening (Sussman and Rosenfeld, 1978). Moreover, men and women benefit and experience different reward stimuli in different ways, including on a neurological level (Spreckelmeyer et al., 2009). Therefore, future studies should investigate whether the current results refer to both or whether there exist gender-specific differences regarding social touch rewards. In order to avoid the artificial laboratory setting, the only way out is field research, whereby the observation of parent-child dynamics is of course particularly suitable, but also the search for natural settings of social touch, such as dance classes or physiological therapies. It would also be worth testing different samples as well as different cultures to learn more about the role and attitude towards social touch that is acquired through society and how this affects our neurological functioning, in particular the endogenous opioid system.

Last but not least, the investigation of a neurological dissociation of wanting and liking in the social reward system should be replicated using other social reward stimuli, as the results are susceptible to misinterpretation due to the direct relationship of the opioid system with touch.

Current relevance of this research

Will social touch become rarer and more intimate if the current COVID 19 pandemic lasts longer or even if there will be others of its kind? People will have to fear more and more physical contact with others. What alternatives are there, eventually also from a technological point of view, so that human growth and well-being won't suffer excessively? The Dutch researcher Gijs Huisman (Frederiks, Kröse & Huisman, 2016) has been propagating a prototype of touch surrogates for a while, which are supposed to identify and transmit touches via a moving vibratory sensor, so that they can also be transmitted over distance. In view of the fact that similar models have been on the market for a long time in the sexual area and have proven to be quite suitable (as the market is very large in this respect), this consideration is perhaps not at all wrong. But what will we miss compared to a person to person physical contact? How will our brains react to it? This is not only an important question in times of pandemic crises, but generally speaking, as the consequences of excessive use of social networks, which in many cases are replacing personal contacts, have not yet been clarified. Psychopathologies related to impairments of social reward processing such as addiction, depression and autism spectrum disorders are also in need of better understanding through research in this area and can be used to improve clinical prevention and treatment.

This research provides a basis on which such questions may be answered in the future, because one thing is clear: touch is essential for survival and a significant part of our social reward system, both in the clinical and the general population.

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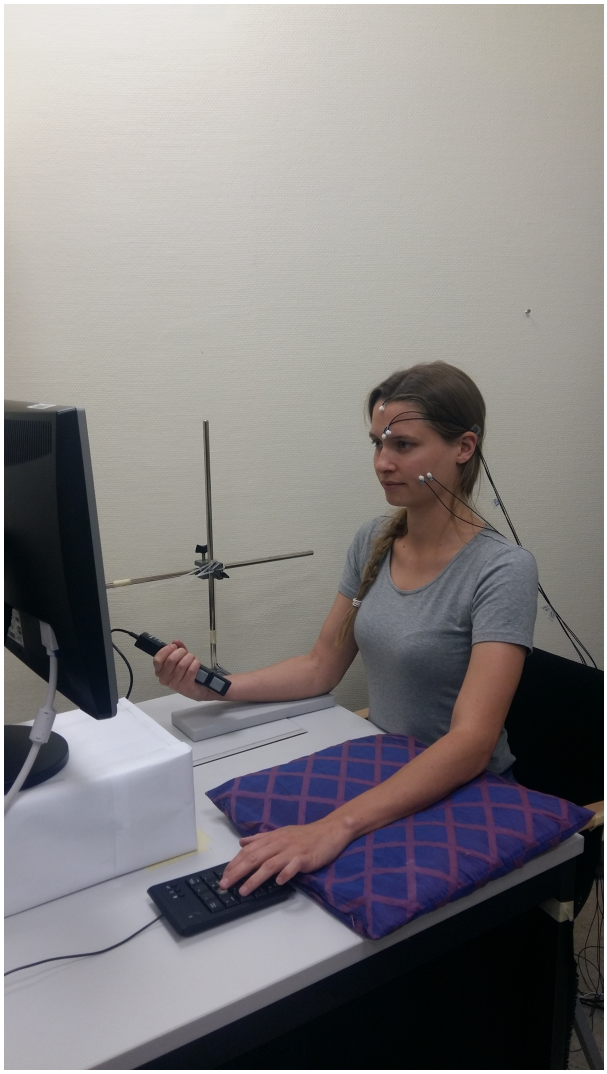
Appendix



Experimental setup in the laboratory

Abstract English

This research deals with two crucial aspects of reward: wanting and liking. Animal research established a clear neurological dissociation between wanting and liking in primary reward. There is strong evidence that dopamine is only involved in the motivational component and that pleasure is mainly regulated and influenced by opioids. However, there do not exist comparable studies in humans, and social reward stimuli such as social touch have been largely neglected or not clearly distinguished from primary rewards. We aim to overcome this knowledge gap by using behavioural paradigms and using psychopharmacological methods in combination with electromyography to investigate the role of endogenous opioids in wanting and liking of social touch stimuli in a differentiated way. For this purpose, a sample of 43 healthy participants was tested in a randomized, double-blind, placebo-controlled experiment. Data partially confirmed that naltrexone reduces wanting and liking, especially when the touch is not very pleasant from the outset. However, there were almost no significant differences between the two groups, possibly due to the high variability of data in the naltrexone group. It was particularly remarkable that the results of the implicit liking did not match the results of the explicit ratings. Overall, the results indicate the pleasant function of slow affective touches. The topic is important not only in times of pandemic crises, but in general, as the consequences of social and tactile deprivation are not yet fully understood. Psychopathologies related to impairments in social reward processing such as addiction, depression and autism spectrum disorders also require better understanding through research in this area.

Abstract German

Diese Arbeit befasst sich mit zwei grundlegenden Aspekten des Belohnungssystems: Wollen und Mögen. Im Rahmen von Tierstudien wurde eine klare neurologische Unterscheidung zwischen Wollen und Mögen bei der primären Belohnung festgestellt. Es gibt überzeugende Belege dafür, dass Dopamin nur die motivierende Komponente betrifft und dass das Lustgefühl hauptsächlich durch Opioide reguliert und beeinflusst wird. An Menschen gibt es bislang keine vergleichbaren Studien, und soziale Belohnungsreize wie soziale Berührung wurden in der Forschung weitestgehend ausgelassen oder nicht klar von primärer Belohnung unterschieden. Diese Wissenslücke wollen wir überwinden, indem wir etablierte Verhaltensparadigmen anwenden und psychopharmakologische Methoden in Kombination mit Elektromyografie einsetzen, um die Bedeutung endogener Opioide für das Wollen und Mögen von sozialen Berührungsreizen differenziert zu untersuchen. Hierfür wurde eine Stichprobe von 43 gesunden Teilnehmern in einem randomisierten, doppelblinden, Placebo-kontrollierten Experiment getestet. Anhand der Daten konnte teilweise bestätigt werden, dass Naltrexon das Wollen und Mögen reduziert, insbesondere wenn die Berührung von vornherein nicht sehr angenehm ist. Allerdings gab es fast keine signifikanten Unterschiede zwischen den beiden Gruppen, was möglicherweise auf die hohe Variabilität der Daten in der Naltrexon-Gruppe zurückzuführen ist. Besonders auffallend war, dass die Ergebnisse der impliziten Erhebung nicht mit den Ergebnissen der expliziten Bewertungen übereinstimmten. Insgesamt deuten die Ergebnisse auf die angenehme Wirkungsfunktion von langsamen affektiven Berührungen hin. Die Thematik ist nicht nur in Zeiten von Pandemiekrisen von Bedeutung, sondern im Allgemeinen, da die Folgen von sozialer und taktiler Deprivation noch nicht vollständig ergründet sind. Psychopathologien im Zusammenhang mit Beeinträchtigungen der sozialen Belohnungsverarbeitung wie Sucht, Depression und Störungen im autistischen Spektrum erfordern ebenfalls ein besseres Verständnis durch Forschung in diesem Bereich.