universität wien

MASTERARBEIT / MASTER'S THESIS

Titel der Masterarbeit / Title of the Master's Thesis

„Naltrexone reduces affiliative facial responses towards happy faces"

verfasst von / submitted by

Vera Ritter, BSc

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

Master of Science (MSc)

Wien, 2018 / Vienna 2018

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

Table of Contents

1. Theoretical Background 1
1.1 Facial mimicry 1
1.2 Influences on Facial Mimicry 2
1.2.1 Empathy 2
1.2.2 Current state of the Perceiver 3
1.2.3 Type of Expression the Perceiver Observes 4
1.2.4 Attitudes Towards the Expresser 4
1.2.5 Characteristics of Sender 4
1.2.6 Gender Differences 5
1.3 Functions of Facial Mimicry 7
1.4 Facial Mimicry in Autism Spectrum Disorder 8
1.5.1 Mirror Neuron System 9
1.5.2 Opioid System 11
1.5.3 Naltrexone as an Opioid Antagonist 12
2. Research Question & Hypotheses 14
3. Methods 16
3.1 Participants 16
3.2 Drug Administration 16
3.3 Study Procedure 17
3.3.1 Taste & Touch Study 17
3.3.2 Facial Mimicry Task 18
3.4 Stimuli 19
3.5 Procedure Facial Mimicry Task 19
3.6 Facial EMG Recording 20
3.7 EMG Data Preprocessing 21

3.8 Data Analysis 21
4. Results 23
5. Discussion 28
5.1.1 Presence of Facial Mimicry 28
5.1.2 Gender Differences in Facial Mimicry 29
5.1.3 Influences of Naltrexone on Facial Mimicry 31
5.2 Limitation and Suggestions for Further Studies 33
5.3 Conclusion 35
6. References 36
7. Appendix 48

1. Theoretical Background

Humans are social beings (Caporael, 2001). Almost daily from dawn until dusk (and sometimes from dusk until dawn), our lives are filled with social interactions (Lakin, Jefferis, Cheng, & Chartrand, 2003). We interact with other people when ordering food at the bakery, when saying hello to the bus driver, when talking about the next meeting at work with colleagues, or when catching up with friends in the evening. For this reason, it is not surprising that many scientists deal with the field of social behavior, since it social interactions are crucial and ubiquitous in everyone's life.

Social interactions include a coherent set of vocal components, gestural markers as well as facial expressions (Schweinberger & Schneider, 2014) which are meant to facilitate communication. Thereby, the humans face is one of the most expressive way to communicate (Ekman & Rosenberg, 2005). Facial expressions as a nonverbal channel of communication are crucial for the perception of other people's emotions and intentions and can thus be considered as a key component in daily social communication. It allows rapid transmission of valence information from one person to another (Blair, 2003). Hence, our face and the way we communicate loom large in social interactions.

1.1 Facial mimicry

As mentioned, a lot of communication happens via gestures and facial expressions. A crucial part of countenance is mimicry. Mimicry describes the often unconscious and unintentional imitation of behavior that human show when they interact (Seibt, Mühlberger, Likowski, & Weyers, 2015). Thereby, postures, behavior and facial expressions can be mimicked (Seibt et al., 2015). The latter is called facial mimicry. Facial mimicry is defined as a tendency to mimic the facial expressions of individuals with whom we are interacting and showing congruent facial muscular activations in response to the perceived expression (Argaud et al., 2016). The muscular reactions can be very low in intensity and are usually registered by using electromyography, a diagnostic procedure for recording electrical activity produced by muscles (Fridlund & Cacioppo, 1986). Those changes in muscle electrical activity begin rapidly within the first 300-400 ms after appearance of stimuli (Dimberg & Thunberg, 1998). They are typically automatic, occur without

awareness or conscious control (Dimberg & Lundqvist, 1990; Dimberg & Thunberg, 1998; Dimberg, Thunberg, & Elmehed, 2000), and are difficult to suppress voluntary (Korb, Grandjean, & Scherer, 2010). They even occur in minimal social context (Dimberg, 1982; Likowski, Mühlberger, Seibt, Pauli, & Weyers, 2008) and as a response to subconsciously presented emotional expressions (Dimberg et al., 2000). The assumption that mimicry of facial expressions occurs spontaneously and unconsciously is supported by findings showing that facial mimicry can occur without the conscious perception of the stimulus face (Dimberg et al., 2000). Moreover, facial mimicry develops early in human life and occurs automatically as a reflex-like reaction, which tends to be an evidence for biological preparedness (Field, Woodson, Greenberg, & Cohen, 1982; Meltzoff & Moore, 1977).

1.2 Influences on Facial Mimicry

Both the occurrence and the extent of facial mimicry depend on several factors, such as personality traits, the current state, the relationship between perceiver and expresser, the type of expression the perceiver observed, social motivation, or gender, which is why some individuals tend to mimic more than others (Seibt et al., 2015). In the following, the influence of certain aspects on facial mimicry is discussed in detail.

1.2.1 Empathy

Assuming that facial mimicry is an important factor for social communication and interaction, it can be expected that personality traits which are related to affiliative behavior [1] enhance facial mimicry. One of those traits is empathy, a personal characteristic which is important for social rapport. Empathy can be divided into two sub-constructs: emotional empathy ("I feel what you feel") and cognitive empathy ("I understand what you

[1] any sort of behavior that is enacted with the intent of supporting or improving one's individual union with others or which is connected more so with a drive to build, upkeep, and improve close individual partnerships with others (Nugent, 2013).

feel"; de Waal, 2008). Individuals high in emotional empathy are more likely to show facial mimicry, since they are motivated to show their concern and feel for other persons (Goldman & Sripada, 2005). Cognitive empathy which can be considered as perspective taking may be enabled through facial mimicry, by working as a feedback mechanism about the other person's emotional state (Neal & Chartrand, 2011). Results of studies by Sonnby-Borgström (2002), Dimberg, Andréasson, and Thunberg (2011), and Zajonc, Adelmann, Murphy, and Niedenthal (1987) displayed stronger congruent facial reactions to happy and angry faces in individuals high in self-reported emotional empathy. This suggests that they perceive emotional expressions stronger than low empathic individuals.

Moreover, individuals reporting high levels of empathy do not only show a greater amount of facial mimicry, they also perceived changes between facial expressions (e.g., from anger to happiness) more rapidly (Niedenthal, Brauer, Halberstadt, & Innes-Ker, 2001; Korb et al., 2015). However, it is unclear whether the effect of stronger facial reactions in high empathic individuals can be accounted for by an enhanced sensitivity to emotional signals, enhanced emotional responding or enhanced emotional expressivity (Seibt et al., 2015). Chartrand and Lakin (2013) elucidate the relationship from mimicry to emotional contagion, which is supposed to be a component of emotional empathy. On the other hand, facial mimicry may not be enhanced by empathy, but is crucial for the development of empathy, because it requires the ability to detect and represent the emotional state of another person (Korb et al., 2015).

1.2.2 Current state of the Perceiver

In addition to stable personality factors, the current state of the perceiver can moderate facial mimicry as well. A study by Likowski, Weyers, Seibt, Stöhr, Pauli, and Mühlberger (2011) showed that participants in a good mood displayed stronger mimicry of happy, sad, and angry faces compared to those who were in a sad mood. Participants in fearful mood displayed fearful reactions to angry faces, while those in a sad mood did not show any response to it (Moody, McIntosh, Mann, & Weisser, 2007). Therefore, it can be inferred, that facial mimicry is determined by the quality of the negative mood and not its valence (Seibt et al., 2015). Moreover, the emotional state affects the detection of the offset of an initial expression (Niedenthal et al., 2001). Individuals in a happy state detect the

offset of happiness changing to a sad expression at an earlier point than those in a sad state. Likewise, individuals in a sad mood see the offset of sad expressions earlier than individuals in a happy condition did (Niedenthal et al., 2001). Therefore, the current state has an impact on the extent of how people mimic emotional facial expressions and how quickly they recognize the changes of those.

1.2.3 Type of Expression the Perceiver Observes

Some emotion displays are less likely to be mimicked than others (Hess & Fischer, 2014). Presentations of anger, disgust, and contempt for example are less likely to be imitated, especially not when they are directed towards the observer, whereas happy expressions such as a smile are likely to be mimicked. This can be explained by the fact that anger, disgust, and contempt signals opposition for affiliation, by contrast, smiles signal affiliative intentions and are generally perceived as more relationship enhancing (Hess & Fischer, 2014; Hess, Blairy, & Kleck, 2000).

1.2.4 Attitudes Towards the Expresser

The relationship towards the expresser has a bearing on facial mimicry as well. According to Hess (2001), facial mimicry occurs only in situations where individuals already have a positive or at least neutral relationship. More precisely, happy and sad faces of positively perceived characters evoked congruent facial mimicry, as well as happy and sad faces of negatively perceived characters evoked less or even incongruent reactions (Likowski et al., 2008). In case the relationship is negative, or someone appraises the emotional signal as having a negative consequence for oneself, emotional mimicry does not occur or only in a limited way (Hess & Fischer, 2014).

1.2.5 Characteristics of Sender

Not only perceivers, but also senders have characteristics that influence perceivers' reactions to facial expressions. Eye gaze and its direction, for instance, play an important role in interpreting facial expressions. If the sender of facial expressions shows a direct or

averted gaze towards the perceiver can therefore moderate the perceivers extent of facial mimicry (Seibt et al., 2015). In a study by Schrammel, Pannasch, Graupner, Mojzisch, and Velichowsky (2009) pictures of smiling people with either direct or averted gaze to participants were presented. Self-directed expression, in other words a direct gaze of the sender, induces thereby a stronger Zygomaticus Major activation (a muscle that is known to be involved in smiling) in the perceiver compared to an averted gaze. Hence, a direct eye contact between sender and receiver of an emotional facial expression can be considered as a trigger for spontaneously facial mimicry (Niedenthal, Mermillod, Maringer, & Hess, 2010).

1.2.6 Gender Differences

Women and men differ in their way they behave in social interactions and how they respond to emotional stimuli. Thus, they vary in the way they produce, perceive, and regulate facial expressions (Korb et al., 2015). Thereby, women are more susceptible of emotional expressions and show more facial mimicry compared to men. More precisely, women smile more often than men (Hess & Bourgeois, 2010) and react with a stronger Zygomaticus Major activation to happy faces (Dimberg & Lundqvist, 1990), which means they display mimicry of smiles to a greater extent compared to men. Also, in a study by Schrammel et al. (2009) female participants displayed stronger Zygomaticus Major activation especially to male rather than female happy faces, whereas apart from that it is believed that women show more same sex-smile mimicry (Seibt et al., 2015), indicating that the sex of the sender affects the extent to which the perceiver mimic back. However, there are some studies that found no facial mimicry effects for gender of stimuli / expresser (e.g., Dimberg & Lundqvist, 1990).

The assumption that women show a greater facial mimicry can be explained by their differences in behavior and traits compared to men. Women are generally more emotionally expressive than men (LaFrance & Hecht, 2000) as they exhibit more positive expressions in response to happy movies and more negative expressions in response to sad and fear movies. That is, women may express more emotion because they experience more emotions (Gross & Levenson, 1993; Kring & Gordon, 1998). Those differences can be accounted for by the dissimilar rules boys and girls learn for the expression of emotion. In

general, boys learn to conceal their feeling, whereas girls learn to more freely express their feelings while also learning how to control their expressive behavior (Kring & Gordon, 1998). Women are more accurate than men as well as efficient in processing facial expressions of emotion (Hall & Matsumoto, 2004). Furthermore, women are more empathic, and as mentioned earlier higher scores in empathy are correlated to a greater response in facial mimicry (see Korb et al., 2015). They display higher emotional contagion than men, meaning they share the targets' emotions to a greater extent (Doherty, Orimoto, Singelis, Hatfield, & Hebb, 1995). Women have a higher social sensitivity (McClure, 2000) and are more vulnerable to environmental threats. Additionally, women have different behavior concerning social goals and motives. They show greater motives for affiliation and bonding (Brody & Hall, 2008), which in turn is one reason why they mimic more.

Although studies showed gender differences in expressing positive emotions and in muscle activation towards positive facial expressions, however, results of gender differences for negative emotions are less consistent. Several studies showed no differences in the expression of negative emotions such as anger between women and men (e.g., Levenson, Ekman, & Friesen, 1990). As opposite to this, other studies found gender differences. Friedman, Riggio and Segall (1980), for instance, showed that women display more expressions of anger compared to men whereas other studies found that men are more likely to display expressions of anger (e.g., Rotter & Rotter, 1988). Moreover, studies of facial muscle activity towards negative facial expressions are not coherent. In a study by Soussignan, Chadwick, Philip, Conty, Dezecache, and Grezes (2013) anger expressions of the sender elicited an increased Corrugator Supercilii (a muscle that is known to be involved in frowning) activity in male perceivers. Other studies found that females show greater activity of Corrugator Supercilii when observing videos containing fear-relevant stimuli such as snakes (Thunberg & Dimberg, 2000) or when imagining emotional situations (Schwartz, Brown, & Ahern, 1980). Although brow furrowing which is associated with anger and was found to be more present in males compared to women, McDuff, Kodra, el Kaliouby, and LaFrance (2017) found at the same time inner brow raising significantly more in women. Hence, there are no consistent findings of expressing and imitating negative emotions such as anger between females and males.

As can be seen, many aspects influence the extent to how much expressions are shown. However, the presence of facial mimicry has a crucial role in social interactions.

1.3 Functions of Facial Mimicry

The mimic of facial expressions has several functions. On the one hand, it helps to create social affiliation. As mentioned before, humans are social beings who rely on acceptance into groups and intimate relationships (Hsu et al., 2013). Thereby, humans' contract close social bonds to others. Those bonds as well as social interactions in general are critical for health, well-being and normal functioning (Taylor, 2010). In contrast, the absence of positive social contact and isolation has been shown to negatively affect well-being as well as health (Cacioppo, Cacioppo, Capitanio, & Cole 2015), while possibly causing social withdrawal as well as symptoms of anxiety and depression (Slavich, O'Donovan, Epel, & Kemeny, 2010). Social bonding can therefore be seen as a social need (Baumeister & Leary, 1995), just like water and food are primary needs.

The affiliative function of facial mimicry is based on the idea that individuals who mimic each other will like one another more. Emotional mimicry can thus improve the quality of relationships by indirectly providing subtle signs of empathy, support or pleasure mimicking facial expressions (Hess & Fischer, 2014). Mimicking facial expressions as well as other body motions (such as gestures and postures) can therefore be considered as "social glue", due to its properties of binding individuals together (Hess & Fischer, 2014; Lakin & Chartrand, 2003; Lakin et al., 2003; McIntosh, 2006) and its promotion for affiliation, a process that shapes emotional bonds between individuals (Meier et al., 2016). Thereby, some emotion displays, particularly smiles, are likely to be mimicked than others, presumably because they signal affiliation intention (Hess et al., 2000). In contrast, anger, disgust and probably contempt facial expressions are not likely to be mimicked, because of their antagonism and oppose signal to affiliation (Hess & Fischer, 2014).

Furthermore, mimic facial expression has a rewarding function. Since the act of getting mimicked and the act of mimicking itself is rewarding, the link between mimic and reward can be considered as bidirectional (Hsu, Sims, & Chakrabarti, 2017). More precisely, faces that showed greater mimicry were rated as more rewarding and were more liked (Neufeld & Chakrabarti, 2016). On the other hand, individuals mimic people who they like to a greater extent (Lakin et al., 2003), which in turn leads to being liked more by the opposite. Both, liking and affiliation goals can therefore be considered as processes that influence the reward value of social stimuli (Hsu et al., 2013), meaning the reward value

can be altered due to its spontaneous mimicry (Sims, van Reekum, Johnstone, & Chakrabarti, 2012).

Another function of facial expressions is understanding the emotions of with whom we are interacting, whereas understanding means to recognize other emotions accurately (Hess & Fischer, 2013). Facial mimicry can foster the understanding of the emotion and mental state of the other person during social interaction. This assumption is based on the embodied simulation theory, according to which observers mirror emotion expressions, and these mimicked expressions entrain a feedback process. This in turn induces a tonic muscular change related to a central proprioceptive feedback and thereby elicits a corresponding emotional state in the perceiver (Argaud et al., 2016; Hess & Fischer, 2014; McIntosh, 1996). This facial feedback helps to recognize the displayed emotion (Hess & Fischer, 2014).

Although some studies have shown that deliberately suppressing facial mimicry (for example, by holding a pen in the mouth) could lead to impaired ability to recognize emotions correctly (Oberman, Winkielman, & Ramachandran, 2007; Ponari, Conson, D'Amico, Grossi, & Trojano, 2012), however, other studies found no associations between facial mimicry and emotion recognition (e.g., Hess & Blairy, 2001). The mimicry of facial expressions is therefore not necessary for the recognition of the emotions of the other person. This view is illustrated by studies of people with the Moebius syndrome, a disease characterized by bilateral paralysis of facial muscles. These individuals showed no difference in performance compared to a healthy control group in an emotion recognition task (Bogart & Matsumoto, 2010). The role of facial mimicry in terms of emotion recognition is not conclusive. However, facial mimicry does not always seem to be necessary for recognizing emotions in simple recognition tasks, but it can simplify the recognition of it (Niedenthal et al., 2001; Korb et al., 2015) and influence the speed of categorizing facial expressions (Stel & van Knippenberg, 2008).

1.4 Facial Mimicry in Autism Spectrum Disorder

Although facial mimicry is beneficial in social encounters, there are individuals who generally do not display mimicry when interacting with others. So do, for instance, people

with Autism Spectrum Disorder (ASD). Why they show less facial mimicry and what impact that induces on them will be discussed in the following.

As mentioned earlier, the extent of facial mimicry is influenced by certain character traits, such as empathy. A clinical disorder characterized by low empathy is Autism Spectrum Disorder (ASD; Trimmer, McDonald, & Rushby, 2017), a factor, among others, which can lead to difficulties in social communication (Korb et al., 2015). Members of this group show less affiliative behavior and sensitivity towards social reward, as well as display facial mimicry to a lower extent as typically developed individuals (McIntosh, Reichmann-Decker, Winkielman, & Wilbarger, 2006). Possible reasons for the reduced facial mimicry might be driven by the low reward value ascribed to faces and other stimuli displayed by people with ASD (Chevallier, Kohls, Troiani, Brodkin, & Schultz, 2012), others suggest a deficit in the brains mirror neuron system as a potential cause (e.g., Oberman, Hubbard, McCleery, Altschuler, Ramachandran, & Pineda, 2005). Interestingly, studies have only found reduced mimicry when it was spontaneous and uninstructed, but not in volitional mimicry (McIntosh et al., 2006). This leads to an essential question of what drives spontaneous facial mimicry.

As noted before, some authors believe that deficits in the brain may affect in a diminished facial mimicry. Which brain regions generally are involved in facial mimicry will be explained in more detail below.

1.5 Neurobiological Basis of Facial Mimicry

1.5.1 Mirror Neuron System

One area of the brain that is often associated with imitating and understanding actions is the mirror neuron system (MNS). The MNS was discovered in studies with macaques, in which a system of cortical neurons in the area F5 (the premotor cortex in macaques) and a part of the inferior parietal lobule was discovered, that were both active not only when the monkeys themselves performed an action but also when they observed the same action in someone else (di Pellegrino, Fadiga, Fogassi, Gallese, & Rizzolatti, 1992). They called this system of neurons the MNS because it appeared that the observed action was reflected or internally simulated within the monkey's own motor system. Meanwhile,

there is evidence that humans have such an equivalent system as well. Molenberghs, Cunnington, and Mattingley (2012) reviewed 125 studies on the human mirror neuron system and concluded that there are classic regions that play a major role in MNS, including the inferior parietal lobule, the inferior frontal gyrus, the superior temporal sulcus and the ventral premotor cortex (human homologue of monkeys F5 region).

Imitating actions and, consequently, activating the MNS also plays an essential role in social interactions, such as mirroring facial expressions. Studies provide evidence for an activation in Brodmann area 44 when subjects consciously mimic other people's facial expressions (Carr, Iacoboni, Dubeau, Mazziotta, & Lenzi, 2003). Furthermore, imaging studies were able to show that the inferior frontal gyrus and inferior parietal lobule (both "classical" MNS regions), as well as the superior temporal sulcus, middle temporal gyrus, insula, supplementary motor area, amygdala, the limbic system, and the somatosensory cortex (also called the "extended" MNS) were active during the observation and imitation of facial emotional expressions (Iacoboni, 2005; Likowski, Mühlberger, Gerdes, Wieser, Pauli, & Weyers, 2012; van der Gaag, Minderaa, & Keysers, 2007).

Although a wide range of regions assumed to belong to the classic and extended MNS, only a small number of regions seem to be associated to the observed strength of facial mimicry (Likowski et al., 2012). The regions related to facial mimicry are on the one hand those concerned with the perception and execution of facial movements and their action representations (for example the superior temporal sulcus, superior temporal sulcus, inferior frontal gyrus, and supplementary motor area), on the other hand regions that are associated with emotional processing.

The suggestion of Carr et al. (2003) that the function of the MNS is to decode and to understand other people's action and that the activation of areas concerned with action representation and emotional content helps to resonate, simulate and thereby recognize the emotional expression, overlaps with the embodiment theory of facial mimicry (Likowski et al., 2012). This theory includes the facial feedback hypothesis, according to which information from one's own facial expressions feed back into the brain and triggers emotional responses (McIntosh, 1996). Hence, pre-motor neurons (mirror neurons) fire not only when an action is performed but also when the same action is observed (Goldman & Sripada, 2005). As a result, emotional facial expressions lead to a reliving of past

experiences that have been associated with this kind of facial expressions (Likowski et al., 2012).

1.5.2 Opioid System

The opioid system is one of the underlying neurobiological factors of social affiliation behavior (Meier et al., 2016). As mentioned before, affiliation is associated with facial mimicry and affects the extent of showing such imitation. For this reason, the following will be elaborate on the opioid system with its functions and influences on social behavior, especially on facial mimicry.

The opioid system consists of three types of opioid peptides, including β-endorphin, enkephalins, and dynorphins, and three types of receptors in the brain, including μ- (MOR), δ- (DOR), and κ-receptors (KOR; Benarroch, 2012). The peptides have a distribution in the central and peripheral nervous system. In particular, systems that are involved in pain modulation, reward, response to stress, and autonomic control (Benarroch, 2012), contribute to emotional and cognitive processes regarding the development of addictive behavior (Lutz & Kieffer, 2013). The activation of opioid receptors thereby elicits synaptic inhibition resulting in a wide range of opioid-induced behavioral effects (Benarroch, 2012).

The mu-opioid system is known to be involved, among others, in socio-emotional behavior, to be more specific in affiliation, social bonding, and social reward processing (Meier et al., 2016). In doing so, it modulates and subserves, for instance, the feeling of social connection in humans (Inagaki, Ray, Irwin, Way, & Eisenberger, 2016) and plays an important role regarding motivation and hedonic aspects that regulate automatic and unconscious responses to social reward cues (Chelnokova, Laeng, Eikemo, Riegels, Loseth, Maurud, Willoch, & Leknes, 2014).

Previous studies showed receptor activation of (mu-)opioid in the nucleus accumbens, a main structure of the neural reward circuitry, after positive feedback and attribution to social interactions in humans (Hsu et al., 2013; Meier et al., 2016). Further, MOR activation in the left ventral striatum during acceptance (being liked by others) predicted a greater desire for social interaction, a further prediction for the role of the MOR system in social reward (Hsu et al., 2013). Undergoing social rejection (not being liked by others) for example significantly activated the MOR system (Hsu et al., 2013), which is

consistent with the finding that the endogenous opioid system plays a role in reducing pain (in this case social pain; Benarroch, 2012).

According to the brain opioid theory of social attachment postulated by Panksepp, Herman, Conner, Bishop, & Scott (1978), endogenous opioids (especially mu-opioids) are released by experiencing social bonding. This implies that feelings, such as warmth and affection, that are stemmed from social connections, are mediated by opioids (Loseth, Ellingsen, & Leknes, 2014). Experiencing no social connection on the other hand (for example due to loss or separation) can lead to a reduction of the opioid activity and thus to feelings of disconnection and separation distress (Panksepp et al., 1978). However, feelings of social connection and affiliation can be arbitrarily blocked by opioid antagonist, such as naltrexone, and thus influence one's social behavior (Inagaki et al, 2016).

1.5.3 Naltrexone as an Opioid Antagonist

Naltrexone is a non-selective opioid antagonist, which is most selective to the mu-opioid system (Lee, Wagner, Tanada, Frost, Bice, & Dannals, 1988) with a high affinity for the μ-opioid receptors (Ki = 0.08 nM), an intermediate affinity for κ-opioid receptors (Ki = 0.50 nM), and a very low affinity for δ-opioid receptors (Ki = 8.2 nM) (Codd, Shank, Schupsky, & Raffa, 1995). As a result, naltrexone occupies opioid receptors, abolishing the effects of opioids there.

As mentioned earlier, blocking the mu-opioid system due to naltrexone administration can affect feelings of social connection and affiliation behavior. In a study described by Depue and Morrone-Strupinsky (2005) naltrexone reduced an increase in warm, affectionate feelings when watching affiliative video clips compared to a neutral clip. As demonstrated in an experiment by Inagaki and colleagues (2016), individuals also showed a reduced experience of social connectivity and affiliation after an intake of naltrexone over four days. Although generally positive feelings are reduced by naltrexone in this study, feelings of social connection, however, do to the largest extent.

These results are in line with the assumption that opioids play an important role in reward experiencing. Next to affecting social affiliation and social bonding, opioid antagonists such as naltrexone have shown to reduce liking of non-social stimuli, such as food (Yeomans & Gray, 1997) or gambling wins (Petrovic et al., 2008). Therefore, opioid

antagonists do not only have an impact on social stimuli, but rather are specific to the most valued or rewarding ones. It follows that opioid antagonists influence the sensitivity for rewarding stimuli. That is, opioid antagonists may affect one's subjective experience in response to the greatest reward available (Inagaki et al, 2016).

Moreover, there is a change in facial mimicry due to naltrexone intake. As already mentioned, the mimicking of facial expressions is essential for social interactions and relevant to promote social bonds and affiliation. Since Naltrexone reduces affiliative behavior, it was assumed that this is also expressed by a diminished facial mimicry of facial expressions. Meier et al. (2016) were able to confirm this assumption in their experiment and showed that naltrexone administration results in an increase of negatively facial responses to affiliative facial cues in females. More precisely, they found an increase in Corrugator Supercilii activation (a muscle that is known to be involved in frowning) and a near-significant increase of depressor activity to happy faces.

2. Research Question & Hypotheses

As mentioned above, social interactions are essential for our health, well-being and normal functioning (Taylor, 2010). Facial mimicry plays an important role in social behavior, as it promotes affiliation and thus acts as a social glue in interaction with others. The extent of imitating others emotional facial expressions and therefore affiliative behavior is influenced by numerous factors, such as personal characteristics, relationship towards the other person with whom someone is interacting, and the motivation and ambition for social interaction (see Seibt et al., 2016, for a review). But also, neurobiological factors affect our social behavior.

There has been a great amount of research recently done on facial mimicry in humans, which focused mainly on the effects (such as the proper recognition of emotions) or on factors that affect the extent of facial mimicry (e.g., traits and states, the presence of mental disorder like ASD, differences between genders, or social settings). The influence of the mu-opioid system on social behavior, in which facial mimicry is known to play a major role, has already been demonstrated extensively in rodents as well as in humans. However, so far, little attention has been paid to the impact of underlying neurobiological mechanisms such as the opioid system on facial mimicry.

For this reason, the aim of the present paper is to investigate how facial mimicry is modulated by the opioid system. In particular, which influence does blocking the opioid system by naltrexone, an opioid antagonist, have on emotional mimicry of emotional facial expressions and therefore on social affiliative behavioral responses?

Based on the literature on facial mimicry, the opioid system, social affiliation and reward behavior, it can be hypothesized that 1) there are changes in the measured muscle activity in response to observed facial expressions. More precisely, activity of Corrugator Supercilii is only expected to increase when angry facial expressions are observed, and activity of Zygomaticus Major only when happy faces are shown. Further, it is expected that 2) there are gender differences. Since findings concerning expressing and mimicking negative emotions are less consistent, only gender differences for positive emotions are assumed. In specific, women who normally display stronger affiliative behavior show greater facial mimicry when observing positive emotional facial expressions. Moreover, since naltrexone has a reputation to reduce affiliative behavior in social interactions, it is

assumed that 3) participants in the naltrexone group will show a diminished activity of Zygomaticus Major towards happy facial expressions as well as an increased activity of Corrugator Supercilii towards happy faces. Moreover, due to the greater affiliative behavior in females it is assumed that 4) women will be more significantly influenced by the administration of naltrexone in their mimics of facial expressions. More precisely, the decrease in Zygomaticus Major activation under naltrexone intake is supposed to be more pronounced in female participants.

Overall, the hypotheses are as follows:

H1: There are changes in muscle activity when observing emotional facial expressions.

1a. Corrugator Supercilii activation increases when observing angry facial expressions.

1b. Zygomaticus Major activation increases when observing happy facial expressions.

H2: Females show a greater activation of Zygomaticus Major towards happy faces.

H3: Naltrexone influences the extent of facial mimicry.

3a. Naltrexone reduces activity of Zygomaticus Major when observing happy facial expressions.

3b. Naltrexone increases activity of Corrugator Supercilii when observing happy facial expressions.

H4: Reduction of Zygomaticus Major activity towards happy faces is more pronounced in females compared to males.

3. Methods

3.1 Participants

As the current study examines the general exploration of how facial mimicry is modulated by the opioid system, a non-probability sampling was done. Participants for this study were recruited via internet platforms, flyers, and "Laboratory Administration for Behavioral Sciences" (LABS), a recruitment tool by the University of Vienna, between February 2018 and July 2018. The sample included 43 volunteers (31 females and 12 males) and was aged 18-35 years (M = 23.12, SD = 4.10). All participants were fluent in German language and reported normal or corrected-to-normal visual acuity, to have no history of current or former drug abuse, and to be free of psychiatric or neurological disorders (for this purpose, they were screened before testing). Participants gave written informed consent prior to participation and were briefed about the side effects as well as the confidential and anonymous aspect of their involvement in this study (which was approved by the ethical committee of the Medical University Vienna). In the end of the experiment everyone received a monetary compensation (which was at least 90 € for the whole "Taste & Touch" study).

3.2 Drug Administration

Approximately 4 h before the facial mimicry task, participants were given orally either Dependex (1 x 50 mg naltrexone, encapsulated) or a placebo capsule containing mannitol, once in a randomized, double blind and counter balanced manner. In this study, 50 mg of naltrexone were administered as this is a standard dosage were mu-opioid receptors are known to be blocked more than 90% (Weerts et al., 2013), which induces a plasma concentration plateau approximately 1 h after intake (Lugo & Kern, 2002). The active ingredient naltrexone has been tested in several studies without any serious side effects (e.g., Chelnokova et al., 2014; Inagaki et al., 2016). On that account, with the dose of 50 mg used in this study and onetime administered, no significant side effects are to be expected. See figure 1 for an overview of the distribution of women and men in naltrexone and placebo group.

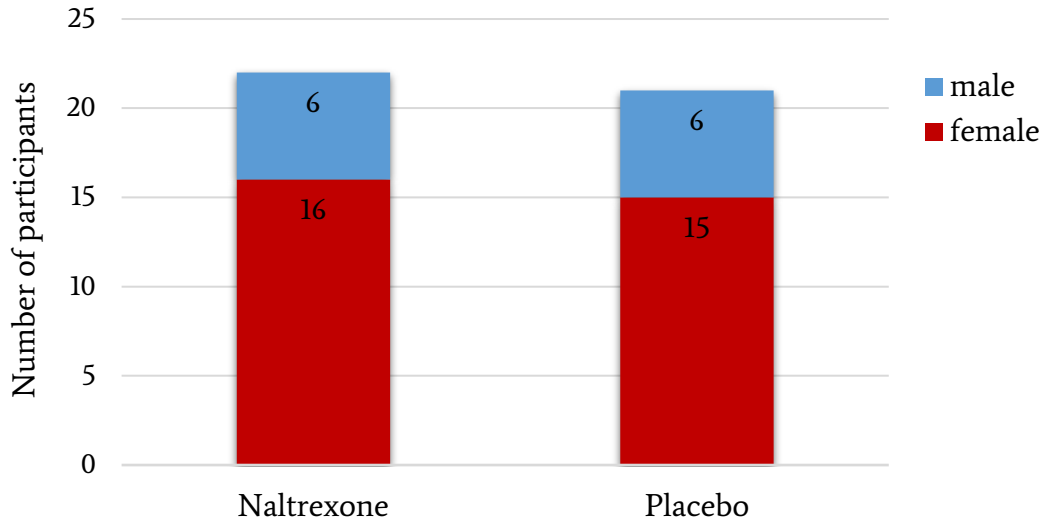

Figure 1. Quantity and gender distribution in naltrexone and placebo group.

3.3 Study Procedure

The facial mimicry task was one part of a study called "Taste & Touch" conducted by Silani and colleagues, a basic research study (monocentric, randomized, double-blind, placebo-controlled, three-armed parallel design) which investigates the psychopharmacological distinction of wanting and liking of primary and social rewards and took part at the Department of Psychiatry and Psychotherapy, Medical University of Vienna (General Hospital [AKH], Währinger Gürtel 18-20, 1090 Vienna). In the following, the procedure of the whole "Taste & Touch" study will be described roughly, followed by a closer look at the facial mimicry task presented in this paper.

3.3.1 Taste & Touch Study

The study consisted of two test times. The first day includes an extensive pre-screening (T0), the second day (T1) the actual investigation of the role of dopamine and opioid system in wanting and liking of primary and social rewards. At the first test time (T0), the participants did a short computer task (an experiment measuring the creation of stimulus-reward relationships) and were then tested by the doctor in detail on their mental and physical health (electrocardiography, examination of the blood, psychiatric questionnaire) to the suitability of the study. If the medical examination was without pathological findings, participants were invited to the second test time, which took place

one to a maximum of 60 days after the first test and was scheduled for 6 hours. The second day of testing (T1) was scheduled for a total of 6 hours. After drug administration, the psychophysiological study began, including testing the wanting and liking of primary and social rewards, the facial mimicry task, as well as three shorter computer experiments (an experiment for probability weighting, again the reward learning task, and a task about working memory). Throughout the experiment, the state of health and the occurrence of side effects was assessed by the doctor 180 and 300 minutes after drug administration.

3.3.2 Facial Mimicry Task

This facial mimicry task is a behavioral experiment which was done on the computer. Therefore, participants sat about 50 cm in front of the screen and were observing stimuli containing emotional faces. In what kind of modality the stimuli were presented (static or dynamic) is particularly important in the recognition of facial expression as well as for the extent on facial mimicry. Several studies (e.g., Dimberg & Lundqvist, 1990) are using static imagines to measure mimicry. However, recent studies reveal dynamic advantages in emotion recognition (e. g., Hyniewska & Sato, 2015; Calvo, Avero, Fernández-Martín, & Recio, 2016), a better representation of social encounters, and a greater observed emotion consistent EMG activity (e.g., Weyers, Muehlberger, Hefele, & Pauli, 2006). Particularly, higher intensities of core smile movements have been reported when participants watched dynamic rather than static expressions of happiness. Also, dynamic materials have a higher ecological validity, given that in everyday social interactions facial expressions are fluid and rapidly changing depending on the situation (Krumhuber, Kappas, & Manstead, 2013; Krumhuber, Skora, Küster, & Fou, 2017). Likewise, past research reveals better recognition and higher arousal scores of emotions when dynamic than static stimuli were shown (e.g., Hyniewska & Sato, 2015; Calvo et al., 2016). Dynamic displays may therefore provide relevant cues which facilitate the decoding of facial expressions and help identifying subtle facial expressions (Krumhuber & Manstead, 2009), which in turn has an impact on facial mimicry. For these reasons, dynamic stimuli were used in this study, which are described in more detail in the following.

3.4 Stimuli

For the facial mimicry task short 5120 ms video sequences as stimuli were shown on a black background. Video clips contained gradual changes of photos containing faces that showed different emotional facial expression which are displayed by men and women. The same photos were successfully used to generate similar stimuli in previous studies (Korb et al., 2015; Halberstadt & Niedenthal, 2001; Niedenthal et al., 2001). Stimuli were constructed with a morphing software (Morpheus Photo Morpher, version 3.17) using angry, happy and neutral expressions by 12 adults (half female, half male faces). Thereby, angry facial expressions morphed into happy facial expressions and other way round (condition AngerToHappy [AH] and HappyToAnger [HA]). Anger and happiness as emotions were chosen because they elicit pattern of facial mimicry that can clearly be distinguished (Korb, Malsert, Strathearn, Vuilleumier, & Niedenthal, 2016). See figure 2 for an example of a stimuli.

Figure 2. Schematic view of one trial showing faces which morph from an angry into a happy expression (stimuli of HappyToAnger condition).

3.5 Procedure Facial Mimicry Task

After approximately 4 h after drug administration, participants did the facial mimicry task. Therefore, they were told to report the moment one emotion completely switched to the other by pressing a button on a keypad. Video clips were shown for their

entire length, regardless of whether and when participants responded. Perceived offset time (reaction time, RT) was measured in milliseconds from the onset of the video clip. After each clip, if a response had been provided, RT was shown for one second on a black screen. Otherwise, the text "No response" was shown. After completion of four practice trials (displaying two stimuli of each condition), 96 trials were shown in two blocks of 48 trials. Between the blocks, participants were free to take a break.

3.6 Facial EMG Recording

To measure the activity of the facial muscles and thus facial mimicry in this study, facial electromyography (EMG) was used. EMG is a way to measure the electrical potential from facial muscles in order to infer muscular contraction. Thereby, electrodes are placed on the skin of the face to measure potential changes in the muscle activity. Those changes in muscle activity were typically reported as difference scores between reaction scores while the subject undergoes various procedures, such as watching pictures or films containing emotional expressions (Fridlund & Cacioppo, 1986). A major advantage of using EMG is its ability to detect muscular activity that would not be recognizable to the human eye. It is a non-invasive, and in psychological research widely used method.

In this study, bipolar EMG responses were measured using Ag/AgCl electrodes with 4 mm inner diameter according to the guidelines established by Fridlund and Cacioppo (1986). The EMG raw signals were measured with a g.USBamp amplifier (g.tec medical engineering GmbH, Austria) with a sampling rate of 1200 Hz. To increase the conductivity of the electrodes they were filled with skin-friendly, highly conductive water electrolyte gel (SignaGel, Parker Laboratories). The electrodes were positioned on the left side of the face in pairs on Corrugator Supercilii (in the following CS), the Zygomaticus Major (in the following ZM), as well as a reference electrode behind the ear and a ground electrode on the upper forehead below the hairline. ZM (a muscle involved in smiling by lifting the corners of the mouth up) was chosen because it responds to positive, happy faces, and CS (a muscle responsible for frowning by drawing the eyebrows together and downwards) because of its response to negative, angry faces (Dimberg, 1990). Before the electrodes were attached, the skin of the participants was first degreased with alcohol and afterwards cleaned with skin peeling to reduce electrode-skin impedance.

3.7 EMG Data Preprocessing

EMG data was post-processed with Matlab, partly using EEGLAB. Data management and statistical analysis were performed using in R 3.5.1 (R Core Team, 2016). For generating tables and figures R as well as Windows Office Excel 2016 was used.

First, for data preparation EMG data was rectified and filtered with a high-pass of 20 Hz, a low-pass of 400 Hz, and a 50 Hz notch filter, and smoothed with a 40 Hz low-pass filter. Subsequently, the EMG scores are expressed as a percentage of the baseline scores and averaged over 1-second windows.

For analysis, trials were excluded if the average of the baseline was more than 2 SDs over or below the average of all the baselines of that subject, or if the peak ampere in the baseline was more than 2 SDs over or below the average of the peaks of the baselines of that subject. In addition, trials were excluded if the average was more than 2 SDs over or below the average for the period after the baseline of that subject or if the peak ampere was more than 2 SDs over or below the average for the period after the baseline of that subject. In addition, trials were excluded for the analysis if EMG data contained artefacts. Therefore, only trials that survived EMG-based rejections were included in analysis of EMG data. On average, 17 trials per person (17.95% of trials per person) were excluded (M = 17.23, SD = 3.88). Numbers of trials rejected in females (M = 17.16, SD = 3.84) and males (M = 17.24, SD = 4.16) did not differ significantly ($t(41) = 0.18$, $p = 0.856$), as well as number of trials in the naltrexone (M = 16.77, SD = 4.04) and placebo group (M = 17.71, SD = 3.76) did not differ significantly ($t(41) = -0.79$, $p = 0.433$).

3.8 Data Analysis

For statistics, data were analyzed with linear mixed models (LMMs) using lme4 (Bates, Maechler, Bolker, & Walker, 2014), a package in the free open-source program R (R Core Team, 2016). An LMM describes the relationship between a dependent variable and other explanatory variables that have been obtained along with the response. It comprises fixed effects, as well as random effects (Magezi, 2015). Using LMMs for analyzing does have several advantages compared to using analysis of variance (ANOVA). LMMs are more robust and flexible for analyzing unbalanced data sets when random effects are present

(Bolker et al., 2009), since it can accommodate missing data points often encountered in longitudinal datasets and can model nonlinear, individual characteristics (Krueger & Tian, 2004). Also, LMMs can be extended to higher-level models, meaning repeated observations within individuals within clusters. Moreover, LMMs can include random effects for both participants and stimuli, which entails a reduction of type I errors (Korb et al., 2016). Since the gender distribution in the samples are not the same size and some values were taken out due to artefacts or insufficient RT exclusion, for these reasons and the advantages over the ANOVA, LMMs were used for data analysis.

To test the hypotheses, several LMMs with random intercepts per subjects were calculated including different factors. In particular, LMMs with EMG for the different emotion conditions were done (LMM with EMG to AH and LMM with EMG to HA) with the within-subjects factor Time (as continuous with five windows from 1 to 5), and the between-subjects factors Muscle (ZM and CS), Drug (naltrexone and placebo) and Gender (female and male) were tested (resulting in two 2x5x2x2 LMMs) to see if there are facial mimicry and gender differences in muscle activity when observing emotional facial expressions and to examine the effect of naltrexone on the activity of facial muscles (EMG). Additionally, LMMs with EMG for specific muscles with congruent emotions were tested (LMM with EMG for ZM to AH and LMM with EMG for CS to HA) with Time, Drug, and Gender as factors (resulting in two 5x2x2 LMMs). Furthermore, possible negatively-valanced muscle responses were analyzed by LMMs with EMG for ZM to HappyToAnger and one for CS to AngerToHappy with the factors Time, Gender, and Drug (resulting in two more 5x2x2 LMMs).

In order to compensate for the possibility of false positive results, the significance threshold α was set to $p = 0.05$.

There is no generally defined way to measure facial mimicry. Consequently, facial mimicry studies vary considerably in the period of measurement. Some studies look at the time progress of muscle activity changes, while others show the mean difference from baseline for an entire stimulus presentation period (Seibt et al., 2015). Since dynamic stimuli were presented in this study, facial mimicry is considered to be a change in facial muscle activity over time (from beginning of the video clip till the end). Thus, for statistical analysis, it is investigated whether the EMG data changes significantly during the observation of video clips.

4. Results

Is there facial mimicry in response to observed facial expressions? Results show significant muscle activity changes over time when observing video clips morphing into happy facial expressions ($F(1, 16353.6) = 44.92$, $p < .001$; Time*Muscle interaction in LMM with EMG to HA) as well as video clips morphing into angry facial expressions ($F(1, 16474.0) = 56.96$, $p < .001$; Time*Muscle interaction in LMM with EMG to HA). Figure 3 illustrates the diverse transition of CS and ZM activity in the HappyToAnger and AngerToHappy condition.

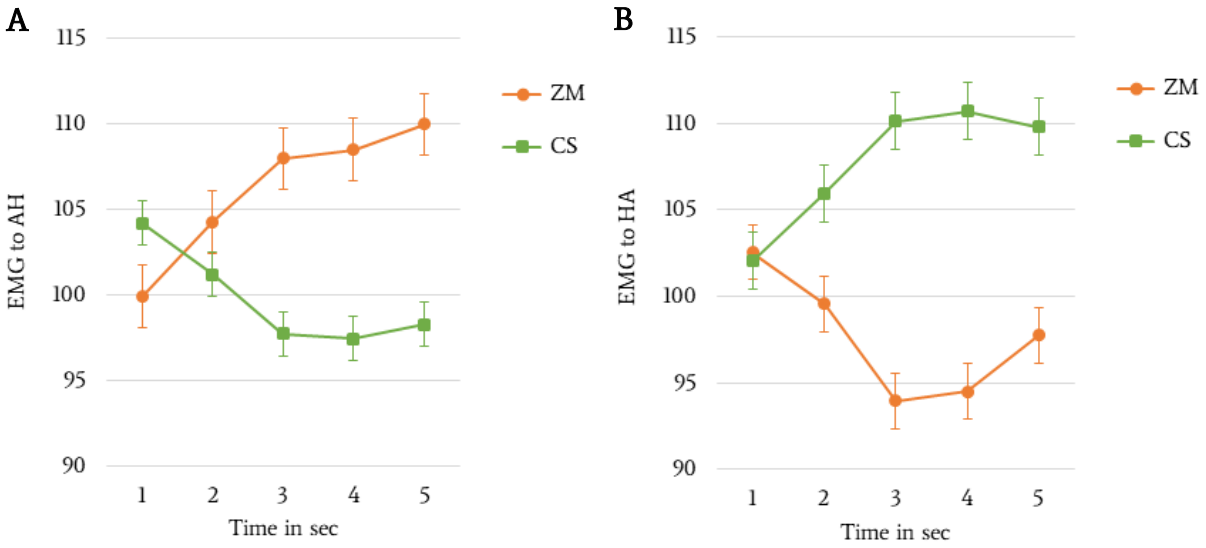

Figure 3. Mean EMG in response to AngerToHappy (left, A) and HappyToAnger (right, B) trials, averaged over 5 consecutive time windows. Significant differences in ZM and CS muscle activity are shown. Error bars indicate standard errors of the means.

According to this, ZM activity significantly increases when observing happy facial expressions ($F(1, 8151.9) = 21.85$, $p < .001$; main effect of Time in LMM with EMG data for ZM to AH), whereas at the same time CS activity significantly decreased ($F(1, 8152.1) = 36.65$, $p < .001$; main effect Time in LMM with EMG for CS to AH).

As opposed to this, a significant increase of CS activation towards angry facial expression could be shown ($F(1, 8212.0) = 58.87$, $p < .001$; main effect Time in LMM with EMG data for CS to HA) with a simultaneous decline in ZM activity ($F(1, 8212.4) = 18.76$, $p < .001$; main effect Time in LMM with EMG for ZM to HA).

Are there gender differences in the way in which positive facial expressions are mimicked? Contrary to the assumption, no significant gender difference in ZM activity could have been shown. Neither for happy faces ($F(1, 65.2) = 2.45$, $p = .122$; no significant effect of Gender in LMM with EMG for ZM to AH), nor for angry faces ($F(1, 95.5) = 3.78$, $p = .055$; only marginally significant effect of Gender in LMM with EMG for ZM to HA).

However, a variation between females and males were found in the extent of CS activation. More specific, there was a significant increase in CS activation towards angry faces over time ($F(1, 8212.0) = 7.02$, $p = .008$; interaction effect of Time*Gender in LMM with EMG of CS to HA;). Thus, females and males differ significantly in the mean EMG of CS activation in the HappyToAnger condition ($t(41) = -2.90$, $p = .008$). For a graphical depiction of difference in CS activity over time, see figure 4.

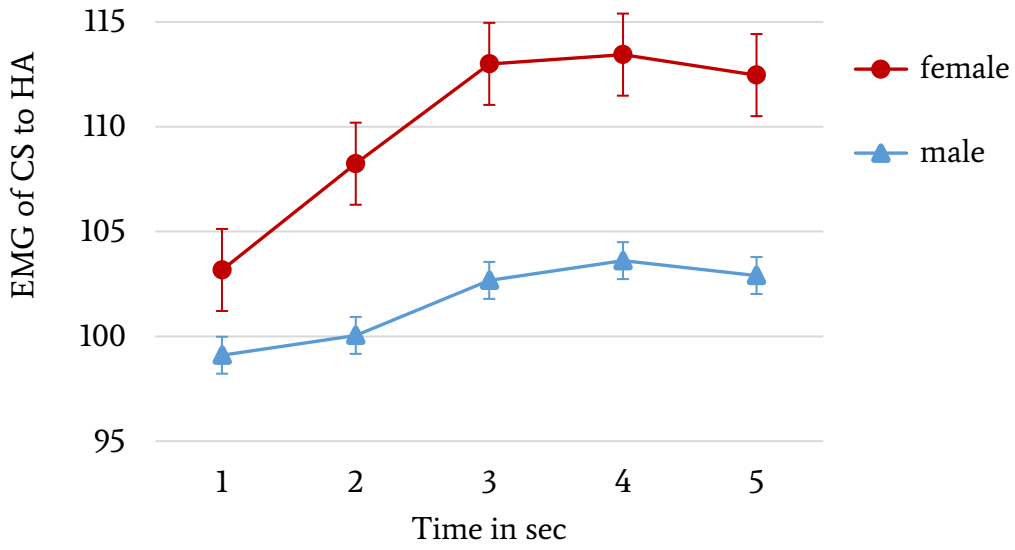

Figure 4. Mean EMG for CS during HappyToAnger trials averaged over 5 consecutive time windows, showing greater increase of CS activation in females compared to males (standard errors indicated).

In addition, significant differences by gender in the increase of CS activity over time was found for the AngerToHappy condition ($F(1, 52.7) = 5.08$, $p = .028$; interaction effect of Time*Gender in LMM with EMG of CS to AH). Figure 5 illustrates the difference of females and males in CS changes over time when observing AngerToHappy videos.

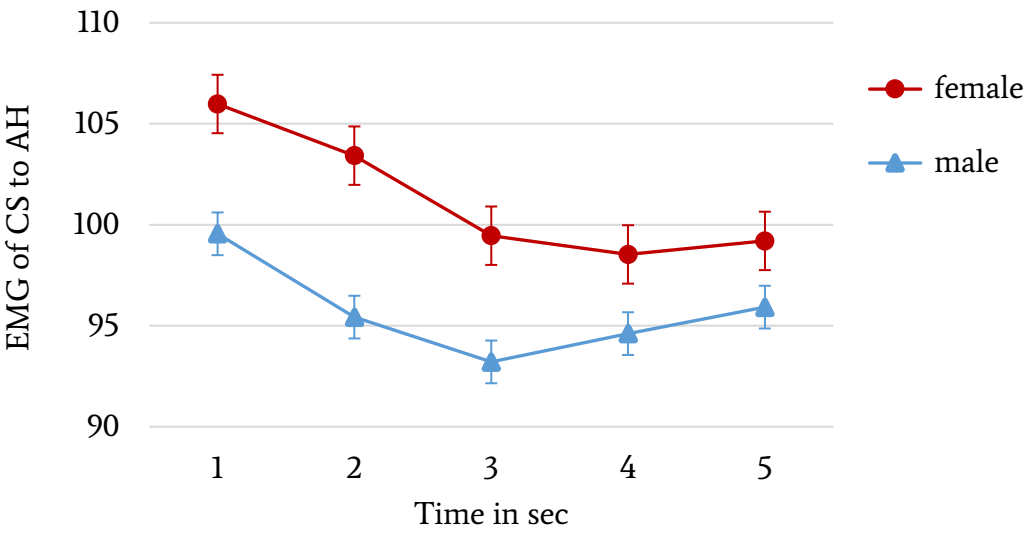

Figure 5. Mean EMG for CS during AngerToHappy trials averaged over 5 consecutive time windows, showing lower decrease of CS activation in females compared to males (standard errors indicated).

However, when comparing the mean EMG of CS activation in AngerToHappy condition overall, no significant difference can be found ($t(14) = -1.96$, $p = .060$; see figure 6).

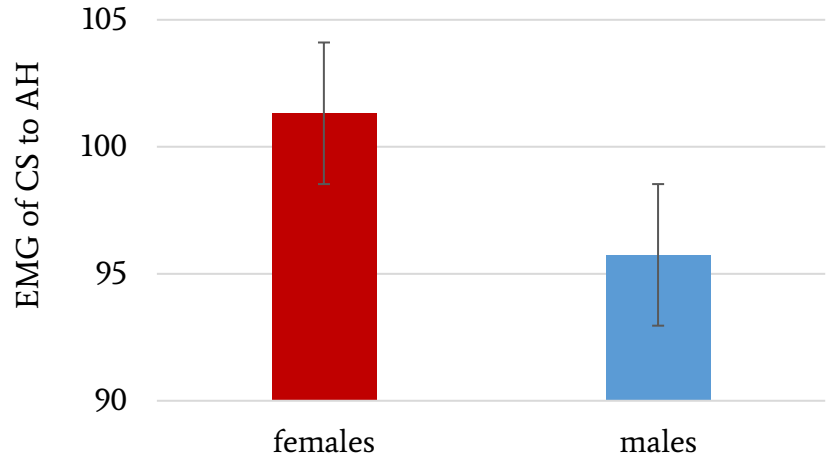

Figure 6. Mean EMG for CS averaged over all time windows in AngerToHappy trials, showing no significant differences in CS activation between females compared to males (standard errors indicated).

Does naltrexone have an impact on how participants mimicry? When looking at the ramification of naltrexone on happy facial expressions, a significant interaction effect of Drug*Time could have been shown in the EMG ($F(1, 16353.6) = 4.76$, $p = .029$; LMM with EMG to AH), indicating a significant difference in the change of muscle activity between naltrexone and placebo group towards happy facial expressions over time.

Results further showed a significant interaction effect of Drug*Time in ZM activity to AH ($F(1, 8151.9) = 4.00$, $p = .046$; LMM with EMG of ZM to AH), implicating a different ZM activity change towards happy facial expression between naltrexone and placebo group. Figure 7 represents the various increases in ZM activity when observing happy faces.

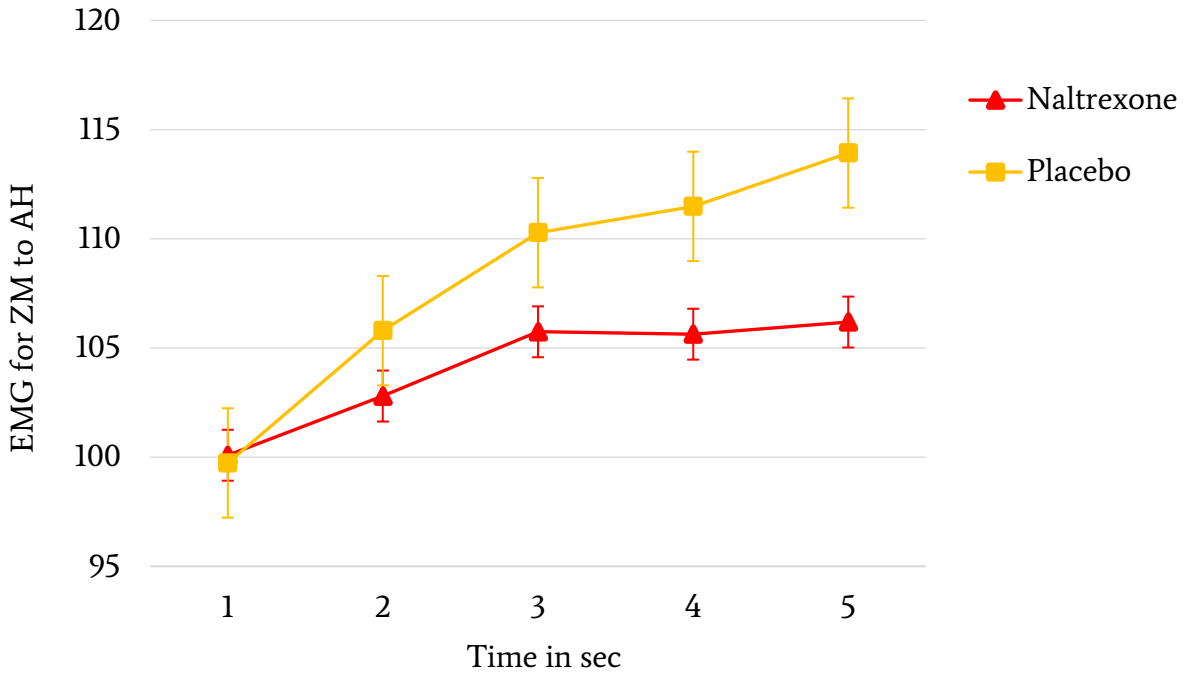

Figure 7. Mean EMG for Zygomaticus Major in naltrexone and placebo group during trials with AngerToHappy condition averaged over 5 consecutive time windows. Significant lower increase of ZM activation towards happy faces in naltrexone group compared to placebo group. Error bars indicate standard errors of the means.

No such Drug*Time interaction was found for CS activity to happy facial expressions ($F(1, 8152.1) = 1.03$, $p = .311$; LMM with EMG for CS to AH), indicating that naltrexone group do not differ from placebo group in CS activity changes towards happy faces.

Moreover, no influence of naltrexone on muscle activation over time towards angry facial expressions could have been shown ($F(1, 16474.0) = 1.15$, $p = .284$; no interaction of Drug*Time in LMM with EMG to HA), neither on CS activity ($F(1, 8212.0) = 0.27$, $p = .601$; no interaction of Drug*Time in LMM with EMG for CS to HA), nor on ZM activity ($F(1, 8212.4) = 2.53$, $p = .112$; no interaction of Drug*Time in LMM with EMG of ZM to HA).

Is the influence of naltrexone intake on facial mimicry more pronounced in females? As mentioned above, naltrexone shows a significant impact on ZM activity over time towards happy faces. But is this influence more pronounced in one gender? For happy faces, results show no significant Drug*Gender interaction ($F(1, 65.2) = 0.53$, $p = .468$; LMM with EMG of ZM to AH), indicating that there is a no difference in ZM changes over time in females and males between naltrexone and placebo group when observing video clips morphing into happy faces. Figure 8 shows the EMG of ZM in the AngerToHappy condition for females and males in naltrexone group.

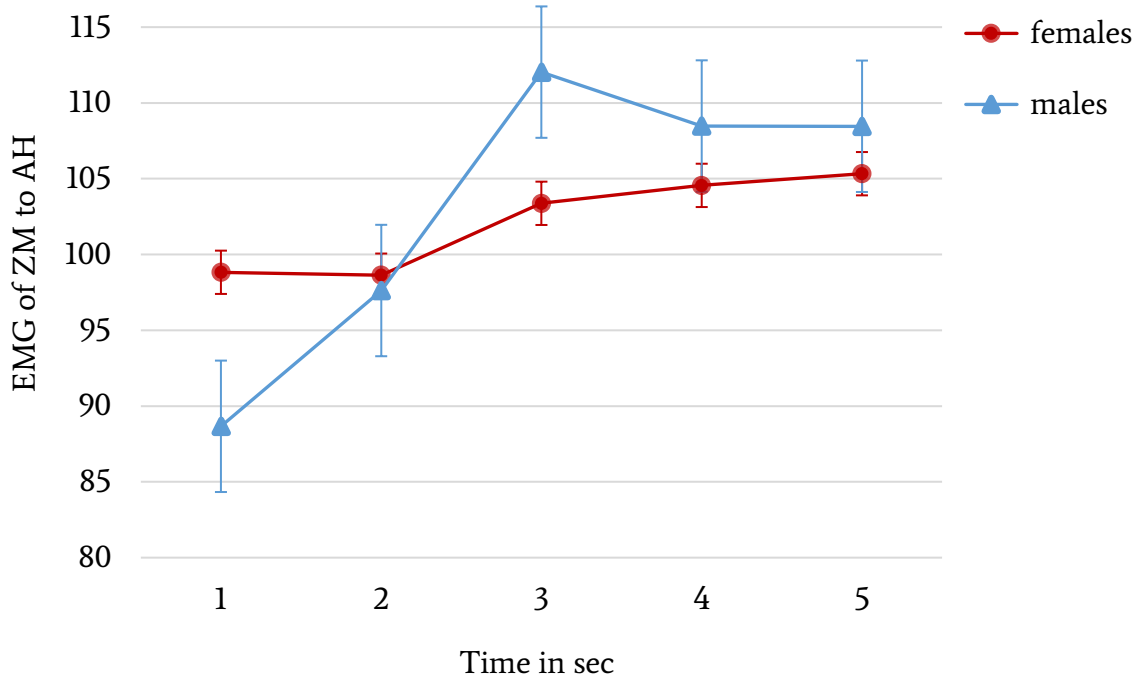

Figure 8. Means of EMG for ZM activity in AngerToHappy condition of females and males in naltrexone group (including standard errors) condition averaged over 5 consecutive time windows, indicating a slight tendency for a lower activation of ZM in females when observing faces morphing into happy expressions.

5. Discussion

Imitating facial expressions is an essential part of social interactions. It is helpful for a better and faster understanding of emotions and promotes affiliation and liking. Aim of this study was to investigate the impact of the opioid system on the ability and extent of mimicking emotional facial expressions, more precisely, how naltrexone, an opioid antagonist, modulates mimicry of emotional facial expressions and therefore responds to social affiliative behavior. Therefore, 43 participants divided into two different groups (were either naltrexone or placebo were administered) observed 96 short video clips containing pictures of faces morphing from either happy to angry facial expressions or the other way around. To compare muscle activation, activity of ZM and CS were assessed using EMG. The results illustrated that first, as hypothesized, there is activation of facial muscles to congruent emotional expressions associated with them. Second, and different from what was assumed, women respond with a greater CS activity towards negative as well as positive facial expressions compared to men. No gender difference was found for ZM activation. Third, naltrexone has an impact on the extent of the imitation of ZM activation towards emotional facial expressions, which corroborate the hypothesis. An influence of naltrexone on CS activity could not be shown. In specific, a reduced ZM activity towards happy faces in women and an increased ZM activity towards angry faces in men has been shown. Fourth, no significant effect was found that the non-affiliative fostering impact of naltrexone is more pronounced in females.

5.1 Interpretation of Results

5.1.1 Presence of Facial Mimicry

The present study displayed that facial mimicry was reliably triggered by both emotions. In particular, when observing faces morphing into a happy expression, participants display an increase in ZM activity and reduction in CS activity. In contrast, CS activity increases and ZM activity decreases when watching faces morphing into an angry emotion. This illustrates that ZM mainly responds to positive, happy faces and CS to negative, angry faces. The increased activity could not be attributed to a generalized

increase in all facial muscle activity as there was no such trend observed for the ZM towards angry facial expressions and for CS in response to happy facial expressions. Those results are in line with earlier studies investigating differences in muscle feedback to observed emotional stimuli (Dimberg, 1990; Hess & Blairy, 2001).

5.1.2 Gender Differences in Facial Mimicry

The statistics show gender differences in facial mimicry. Specifically, to the extent of activation of CS. Thus, women differed significantly from men in the extent of CS activation when observing angry faces as well as happy faces. However, the assumption that women show facial mimicry towards positive social reward cues (happy facial expressions) to a greater extent than men could not be confirmed. This result is in contrast with earlier findings from studies showing that females in general exhibited greater facial EMG response that were most pronounced to positive facial expressions (e.g., Dimberg & Lundqvist, 1990) and which can be explained due to a generally more affiliative behavior compared to men (Brody & Hall, 2008). Thus, although there have been proven differences in social behavior and affiliative motives, which suggests that women show more facial mimicry to smiles, this could not be confirmed in this study.

Why do women show no greater activity of ZM compared to men in this study? One possible explanation for the absence of gender differences in the extent of ZM activation might be because participants who naltrexone were not partitioned out when calculating gender differences. Since the two antagonists are related to the extent of facial mimicry, this may be the reason why the results show no differences between women and men. However, even if only participants who received a placebo are considered for exploring gender differences, and thus no effects of naltrexone on the extent of muscle activation can exist, no significant gender differences in the activation of the ZM can be seen (only a tendency for women to show more ZM muscle activity towards happy faces).

Given the fact that in the placebo group is a slight disposition for women to show more ZM muscle activity, the insignificant difference might be due to the fact that the placebo group was quite small (N = 21) and unequal in size (15 female and 6 male

participants). Having more women and men in the placebo group, gender differences in muscle activity on happy faces may be shown significantly.

Moreover, the findings not only show that women do not response with a greater ZM activity to happy facial expression but also that they show a greater CS activity towards angry emotional faces. Results for CS activity and in general for expressing negative emotions are less consistent. There are studies which are in line with the current finding, revealing a greater display of anger in females compared to males (Levenson et al., 1990) as well as a greater CS activity in females than males when observing videos of snakes (Thunberg & Dimberg, 2000) and when imagining emotional situations (Schwartz et al., 1980). However, some studies found the exact opposite (i.e. more pronounced CS increase in males when observing angry facial expressions, see Soussignan et al., 2013), whereas some found no differences between genders (e.g., Levenson et al., 1990). As can be seen, previous studies of differences between women and men in the expression of anger are not in agreement. McDuff et al. (2017) suggest that there is no universal norm for women to express fewer negative emotions than men and that gender differences may be more state specific. As can be seen, the results on gender differences in CS activity are relatively uneven. Apparently, it depends on which stimuli are presented, how the structure of the study was, in which setting the facial muscle activity was measured, and on specific states and traits of participants.

But why did females in this study displayed more CS activity towards angry faces compared to men? An influence of naltrexone can be ruled out as a possible reason, since females in the placebo group also show more CS activation towards angry faces than males. However, the reason might be that women are more emotional expressive (LaFrance & Hecht, 2000) and therefore are more likely to be infected by feelings of others. Due to the greater emotional contagion (Doherty et al., 1995) females may also be more affected by the observed angry facial expressions. Studies also show that negative emotions are perceived stronger and faster than positive emotions (Cacioppo, Gardner, & Berntson, 1997). Thus, angry facial expressions in the videos affect the extent the observer feels faster and stronger. Aside from that, contagion is closely linked with empathy (Hatfield, Bensman, Thornton, & Rapson, 2014), which also shows women in a more pronounced sense than

men (Davis, 1983). Higher emotional affection as well as more pronounced empathy might therefore be the reason for greater mimicry of angry facial expressions in females.

Further, it has been shown that gender vary in CS activation changes when observing AngerToHappy trials. However, there was no significant difference in EMG of CS for whole AH trials. This illustrates that while there is a difference in the change in CS activity in women and men throughout the video, no such difference was found for an average of CS activation throughout the trial (see figure 6). This may be explained by the fact that women display an increased CS activation to angry facial expressions. Since faces with an angry expression are shown in the first few seconds in the AngerToHappy condition, the difference between genders is more pronounced in the beginning and decreases in the last seconds when happy faces are shown (see figure 5). That is, the significantly different changes in CS activation in the AH condition is due to the fact that women respond more strongly to angry facial expressions. This assumption is supported by the fact that there is no significant difference between the sexes in the CS activation averaged over all five time windows. Thus, it can be concluded that there are no differences between women and men in facial mimicry to happy faces.

5.1.3 Influences of Naltrexone on Facial Mimicry

In addition, the present study showed that naltrexone has an influence on the extent participants mimicked emotional facial expressions. Thus, as it was expected, there was a significant difference in the muscle activity in the AngerToHappy condition by taking naltrexone. More specifically, a significantly diminished increase in ZM activity towards happy facial expressions could be demonstrated. This indicates that blocking the (mu-) opioid system reduces the facial mimicry of happy facial expressions. Those findings are in line with current literature that blocking the opioid system diminishes affiliative behavior and affects the sensibility for rewarding stimuli (Chelnokova et al., 2014; Depue & Morrone-Strupinsky, 2005; Inagaki et al., 2016; Meier et al., 2016). The present study extends these findings by demonstrating that the mu-opioid system modulates the automatic and unconscious behavioral response towards social reward cues like positive happy faces.

Further, the hypotheses that naltrexone increases CS activity to happy faces cannot be confirmed. This result stands in contrast to the finding of Meier et al. (2016), who showed that naltrexone lead to an increase of CS activation when observing positive facial expressions. Thus, no increase of negatively facial responses to affiliative facial cues could have been shown and reproduced in this study. This could indicate that merely positive facial expressions appear to be affected in their response to happy faces by blocking the opioid system. Thus, as in the study by Inagaki et al. (2016), behaviors that are especially related to positive feelings (in this case smiles) seem to be only affected through the intake of naltrexone.

Moreover, and also contrary as it was suggested, it has not been shown in this study that the influence of naltrexone on facial mimicry is more pronounced in women. Although women show more behavior that signal the desire to get in touch with others (Brody & Hall, 2008), the reduction of affiliative behavior by naltrexone has not been revealed especially on women. However, females show a slight tendency for a lower ZM activity towards happy faces. This suggests that females tend to be influenced by naltrexone in a more pronounced way. Having a bigger sample probably might show such tendency to a greater extent.

Why did naltrexone particularly reduce facial mimicry of smiles? How attractive a stimulus is perceived and how much one strives for it, is driven by various aspects: on the one hand it is influenced by wanting (motivational aspect) and on the other hand by liking (hedonic aspect). In a study by Chelnokova et al. (2014) it has been shown that the opioid system contributes to both components of reward, but especially to the hedonic value. Such influences are the strongest for the most valuable stimuli. When the opioid system is increased (for example by the intake of an opioid agonist such as morphine), motivation for the most valuable stimuli as well as motivation to avert the least valuable stimuli increases. Naltrexone as an opioid antagonist does exactly the opposite. It reduces liking of the most valuable stimuli. The diminished liking, in turn, results in a decreased motivation for these stimuli (Chelnokova et al., 2014). This suggests that opioids can enhance the social reward of certain stimuli while arbitrating social motivation by enhancing the salience and reward appraisal of the most valuable stimuli. In terms of facial mimicry, this means that stimuli with the highest reward value (smiles) are less rewarding and valuable when

lowering the opioid system by naltrexone administration, which results in a diminished motivation for affiliative behavior (i.e. that is to mimic facial expressions).

In sum, it has been shown that facial mimicry is diminished towards positive facial expressions by reducing the opioid system. Whether the reduced facial mimicry is due to perceiving faces as less rewarding or due to a diminished motivation for social connection is in doubt. In order to be able to pursue this question more closely, the general motivation for affiliation should be inquired in future studies, as well as the value of the individual stimuli for participants. This might help to pinpoint which aspect may be more responsible for the reduced mimicry of positive facial expressions towards people with whom once interact with. In addition to this, other issues which should be taken into account in further studies to control possible confounding factors or moderators are addressed in the following.

5.2 Limitation and Suggestions for Further Studies

Although the main hypothesis of the influence of naltrexone on the extent on facial mimicry towards happy facial expressions can be confirmed, the present study indeed has limitations (or at least aspects which may be good to consider in further studies). To begin with, the sample size was relatively small and unbalanced in gender groups. Future studies should include a bigger sample as well as balanced group sizes to get convincing results. Hence, the effect of naltrexone especially in females can be eventually shown significantly.

Further, the EMG data of the participants are based on the assumption that they rivet on the short video clips all the time during the facial mimicry task. Since the task took about 20 minutes, and the participants have been in the lab for more than 3 hours for testing and have done several tasks, it cannot be confirmed that all participants had eyed on the videos clip were altered emotional facial expressions are shown the whole time. For this reason, eye tracking should capture gaze behavior additionally. Hence, it is possible to ascertain when participants did not direct their gaze to the video clips. Sequences in which the stimuli were not observed could be removed from the data analysis to avoid potential distortions in the EMG data and related misinterpretations.

In addition, since people variegate in the extent of how they express emotions with their face and therefore how much they mimic facial expressions, future studies should initially measure voluntary mimicry in the beginning of the task to provide a baseline and to see the unexceptional magnitude of everybody's facial expression. In this way, differences that are not accounted for by naltrexone and conceivably lead to misinterpretations can therefore be eliminated.

As it has been shown in the introduction, facial mimicry is influenced by several aspects. To avoid eventual misinterpretations, further studies may therefore include covariates in the analysis in order to control for certain characteristics. For example, the trait empathy should also be taken into account, given by the results that persons with a high level of empathy show a stronger mimic of facial expressions, both towards happy and angry faces (Sonnby-Borgström, 2002; Dimberg et al., 2011; Zajonc et al., 1987). Further, the current state of the participant should be included, since it has been shown that participants differ in the extent of which they mimic facial expressions according to in which mood they are (Likowski et al., 2011). Additionally, McDuff et al. (2017) suggested that gender differences in facial mimicry are state specific.

Another factor that should be considered in further studies is the gender of the sender. As depending on whether the person or avatar used as stimuli is male or female, the extent of facial mimicry can be affected (see LaFrance & Hecht, 2000; Schrammel et al., 2009; Seibt et al., 2015). Not just the sex of the sender's face, but rather how attractive the sender is considered to be has an impact on facial mimicry, probably due to different expectations towards a potential interaction partner. As mentioned above, manipulation of the opioid system affects the aesthetic evaluation of and the motivation for viewing opposite-sex faces (Chelnokova et al., 2014), wherefore it might be good to know participants' evaluation of attractiveness or value of the shown faces.

Finally, it is of interest to see what effect a change in the opioid system has on facial mimicry in individuals with a mental disorder such as ASD who are known to be less socially affiliative and less sensitive to social rewards.

5.3 Conclusion

In summary, social connections are highly crucial for normal functioning, overall health, happiness, and longevity. For this reason, understanding how humans' bond with and feel socially connected to one another is of utmost importance (Inagaki, 2018). The present study investigated the underlying neurobiological mechanism for social affiliative behavior. Specifically, this work demonstrates the central role of the opioid system in mechanisms that control and influence behavior on social reward cues. Since smiles are such pivotal social cues and indicate social acceptance, this study shows that blocking the mu-opioid system has a non-affiliative promoting effect on facial mimicry towards happy faces. More precisely, naltrexone administration engenders a decreased ZM activity as a response to positive happy faces. These findings elucidate the pivotal role of the opioid system in modulating spontaneous behavioral responses to stimuli of social encounters as well as reward like happy faces.

6. References

Argaud, S., Delplanque, S., Houvenaghel, J.-F., Auffret, M., Duprez, J., Vérin, M., ... Sauleau, P. (2016). Does Facial Amimia Impact the Recognition of Facial Emotions? An EMG Study in Parkinson's Disease. *PLoS ONE, 11*(7): e0160329. doi:10.1371/journal.pone.0160329

Bates, D. M., Maechler, M., Bolker, B. M., & Walker, S. C. (2014). lme4: Linear mixed-effects models using eigen and S4. R package version 1.1-7. Available online at: http://CRAN.R-project.org/package=lme4

Baumeister, R. F. & Leary, M. R. (1995). The need to belong: desire for interpersonal attachments as a fundamental human motivation. *Psychological Bulletin, 117*(3), 497-529. doi:10.1037/0033-2909.117.3.497

Bavelas, J. B., Black, A., Lemery, C. R., & Mullett, J. (1990). Motor mimicry as primitive empathy. In N. Eisenberg & J. Strayer (Eds.), *Empathy and its development* (pp. 317-228). Melbourne: Cambridge University Press.

Benarroch, E. E. (2012). Endogenous opioid system. Current concepts and clinical correlations. *Neurology*, *79*(8), 807-814. doi:10.1212/WNL.0b013e3182662098

Blair, R. J. R. (2003). Facial expressions, their communicatory functions and neurocognitive substrates. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences, 358*(1431), 561-572. doi:10.1098/rstb.2002.1220

Bogart, K. R. & Matsumoto, D. (2010). Facial mimicry is not necessary to recognize emotion: Facial expression recognition by people with moebius syndrome. *Social Neuroscience, 5*(2), 241-251. doi:10.1080/17470910903395692

Bolker, B. M., Brooks, M. E., Clark, C. J., Geange, S. W., Poulsen, J. R., Stevens, M. H. H., & White, J.-S. S. (2009). Generalized linear mixed models: a practical guide for ecology and evolution. *Trends in Ecology & Evolution, 24*(3), 127-135. doi:10.1016/j.tree.2008.10.008

Brody, L. R. & Hall, J. A. (2008). Gender and emotion in context. In M. Lewis & J. M. Haviland (Eds.), *Handbook of emotions* (pp. 395–408). New York: Guilford Press.

Cacioppo, J. T., Cacioppo, S., Capitanio, J. P., & Cole, S. W. (2015). The neuroendocrinology of social isolation. *Annual Review of Psychology, 66*, 733-767. doi:10.1146/annurev-psych-010814-015240

Cacioppo, J. T., Gardner, W. L., & Berntson, G. G. (1997). Beyond bipolar conceptualizations and measures: The case of attitudes and evaluative space. *Personality and Social Psychology Review, 1*(1), 3-25. doi:10.1207/s15327957pspr0101_2

Calvo, M. G., Avero, P., Fernández-Martín, A., & Recio, G. (2016). Recognition thresholds for static and dynamic emotional faces. *Emotion, 16*(8), 1186-1200. doi:10.1037/emo0000192

Caporael, L. R. (2001). Evolutionary psychology: Toward a unifying theory and a hybrid science. *Annual Review of Psychology, 52*, 607-628. doi:10.1146/annurev.psych.52.1.607

Carr, L., Iacoboni, M., Dubeau, M. C., Mazziotta, J. C., & Lenzi,G. L. (2003). Neural mechanisms of empathy in humans: A relay from neural systems for imitation to limbic areas. *Proceedings of the National Academy of Science, 100*(9), 5497-5502. doi:10.1073/pnas.0935845100

Chartrand, T. L. & Lakin, J. L. (2013). The antecedents and consequences of human behavioral mimicry. *Annual Review of Psychology, 64*, 285-308. doi:10.1146/annurev-psych-113011-143754

Chelnokova, O., Laeng, B., Eikemo, M., Riegels, J., Loseth, G., Maurud, H., ... Leknes, S. (2014). Rewards of beauty: The opioid system mediates social motivation in humans. *Molecular Psychiatry, 19*, 746-747. doi:10.1038/mp.2014.1

Chevallier, C., Kohls, G., Troiani, V., Brodkin, E. S., & Schultz, R. T. (2012). The social motivation theory of autism. *Trends in Cognitive Sciences, 16*(4), 231-239. doi:10.1016/j.tics.2012.02.007

Codd, E., Shank, R. P., Schupsky, J. J., & Raffa, R. B. (1995). Serotonin and norepinephrine uptake inhibiting activity of centrally acting analgesics: Structural determinants and role in antinociception. *Journal of Pharmacology and Experimental Therapeutics, 274*(3), 1263-1270.

Davis, M. H. (1983). Measuring individual differences in empathy: Evidence for a multidimensional approach. *Journal of Personality and Social Psychology, 44*(1), 113-126. doi:10.1037/0022-3514.44.1.113

de Waal, F. B. M. (2008). Putting the altruism back into altruism: The evolution of empathy. *Annual Review of Psychology, 59*, 279-300. doi:10.1146/annurev.-psych.59.103006.093625

Depue, R. A. & Morrone-Strupinsky, J. V. (2005). A neurobehavioral model of affiliative bonding: Implications for conceptualizing a human trait of affiliation. *Behavioral and Brain Sciences, 28*(3), 313-350. doi:10.1017/S0140525X05000063

di Pellegrino G., Fadiga, L., Fogassi, L., Gallese, V., & Rizzolatti, G. (1992). Understanding motor events: A neurophysiological study. *Experimental Brain Research, 91*(1), 176-180.

Dimberg, U. (1982). Facial reactions to facial expressions. *Psychophysiology, 19*(6), 643-647. doi:10.1111/j.1469-8986.1982.tb02516.x

Dimberg, U. (1990). Facial electromyography and emotional reactions. *Psychophysiology 27*(5), 481-494. doi:10.1111/j.1469-8986.1990.tb01962.x

Dimberg, U., Andréasson, P., & Thunberg, M. (2011). Emotional empathy and facial reactions to facial expressions. *Journal of Psychophysiology, 25*(1), 26-31. doi:10.1027/0269-8803/a000029

Dimberg, U. & Lundqvist, L.-O. (1990). Gender differences in facial reactions to facial expressions. *Biological Psychology, 30(2)*, 151-159.

Dimberg, U. & Thunberg, M. (1998). Rapid facial reactions to emotion facial expressions. *Scandinavian Journal of Psychology, 39*(1), 39-46. doi:10.1111/1467-9450.00054

Dimberg, U., Thunberg, M., & Elmehed, K. (2000). Unconscious facial reactions to emotional facial expressions. *Psychological Science, 11*(1), 86-89. doi:10.1111/1467-9280.00221

Doherty, R. W., Orimoto, L., Singelis, T. M., Hatfield, E., & Hebb, J. (1995). Emotional contagion: Gender and occupational differences. *Psychology of Women Quarterly, 19*(3), 355-371. doi:10.1111/j.1471-6402.1995.tb00080.x

Ekman, P. & Rosenberg, E. L. (2005). *What the Face Reveals*. Oxford University Press: New York.

Field, T. M., Woodson, R., Greenberg, R., & Cohen, D. (1982). Discrimination and imitation of facial expression by neonates. *Science, 218*(4568), 179-181. doi:10.1126/science.7123230

Fischer, A. & Hess, U. (2017). Mimicking emotions. *Current Opinion in Psychology, 17,* 151-155. doi:10.1016/j.copsyc.2017.07.008

Friedman, H. S., Riggio, R. E., & Segall, D. O. (1980). Personality and the enactment of emotion. *Journal of Nonverbal Behavior, 5*(1), 35-48. doi:10.1007/BF00987053

Fridlund, A. & Cacioppo, J. (1986). Guidelines for human electromyographic research. *Psychophysiology, 23*(5), 567-589. doi:10.1111/j.14698986.1986.tb00676.x

Goldman, A. I. & Sripada, C. S. (2005). Simulationist models of face-based emotion recognition. *Cognition, 94*(3), 193-213. doi:10.1016/j.cognition.2004.01.005

Gross, J. J. & Levenson, R. W. (1993). Emotional suppression: Physiology, self-report, and expressive behavior. *Journal of Personality and Social Psychology, 64*(6), 970-986. doi:10.1037/0022-3514.64.6.970

Halberstadt, J. & Niedenthal, P. M. (2001). Effects of emotion concepts on perceptual memory for emotional expressions. *Journal of Personality and Social Psychology, 81*(4), 587-598. doi:10.1037//0022-3514.81.4.587

Hall, J. A. & Matsumoto, D. (2004). Gender differences in judgments of multiple emotions from facial expressions. *Emotion, 4*(2), 201-206. doi:10.1037/1528-3542.4.2.201

Hatfield, E. & Cacioppo, J. T. (1994). *Emotional contagion*. Cambridge, UK: Cambridge University Press.

Hatfield, E., Bensman, L., Thornton, P. D., & Rapson, R. L. (2014). New perspectives on emotional contagion: A review of classic and recent research on facial mimicry and contagion. *Interpersona, 8*(2), 159-179. doi:10.5964/ijpr.v8i2.162

Hess, U. (2001). The communication of emotion. In A. Kaszniak (Ed.), *Emotion, Qualia and Consciousness* (pp. 397-409). Singapore: World Scientific Publishing.

Hess, U. & Blairy, S. (2001). Facial mimicry and emotional contagion to dynamic emotional facial expressions and their influence on decoding accuracy. *International Journal of Psychophysiology, 40*(2), 129-141. doi:10.1016/S0167-8760(00)00161-6

Hess, U., Blairy, S., & Kleck, R. E. (2000). The influence of expression intensity, gender, and ethnicity on judgments of dominance and affiliation. *Journal of Nonverbal Behavior, 24*(4), 265-283. doi:10.1023/A:1006623213355

Hess, U. & Bourgeois, P. (2010). You smile - I smile: Emotion expression in social interaction. *Biological Psychology, 84*(3), 514-520. doi:10.1016/j.biopsycho.2009.11.001

Hess, U. & Fischer, A. (2013). Emotional mimicry as social regulation. *Personality and Social Psychology Review, 17*(2), 142-157. doi:10.1177/1088868312472607

Hess, U. & Fischer, A. (2014). Emotional mimicry: Why and when we mimic emotions. *Social and Personality Psychology Compass, 8*(2), 45-57. doi:10.1111/spc3.12083

Hsu, D. T., Sanford, B. J., Meyers, K. K., Love, T. M., Hazlett, K. E., Wang, H., ... Zubieta, J.-K., (2013). Response of the mu-opioid system to social rejection and acceptance. *Molecular Psychiatry, 18*, 1211-1217. doi:10.1038/mp.2013.96

Hsu, C. T., Sims, T., & Chakrabarti, B. (2017). How mimicry influences the neural correlates of reward: An fMRI study. *Neuropsychologia, 116*(Pt A), 61-67. doi:10.1016/j.neuropsychologia.2017.08.018

Hyniewska, S. & Sato, W. (2015). Facial feedback affects valence judgments of dynamic and static emotional expressions. *Frontiers in Psychology, 6*: 291. doi:10.3389/fpsyg.2015.00291

Iacoboni, M. (2005). Neural mechanisms of imitation. *Current Opinion in Neurobiology, 15*(6), 632-637. doi:10.1016/j.conb.2005.10.010

Inagaki, T. K. (2018). Opioids and social connection. *Current Directions in Psychological Science, 27*(2), 85-90. doi:10.1177/0963721417735531

Inagaki, T. K., Ray, L. A., Irwin, M. R., Way, B. M., & Eisenberger, N. I. (2016). Opioids and social bonding: Naltrexone reduces feelings of social connection. *Social Cognitive Affect Neuroscience, 11*(5), 728-735. doi:10.1093/scan/nsw006

Korb, S., Grandjean, D., & Scherer, K. R. (2010). Timing and voluntary suppression of facial mimicry to smiling faces in a Go/NoGo task - an EMG study. *Biological Psychology, 85*(2), 347-349. doi:10.1016/j.biopsycho.2010.07.012

Korb, S., Malsert, J., Rocas, V., Rihs, T. A., Rieger, S. W., Schwab, S., ... Grandjean, D. (2015). Gender differences in the neural network of facial mimicry of smiles: An rTMS study. *Cortex, 70*, 104-114. doi:10.1016/j.cortex.2015.06.025

Korb, S., Malsert, J., Strathearn, L., Vuilleumier, P., & Niedenthal, P. (2016). Sniff and mimic - Intranasal oxytocin increases facial mimicry in a sample of men. *Hormones and Behavior, 84*, 64-74. doi:10.1016/j.yhbeh.2016.06.003

Kring, A. M. & Gordon, A. H. (1998). Sex differences in emotion: Expression, experience, and physiology. *Journal of Personality and Social Psychology, 74*(3), 686-703. doi:10.1037/0022-3514.74.3.686

Krueger, C. & Tian, L. (2004). A comparison of the general linear mixed model and repeated measures ANOVA using a dataset with multiple missing data points. *Biological Research for Nursing, 6*(2), 151-157. doi:10.1177/1099800404267682

Krumhuber, E. G. & Manstead, A. S. (2009). Can duchenne smiles be feigned? New evidence on felt and false smiles. *Emotion, 9*(6), 807-820. doi:10.1037/a0017844

Krumhuber, E. G., Kappas, A., & Manstead, A. S. (2013). Effects of dynamic aspects of facial expressions: A review. *Emotion Review, 5*(1), 41-46. doi:10.1177/1754073912451349

Krumhuber, E. G., Skora, L., Küster, D., & Fou, L. (2017). A review of dynamic datasets for facial expression research. *Emotion Review, 9*(3), 280-292. doi:10.1177/1754073916670022

LaFrance, M. & Hecht, M. A. (2000). Gender and smiling: A meta-analysis. In A. H. Fischer (Ed.), *Studies in emotion and social interaction. Second series. Gender and emotion: Social psychological perspectives* (pp. 118-142). New York, NY, US: Cambridge University Press. doi:10.1017/CBO9780511628191.007

Lakin, J. L. & Chartrand, T. L. (2003). Using nonconscious behavioral mimicry to create affiliation and rapport. *Psychological Science, 14*(4), 334-339. doi:10.1111/1467-9280.14481

Lakin, J. L., Jefferis, V. E., Cheng, C. M., & Chartrand, T. L. (2003). The chameleon effect as social glue: Evidence for the evolutionary significance of nonconscious mimicry. *Journal of Nonverbal Behavior, 27*(3), 145-162. doi:10.1023/A:1025389814290

Lee, M. C., Wagner, H. N., Tanada, S., Frost, J. J., Bice, N., & Dannals, R. F. (1988). Duration of occupancy of opiate receptors by naltrexone. *Journal of Nuclear Medicine, 29*(7), 1207-1211. Retrieved from: http://jnm.snmjournals.org

Levenson, R. W., Ekman, P., & Friesen, W. V. (1990). Voluntary facial action generates emotion-specific autonomic nervous system activity. *Psychophysiology, 27*(4), 363-384. doi:10.1111/j.1469-8986.1990.tb02330.x

Likowski, K. U., Mühlberger, A., Gerdes, A. B. M., Wieser, M. J., Pauli, P., & Weyers, P. (2012). Facial mimicry and the mirror neuron system: Simultaneous acquisition of facial electromyography and functional magnetic resonance imaging. *Frontiers in Human Neuroscience, 6*: 214. doi:10.3389/fnhum.2012.00214

Likowski, K. U., Mühlberger, A., Seibt, B., Pauli, P., & Weyers, P. (2008). Modulation of facial mimicry by attitudes. *Journal of Experimental Social Psychology, 44*(4), 1065-1072. doi:10.1016/j.jesp.2007.10.007

Likowski, K. U., Weyers, P., Seibt, B., Stöhr, C., Pauli, P., & Mühlberger, A. (2011). Sad and lonely? Sad mood suppresses facial mimicry. *Journal of Nonverbal Behavior, 35*(2), 101-117. doi:10.1007/s10919-011-0107-4

Loseth, G. E., Ellingsen, D., & Leknes, S. (2014). State-dependent mu-opioid modulation of social motivation. *Frontiers in Behavioral Neuroscience, 8*: 430. doi:10.3389/fnbeh.2014.00430

Lugo, R. A. & Kern, S. E. (2002). Clinical pharmacokinetics of morphine. *Journal of Pain & Palliative Care Pharmacotherapy, 16*(4), 5-18. doi:10.1080/J354v16n04_02

Lutz, P. E. & Kieffer, B. L. (2013). The multiple facets of opioid receptor function: Implications for addiction. *Current Opinion in Neurobiology, 23*(4), 473-479. doi:10.1016/j.conb.2013.02.005

Magezi, D. A. (2015). Linear mixed-effects models for within-participant psychology experiments: An introductory tutorial and free, graphical user interface (LMMgui). *Frontiers in Psychology, 6*: 2. doi:10.3389/fpsyg.2015.00002

McClure, E. B. (2000). A meta-analytic review of sex differences in facial expression processing and their development in infants, children, and adolescents. *Psychological Bulletin, 126*(3), 424-453. doi:10.1037/0033-2909.126.3.424

McDuff, D., Kodra, E., el Kaliouby, R., & LaFrance, M. (2017). A large-scale analysis of sex differences in facial expressions. *PLoS ONE, 12*(4): e0173942. doi:10.1371/journal.pone.0173942.

McIntosh, D. N. (1996). Facial feedback hypotheses: Evidence, implications, and directions. *Motivation and Emotion, 20*(2), 121-147. doi:10.1007/BF02253868

McIntosh, D. N. (2006). Spontaneous facial mimicry, liking and emotional contagion. *Polish Psychological Bulletin, 37*(1), 31-42. Retrieved from: http://pdfs.semanticscholar.org/ffe5/4ead63fd68dde9715271ac8dde0233c3a72e.pdf

McIntosh, D. N., Reichmann-Decker, A., Winkielman, P., & Wilbarger, J. L., (2006). When the social mirror breaks: Deficits in automatic, but not voluntary, mimicry of emotional facial expressions in autism. *Developmental Science, 9*(3), 295-302. doi:10.1111/j.1467-7687.2006.00492.x

Moody, E. J., McIntosh, D. N., Mann, L. J., & Weisser, K. R. (2007). More than mere mimicry? The influence of emotion on rapid facial reactions to faces. *Emotion, 7*(2), 447–457. doi:10.1037/1528-3542.7.2.447

Meier, I. M., Bos, P. A., Hamilton, K., Stein, D. J., van Honk, J., & Malcolm-Smith, S. (2016). Naltrexone increases negatively-valenced facial responses to happy faces in female participants. *Psychoneuroendocrinology*, *74*, 65-68. doi:10.1016/j.psyneuen.2016.08.022

Meltzoff, A. N. & Moore, M. K. (1977). Imitation of facial and manual gestures by human neonates. *Science, 198*(4312), 75-78. doi:10.1126/science.198.4312.75

Molenberghs, P., Cunnington, R., & Mattingley, J. B. (2012). Brain regions with mirror properties: A meta-analysis of 125 human fMRI studies. *Neuroscience & Biobehavior Review, 36*(1), 341-349. doi:10.1016/j.neubiorev.2011.07.004

Neal, D. T. & Chartrand, T. L. (2011). Embodied emotion perception amplifying and dampening facial feedback modulates emotion perception accuracy. *Social Psychology and Personality Science, 2*(6), 673-678. doi:10.1177/1948550611406138

Neufeld, J. & Chakrabarti, B. (2016). Empathy modulates the rewarding effect of mimicry. *Scientific Reports, 6*: 27751. doi:10.1038/srep27751

Niedenthal, P. M., Brauer, M., Halberstadt, J. B., & Innes-Ker, A. H. (2001). When did her smile drop? Facial mimicry and the influences of emotional state on the detection of change in emotional expression. *Cognition and Emotion, 15*(16), 853-864. doi:10.1080/02699930143000194

Niedenthal, P. M., Mermillod, M., Maringer, M., & Hess, U. (2010). The simulation of smiles (SIMS) model: Embodied simulation and the meaning of facial expression. *Behavioral and Brain Sciences, 33*(06), 417-433. doi:10.1017/S0140525X10000865

Nugent, P. M. S. (2013, April 7). Affiliative behavior. *Psychology Dictionary.* Retrieved August 24, 2018, from http://psychologydictionary.org/affiliative-behavior/

Oberman, L. M., Winkielman, P., & Ramachandran, V. S. (2007). Face to face: Blocking facial mimicry can selectively impair recognition of emotional expressions. *Social Neuroscience, 2*(3-4), 167-178. doi:10.1080/17470910701391943

Oberman, L., Hubbard, E., McCleery, J., Altschuler, E., Ramachandran, V., & Pineda, J. (2005). EEG evidence for mirror neuron dysfunction in autism spectrum disorders. *Cognitive Brain Research, 24*(2), 190-198. doi:10.1016/j.cogbrainres.2005.01.014

Panksepp, J., Herman, B., Conner, R., Bishop, P., & Scott, J. P. (1978). The biology of social attachments: Opiates alleviate separation distress. *Biological Psychiatry, 13*(5), 607-618.

Petrovic, P., Pleger, B., Seymour, B., Klöppel, S., De Martino, B., Critchley, H., & Dolan, R. J. (2008). Blocking central opiate function modulates hedonic impact and anterior cingulate response to rewards and losses. *Journal of Neuroscience, 28*(42), 10509-10516. doi:10.1523/JNEUROSCI.2807-08.2008.

Ponari, M., Conson, M., D'Amico, N. P., Grossi, D., & Trojano, L. (2012). Mapping correspondence between facial mimicry and emotion recognition in healthy subjects. *Emotion, 12*(6), 1398-1403. doi:10.1037/a0028588

R Core Team (2016). *R: A language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing. Retrieved from http://www.R-project.org

Rotter, N. G. & Rotter, G. S. (1988). Sex differences in the encoding and decoding of negative facial emotions. *Journal of Nonverbal Behavior, 12*(2), 139-148. doi:10.1007/BF00986931

Sachisthal, M. S., Sauter, D. A., & Fischer, A. H. (2016). Mimicry of ingroup and outgroup emotional expressions. *Comprehensive Results in Social Psychology, 1*(1-3), 86-105. doi:10.1080/23743603.2017.1298355

Schrammel, F., Pannasch, S., Graupner, S.-T., Mojzisch, A., & Velichowsky, B. M. (2009). Virtual friend or threat? The effects of facial expression and gaze interaction on psychophysiological responses and emotional experience. *Psychophysiology, 46*(5), 922-931. doi:10.1111/j.1469-8986.2009.00831.x

Schwartz, G. E., Brown, S. L., & Ahern, G. L. (1980). Facial muscle patterning and subjective experience during affective imagery: Sex differences. *Psychophysiology, 17*(1), 75-82. doi:10.1037/0021-843X.91.1.25

Schweinberger, S. R. & Schneider, D. (2014). Wahrnehmung von Personen und soziale Kognitionen. *Psychologische Rundschau., 65*, 212-226. doi:10.1026/0033-3042/a000225

Seibt, B., Mühlberger, A., Likowski, K. U., & Weyers, P. (2015). Facial mimicry in its social setting. *Frontiers in Psychology, 6*: 1122. doi:10.3389/fpsyg.2015.01122

Sims, T. B., van Reekum, C. M., Johnstone, T., & Chakrabarti, B. (2012). How reward modulates mimicry: EMG evidence of greater facial mimicry of more rewarding happy faces. *Psychophysiology, 49*(7), 998-1004. doi:10.1111/j.1469-8986.2012.01377.x

Slavich, G. M, O'Donovan, A., Epel, E. S., & Kemeny, M. E. (2010). Black sheep get the blues: A psychobiological model of social rejection and depression. *Neuroscience & Biobehavioral Reviews, 35*(1), 39-45. doi:10.1016/j.neubiorev.2010.01.003

Sonnby-Borgström, M. (2002). Automatic mimicry reactions as related to differences in emotional empathy. *Scandinavian Journal of Psychology, 43*(5), 433-443. doi:10.1111/1467-9450.00312

Soussignan, R., Chadwick, M., Philip, L., Conty, L., Dezecache, G., & Grezes, J. (2013). Self-relevance appraisal of gaze direction and dynamic facial expressions: effects on facial electromyographic and autonomic reactions. *Emotion 13*(2), 330-337. doi:10.1037/a0029892

Spreckelmeyer, K. N., Krach, S., Kohls, G., Rademacher, L., Irmak, A., Konrad, K., ... Gründer, G. (2009). Anticipation of monetary and social reward differently activates mesolimbic brain structures in men and women. *Social Cognitive and Affective Neuroscience, 4*(2), 158-165. doi:10.1093/scan/nsn051

Stel, M. & van Knippenberg, A. (2008) The role of facial mimicry in the recognition of affect. *Psychological Science, 19*(10), 984-985. doi:10.1111/j.1467-9280.2008.02188.x.

Stevens, J. S. & Hamann, S. (2012). Sex differences in brain activation to emotional stimuli: A meta-analysis of neuroimaging studies. *Neuropsychologia, 50*(7), 1578-1593. doi:10.1016/j.neuropsychologia.2012.03.011.

Taylor, S. E. (2010). Mechanisms linking early life stress to adult health outcomes. *Proceedings of the National Academy of Sciences, 107*(19), 8507-12. doi:10.1073/pnas.1003890107

Thunberg, M. & Dimberg, U. (2000). Gender differences in facial reactions to fear-relevant stimuli. *Journal of Nonverbal Behavior., 24*(1), 45-51. doi:10.1023/A:1006662822224

Trimmer, E., McDonald, S., & Rushby, J. A (2017). Not knowing what I feel: Emotional empathy in autism spectrum disorders. *Autism, 21*(4), 450-457. doi:10.1177/1362361316648520

van der Gaag, C., Minderaa, R. B., & Keysers, C. (2007). Facial expressions: What the mirror neuron system can and cannot tell us. *Social Neuroscience, 2*(3-4), 179-222. doi:10.1080/17470910701376878

Weerts, E. M., McCaul, M. E., Kuwabara, H., Yang, X., Xu, X., Dannals, R. F., ... Wand, G. S. (2013). Influence of OPRM1 Asn40Asp variant (A118G) on [11C] carfentanil binding potential: Preliminary findings in human subjects. *International Journal of Neuropsychopharmacolpgy, 16*(1), 47-53. doi:10.1017/S146114571200017X

Weyers, P., Muehlberger, A., Hefele, C., & Pauli, P. (2006). Electromyographic responses to static and dynamic avatar emotional facial expressions. *Psychophysiology 43*(5), 450-453. doi:10.1111/j.1469-8986.2006.00451.x

Yeomans, M. R. & Gray, R. W. (1997). Effects of naltrexone on food intake and changes in subjective appetite during eating: Evidence for opioid involvement in the appetizer effect. *Physiology & Behavior, 62*(1), 15-21. doi:10.1016/S0031-9384(97)00101-7

Zajonc, R. B., Adelmann, P. K., Murphy, S. T., & Niedenthal, P. M. (1987). Convergence in the physical appearance of spouses: An implication of the vascular theory of emotional efference. *Motivation and Emotion, 11*(4), 335-46. doi:10.1007/BF00992848

7. Appendix

Abstract (English)

Facial mimicry plays an important role in social interactions. It promotes affiliation and can be considered as “social glue”, due to its properties of binding individuals together. Although it has been shown that blocking the opioid system leads to a diminished sense of social connection and affiliation, little attention has been paid to the impact of underlying neurobiological mechanisms such as the opioid system on facial mimicry. For this reason, the present study investigates in a randomized, double blind, and placebo-controlled design how facial mimicry is modulated by the opioid system. More precisely, what influence naltrexone, an opioid antagonist, has on mimicry to emotional facial expressions. Therefore, 43 participants (whom either naltrexone or a placebo were administered) observed short video clips containing dynamic facial expressions changing from happy to angry, or vice versa. Facial mimicry was measured by electromyography (EMG) on two facial muscles, the Zygomaticus Major (which is known to be active during smiling) and Corrugator Supercilii (which is known to be involved in frowning). The results demonstrated a decrease of Zygomaticus Major activity towards happy facial expressions after naltrexone compared to placebo. Since happy faces are pivotal social cues for social affiliation and indicate social acceptance, this study showed that blocking the mu-opioid system has a non-affiliative promoting effect on facial mimicry towards happy faces. Further, it elucidate the pivotal role of the opioid system in modulating spontaneous behavioral responses to stimuli of social encounters as well as reward like happy faces.

Keywords: Facial Mimicry, Naltrexone, Opioid Systems, EMG, Social Affiliation, Gender Differences

Abstract (German)

Soziale Beziehungen sind wichtig für ein gesundes Leben. In der Interaktion mit Anderen spielt dabei das Mimicken von Gesichtsausdrücken eine bedeutende Rolle, da es Zugehörigkeit und Zuneigung fördert. Wenig ist allerdings bekannt welche Auswirkung neurobiologische Faktoren, auf das Mimicken von Gesichtsausdrücken hat. Jedoch konnte in Studien bereits nachgewiesen werden, dass eine Blockierung durch einen Opioid-Antagonisten zu einem verminderten Gefühl der gesellschaftlichen Beziehungen und der sozialen Zuwendungen führt. Aus diesem Grund untersuchte diese Studie in einem Verhaltensexperiment (mit einem randomisierten, doppelblind und placebokontrollierten Design) inwieweit Naltrexon, ein Opioid-Antagonist, Mimikry beeinflusst. Dafür wurden 43 ProbandInnen (welchen entweder Naltrexon oder ein Placebo-Medikament verabreicht wurden) gebeten kurze Videos mit emotionalen Gesichtern anzusehen, deren Ausdruck sich von glücklich auf verärgert ändert, oder umgekehrt. Mimikry wurde mittels Elektromyographie (EMG) an zwei Gesichtsmuskeln, dem Zygomaticus Major (ein Muskel, der während des Lächelns aktiv ist) sowie dem Corrugator Supercilii (ein Muskel, der während des Stirnrunzelns aktiv ist) gemessen. Es konnte gezeigt werden, dass Naltrexon die Aktivierung des Zygomaticus Major auf glückliche Gesichtsausdrücke vermindert. Da positive, lächelnde Gesichter ein Hinweis für das Interesse an sozialer Zugehörigkeit und Zuwendung ist, reduziert demnach das Blockieren des Mu-Opioid Systems durch Naltrexon Verhaltensweisen, die förderlich für die Aufnahme sozialer Kontakte sind. Somit konnte also die zentrale Rolle des Opioid-Systems in der Modulation spontaner Verhaltensreaktionen hinsichtlich der Zuwendung und Aufnahme sozialer Kontakte verdeutlicht werden.

Schlüsselwörter: Gesichtsmimikry, Naltrexon, Opioid System, EMG, Soziale Zugehörigkeit, Geschlechterunterschiede

List of Figures

Figure 1 Quantity and gender distribution in naltrexone and placebo group 17

Figure 2 Schematic view of one trial showing emotional faces which morph from an angry into a happy expression 19

Figure 3 Mean EMG over time for both muscles in response to AngerToHappy and HappyToAnger trials 23

Figure 4 Mean EMG for CS over time during HappyToAnger trials in females and males 24

Figure 5 Mean EMG for CS over time during AngerToHappy trials in females compared to males (standard errors indicated) 25

Figure 6 Mean EMG for CS averaged over all time windows in AngerToHappy trials for females and males 25

Figure 7 Mean EMG for ZM over time in naltrexone and placebo group during AngerToHappy trials 26

Figure 8 Mean of EMG for ZM activity in AngerToHappy condition of females and males in in naltrexone and placebo group 27

List of Abbreviations

ANOVA	analysis of variance
AH	AngerToHappy condition
ASD	autism spectrum disorder
CS	Corrugator Supercilii
EMG	electromyographically
HA	HappyToAnger condition
LMM	linear mixed model
MNS	mirror neuron system
MOR	mu-opioid receptor
RT	reaction time
ZM	Zygomaticus Major