MASTERARBEIT / MASTER'S THESIS

Titel der Masterarbeit / Title of the Master's Thesis

„Wanting and Liking" – Pharmacological Investigation of the Opioid-related Changes of "Wanting" and "Liking" of Food Rewards

verfasst von / submitted by

Frederic- Jan Schwetz, BSc

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

Master of Science (MSc)

Wien, 2019 / Vienna 2019

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, Privatdoz., PhD
Mitbetreut von / Co-Supervisor:	Dr. Sebastian Korb, PhD

Acknowledgments

“Patience is a virtue”, is my first thought when thinking of my advisor Dr. Giorgia Silani, Privatdoz., PhD. Thank you, dear Giorgia, for giving me the chance to be part of your project as well as for your patience with my theses. It was a great experience and learning opportunity to boost my knowledge and work on my personality.

“Sh.. happens, but we can fix it.” Accordingly, thanks to Dr. Sebastian Korb for being there when I needed him. Sebastian, it was great that you always stayed calm and patient all the way through. Furthermore, it was good for my learning experience to stay motivated do things by myself. Being able to finish this thesis now has filled me with lots of joy.

I would also like to express my thanks to Claudia Massaccesi, MSc who gave us a great training opportunity while being part of the project. Claudia, I highly appreciated that you were always persistent as regards the material, and kept sending out important messages to facilitate professional working.

Sebastian Götzendorfer, MSc. deserves my thanks due to his professional view on my process optimization. Sebastian, you really did a great job when having an eye on eight students doing the right things at the right time while sticking to the scientific objectiveness required for this project.

It is, however, also my great wish to thank my whole family for being optimistic about my personal, academic and professional future all the time!

Dear Benedikt, let me also express my sincere thanks for being my true friend! I guess you know how I highly appreciate your linguistic and intellectual expertise! In other words, thank you for (the) great friendship! ;)

Finally, it is my utmost wish to especially thank my beloved girlfriend Christina as well as her lovely daughter Pia Sophie and my son (soon to be born) who make my life better and happier than I would have ever imagined! Let me assure you that I really “want” you and “like” you, you always fill my life and brain with both pleasure and happiness. Best rewards ever!

Content

Introduction

Rewards

Every human being likes or wants something. According to Maslow's theory of needs and motivation humans first need and then try to get things to survive (Maslow, 1943). Further, he suggested human are driven by innate needs for more than just survival but also for safety, love and belonging, esteem, and self-realization (Abulof, 2017). Starving men tend to think that food is the only commodity they would need to be happy (Malow, 1943). It is all about happiness and pleasure. Human beings behave, do and act to get things that generate feelings of pleasure and happiness – rewards. They are motors to get food, water and mating partners for reproduction. In evolution theory living creatures who earn the better rewards will survive (Schultz, 2015). Rewards can be objects, acts or inner states with a subjective, positive value that can evoke approaching behavior (Schultz, Dayan and Montague, 1997). Rewards are essential for pleasure and well-being. Therefore, they play a fundamental part for many affective disorders like depression, schizophrenia and addiction (Berridge & Kringelbach, 2008).

It's not possible to measure the value of a reward on its own because the value depends on the subjective ascriptions of the receiver (Cabanac, 1971). That means the response to a reward depends on both the needs of the subject and the usefulness for survival and reproduction (Cabanac, 1979).

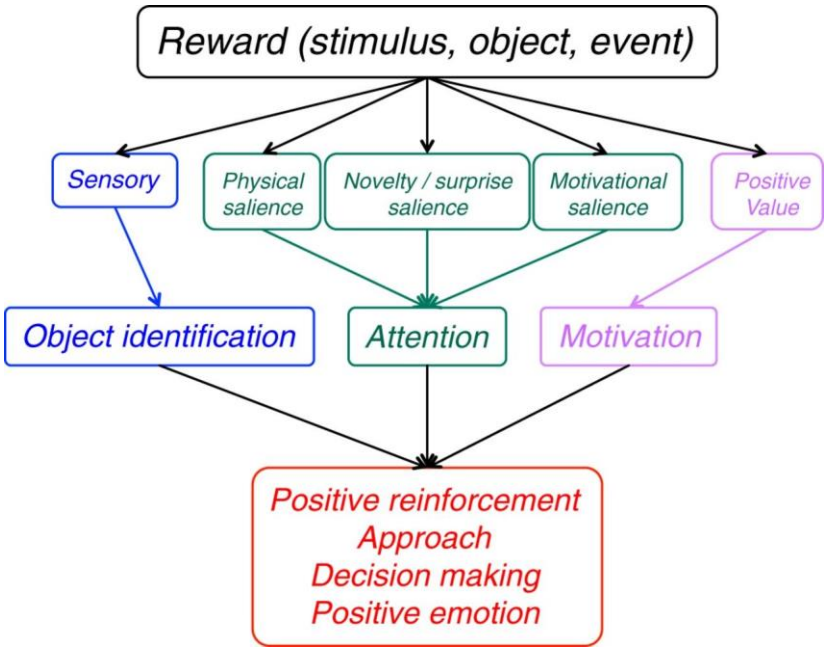

FIG. 1. Reward components and their functions (Schutz, 2015)

Schultz (2015) describes rewards within three main components. The sensory component (Fig.1 left) includes the physical properties of rewarding stimuli (size, form, etc.). Second, the salient component (Fig.1 middle) explains the essential function of rewards to arouse attention and their motivational impact. Third, the value component (Fig. 1 right) is independent from the sensory and attentional components. The positive value of rewards determines the motivational distinction from punishment (Schultz, 2015).

Berridge & Robinson (2003) describe other three components of reward: wanting, liking and learning. These components reflect incentive salience (wanting), hedonic impact (liking) and learning.

“I want chocolate now, because I did my homework” characterizes the meaning of “wanting”. The motivational value of a reward influences our behaviour and thus our “effort” to get a reward (Berridge, 2009; Berridge & Robinson, 1998; Everitt & Robbins, 2005). Here “wanting” is understood as kind of “incentive salience”, a type of motivation towards rewards and their consumption (Berridge, Robinson, & Aldridge, 2009).

The process of “wanting” can run unconsciously or deliberately. If it is running deliberately it results in desires or cognitive goals (Berridge & Robinson, 2003).

“I like chocolate, because it is so yummy”. “Liking” displays the hedonic and affective part of reward processing. Things we “like” play an essential part of the phenomenon of pleasure (Berridge & Robinson, 2003). For example hedonic impact or "liking" is shown within behavioral affective reactions elicited by tastes in human infants, monkeys and rats (Berridge, 2000; Steiner, 1979; Steiner, Glaser, Hawilo, & Berridge, 2001). It has been shown that there is no need for conscious awareness for processing “liking”. (Berridge & Kringelbach, 2008).

“Learning” includes knowledge of past experiences and cognitive predictions (Berridge & Kringelbach, 2008). There are several reinforcement theories. They explain reward “learning” by a process which strengthens or weakens behavior by the consequence that will follow (Berridge, 2000). Skinner (1950) even describes an anti-theoretical model of learning. It does not question “why” reinforcement works, it simply shows the relation between behavior changes according to received stimuli like food or water (Skinner, 1950). “Hullian learning theory” (Hull, 1943) explains reward “learning” by the process of drive reduction. He argues that for example hunger forces behavior to reduce that drive and motivates a person to get something

to eat. In that sense food becomes a reinforcer and leads to satiety. In essence drive reduction represents reward (Hull, 1943). Another theory is called the “incentive learning theory”. It argues that stimuli associated with positive respectively rewarding experiences modulate behavior (Bindra, 1974; Bolles, 1972).

Types of rewards

Certain human needs depend on previously satisfied needs. Maslow (1943) describes basic needs and higher needs in a hierarchical order. Maslow’s pyramid of needs puts the fact that man needs more than just food and water in a theoretical model. It was shown that seeking for belonging and for interpersonal actions are fundamental drives in human behaviour (Baumeister & Leary, 1995).

Inner negative states make people seek for rewarding stimuli (Hull, 1943) or broadly speaking rewards. What is rewarding is determined by biological, personal, cultural and situational factors (Maslow, 1943). Following Maslow (1943) and Hull (1943) a distinction between basic, physiological respectively primary needs and higher respectively secondary needs became common concepts in the scientific community. We have known for a long time that animals differentiate between primary rewards (e.g. water, apple and cacao) and social rewards (e.g. hugs, playing games, compliments and stroking) (Mason, Saxon, & Sharpe, 1963). Animal studies using primary rewards show that there are even two different ways of processing rewards (Berridge, 1996; Berridge & Robinson, 1998). Castro and Berridge (2014) propose that reward processing in rats can be understood through the model of “wanting” and “liking”.

In animal research this process differentiation is worked out clearly but there is need for more scientific efforts exploring these mechanisms in humans. Several studies on humans tried to dissociate “wanting” from “liking” (Finlayson et al. 2008; Finlayson et al. 2007; Zandstra et al. 2000).

Studies exploring rewards show that even pleasant tastes and odors (Zald, Lee, Fluegel, & Pardo, 1998; Zald & Pardo, 1997), pleasant touch (Francis et al., 1999), pleasant music (Blood, Zatorre, Bermudez, & Evans, 1999), and monetary achievements (Thut et al., 1997) lead to positive reactions.

The distinction between “wanting” and “liking” is relevant for addiction research (Robinson & Berridge, 2003) and research in clinical disorders. Studies revealed that some clinical disorders (e.g. autism, depression, schizophrenia) are characterized by

a lower extent of “wanting” (Barch, Treadway, & Schoen, 2014; Treadway & Zald, 2011).

Reward processes in the brain

Both “wanting” and “liking” are connected to reward seeking behaviour. Understanding reward includes the idea that rewards are defined by reactions of the brain and not only by the stimulus itself (Berridge & Kringlebach, 2008). Rewards contain different psychological components that are processed in discriminable neurobiological mechanisms (Berridge & Robinson, 2003; Dickinson & Balleine, 2002; Everitt & Robbins, 2005; Kringelbach, 2005; Kringelbach & Berridge, 2008; Leknes & Tracey, 2008; Schultz, 2006). Berridge (1996) proposes that food rewards can be split into the two components of appetite/”wanting” and pleasure/”liking” with differential neural activities.

The two brain structures nucleus accumbens (NAcc) and ventral pallidum (VPa) have emerged playing big parts in “wanting“ and “liking” (Peciña et al., 2006). Smith et al. 2009) found that “liking” and “wanting” mechanisms are localized in the VPa. Further it was shown that multiple signals for reward including hedonic impact (“liking”), motivation (“wanting”), and “learning” are processed within the NAcc and VPa (Smith et al., 2011). Figure 2 shows rewarding hotspots in the NAcc (Berridge, 2009). Individuals with high activation of accumbens surroundings (green) show higher “wanting” for food (Robinson & Berridge, 2003).

Whereas “liking” is localized to a sub region of the medial nucleus accumbens shell, “wanting” is widely distributed within the NAcc (Peciña, 2008).

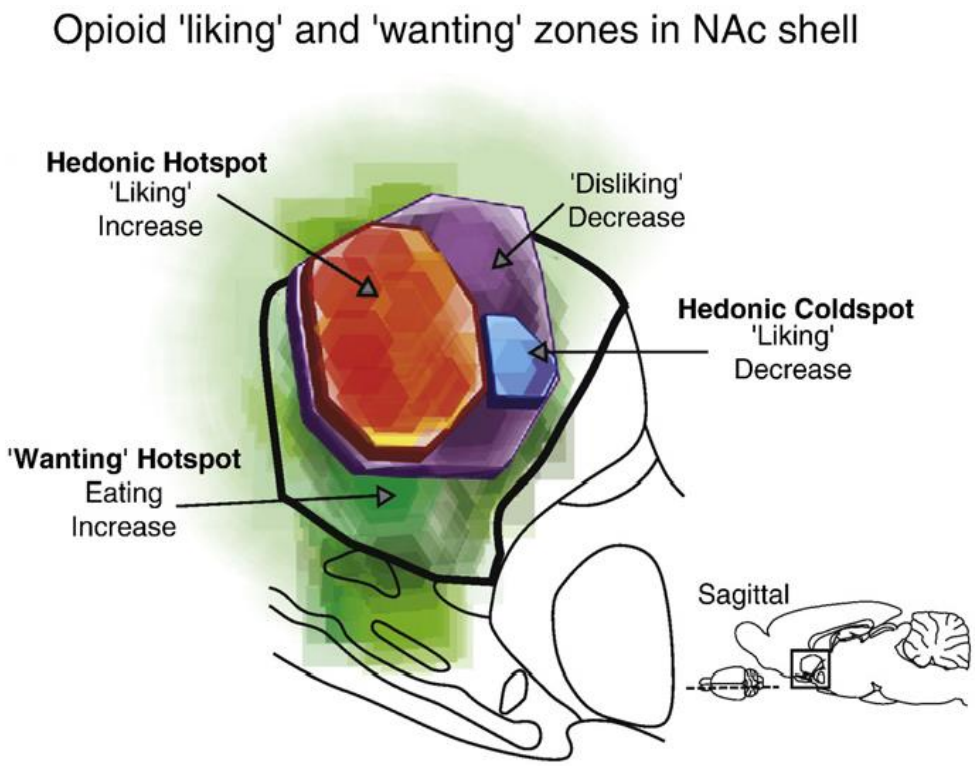

FIG. 2. Hotspots in the nucleus accumbens (medial shell region shown in sagittal view; right), (Berridge, 2009).

Berridge (1996) shows that VPa has a key role in the neural system for eating and “wanting” food. Neuroimaging studies report that consumption of pleasant food or juices activates the NAcc (Berns et al., 2001).

Food is essential for survival and it was shown that the sensory system of taste and smell plays a crucial role in the natural reward system (Kelley & Berridge, 2002). μ-opioid receptor stimulation within the NAcc and surrounding ventral striatal areas enhances food intake and offers an opportunity exploring reward processes (Bakshi and Kelley 1993; Kelley et al.1996). This goes in line with other studies using micro injections that determine effects on food intake (Bodnar, 2004). Especial the opioid systems in the medial shell of NAcc and VP have high impact on hedonic “liking” (Peciña & Berridge, 2005; Peciña et al., 2006). Baldo and Kelley (2007) argue that dopamine receptors correspond to “wanting” and opioid receptors correspond to “liking”. In this project we use Naltrexone as an opioid receptor antagonist and Amisulpride as a dopamine receptor antagonist to explore the effects on “wanting” and “liking”.

Naltrexone

The effects of Naltrexone have already been explored in animals (e.g. Burattini, Burbassi, Aicardi, & Cervo, 2008) and humans (e.g. Murray et al., 2014). It was shown that naltrexone decreases intake of palatable, sweet and fatty food (Giraudo et al. 1993; Agmo et al. 1995; Cleary et al. 1996).

Naltrexone has a high affinity to the μ-opioid receptor which plays a central role in "wanting" regarding social rewards (Loseth, Ellingsen, & Leknes, 2014).) Murray et al. (2014) provide evidence for Naltrexone modulating reward-related brain activity in human. Naltrexone is one of the drugs which is used for treatment of alcoholism, other substance addictions and impulse-control disorders. Naltrexone reduces ethanol consumption in human subjects (Anton et al., 1999, Davidson et al., 1999, Heidbreder, 2005, Hernandez-Avila et al., 2006, O'Brien et al., 1996), and reduces self-administration of ethanol in trained animals (Boyle et al., 1998, Stromberg et al., 1998). Additional Naltrexone reduces drug-seeking behaviour in animals (Ciccocioppo et al., 2003, Ciccocioppo et al., 2002, Liu and Weiss, 2002) and alcohol-cue induced craving in human alcoholics (Monti et al., 1999, O'Malley et al., 2002, Rohsenow et al., 2000). Further on it has been shown that Naltrexone blocks most of the opioid receptors in the brain (Lee et al., 1988, Weerts et al, 2013). Naltrexone is highly compatible for healthy participants and shows only minor side effects (Miotto et al., 2002). Although Naltrexone reaches its maximum plasma concentration after one hour (Verebey et al., 1976), the binding on opioid related receptors remains for multiple hours and that up to 90% (Meyer, Straughn, Lo, Schary, & Whitney, 1984).

Yeomans and Gray (1996) explore changes in food intake for participants receiving Naltrexone. They argue that Naltrexone reduces the caloric intake compared to a placebo. They propose that Naltrexone could have the possibility to modify hedonic evaluation of food.

Although there are many studies on using Naltrexone and exploring its effects, the implications for reward processing are still not clear.

Amisulpride

It is shown that Amisulpride has a high affinity to D2/D3-receptors in animals and, therefore, is expected to have high clinical efficacy in the treatment of schizophrenia (Perrault, Depoortere, Morel, Sanger & Scatton, 1997; Schoemaker et al., 1997).In

the meantime this medication is used in the treatment of both negative and positive symptoms of schizophrenia in humans (Curran & Perry, 2001).
McKeage and Plosker (2004) demonstrate that low dosages preferentially block D2/D3 receptors. It is shown that dopamine receptor blocking modulates neural activations in response to both rewarding and aversive stimuli in healthy volunteers (McCabe, Huber, Harmer, & Cowen, 2011). Therefore, the dopamine system plays a fundamental role for processes of "wanting" rather than for processes of "liking" (Lau, Wang, Hsu, & Liu, 2013). Additionally Amisulpride is a well-tolerated drug and has fewer side effects than other antipsychotics (Rosenzweig et al., 2002).

Facial Electromyography

Facial expressions have an evolutionary origin and are manifested throughout our biological heritage (Dimberg, 1990). Several studies demonstrate that the facial expressions of emotions come up spontaneously and show similar patterns across species and cultures (Berridge, 2008; Ekman & Friesen, 1971; Izard, 1992). Facial Electromyography (fEMG) tracks changes in muscle activation and even collects data which remain invisible to the eye (Fridlund & Izard, 1982).
Further, fEMG captures data of positive and negative affective states (Franzen & Brinkmann, 2016). It allows the recording of muscle action potential from skin and connective tissue (Tassinary and Cacioppo, 1992).
Already Hjortsjö (1970) showes that negative thoughts increased the corrugator supercilii. On the other hand Schwartz et al. (1972) indicate that pleasant thought activates the zygomaticus major which reflects "smiling".

Aim of the study

The study is based on a bigger project which investigates a differentiation of processing primary and social rewards. In this thesis the focus was on exploring opioid-related changes between "wanting" and "liking" of primary rewards, especially food rewards. The participants received milk or cacao drinks respectively as rewards. Food is essential for pleasure and provides accessible experimental methods for scientific studies about rewards and pleasure (Kringelbach, 2005; Peciña et al., 2006; Rozin, 1999; Small et al., 2001).
We tested healthy female and male participants in a real effort task. We explored changes in face muscle activity, subjective ratings and effort performed meanwhile

opioid receptors were blocked. We used fEMG to measure the face muscle activity of the corrugator supercilii and the zygomaticus major. For measuring the effort performed we used a hand dynamometer.
The most relevant receptors for the project are the dopamine D2 receptors (Robbins & Everitt, 1992) and the opioid receptors (Eikemo et al., 2016; Nathan et al., 2012). The dopamine receptors are explored related to Parkinson disease and schizophrenia (Heiss & Herholz, 2006). For the opioid receptors mainly animal studies explore their modulating effect on hedonic pleasure (Trezza, Baarendse, & Vanderschuren, 2010).
For the project participants received either Amisulpride, Naltrexone or a placebo to block according receptors.

Prior hypotheses

Wyvell and Berridge (2000) propose that activation of the opioid receptors increases both “liking” and “wanting” for food, whereas dopamine receptor activation does not enhance sucrose “liking” of sweet taste. A study from 2007 shows that dopamine receptors correspond to “wanting” whereas opioid receptors correspond to “liking” (Baldo & Kelley, 2007).
Therefore, I suggested that receiving an opioid receptor antagonist (Naltrexone) will reduce “liking” and will reduce “wanting” to a lesser extent.
Most facial and chewing muscles of adult humans show greater responses to tastes disliked than to those preferred or less preferred (Horio, 2003). Hu et al. (1999) demonstrate that during reward consumption “liking” is less related to positive facial expressions but more related to negative facial expressions like disgust.
Therefore, food rewards with low ratings of “liking” were expected to result in higher activation of the corrugator supercilii and not to affect the zygomaticus major.
For measuring “wanting” we used a real effort task, where participants had to squeeze a hand dynamometer measuring the motivation towards a reward. Pessiglione et al. (2007) show that people make more of an “effort” when the value of the reward is higher classified. According to this motivation theory, I assumed that participants receiving Naltrexone will press the dynamometer with less “effort” than people receiving a placebo.
Additionally I had a look at subjective ratings exploring differences in “wanting” and “liking” giving Naltrexone. Because of the high affinity of Naltrexone to the μ-opioid

receptor (Loseth, Ellingsen, & Leknes, 2014) I assumed that participants of the experimental group will rate consumed rewards lower for “liking” than participants receiving the placebo. At the same time I assumed that participants will rate announced rewards lower for “wanting” as people receiving a placebo in lower extent than for “liking”.

Methods and Materials

Participants

61 healthy volunteers (44 females and 17 males) took part in the whole project. For answering the hypotheses of this thesis the sample consisted of 42 volunteers including 32 females (~74%) and 11 males (~26%). The participants were aged from 17 to 35 with an average of M = 22,98 (SD = 3.82).
One participant was excluded because of statistical outliers. He rated the received rewards lower than 1,5 standard deviations from the average. Although participants where asked before the experiment if they like chocolate/cacao drinks. Therefore, he was excluded. For taking part participants needed to fulfil requirements which are described in the procedure. Participants’ average Body Mass Index (BMI) was M = 22,31 (*SD* = 2.60, range 17,7 – 27,6). They received 90-120€ as monetary compensation for taking part.

Procedure

The study was approved by the ethics committee of the Medical University of Vienna, and followed the regulations of the Declaration of Helsinki (World Medical Association, 2013). Participants were contacted per email and were invited to fill in an online questionnaire. There we checked if they were right-handed, smoked fewer than five cigarettes daily, had no history of current or former drug abuse, liked milk and chocolate, did not suffer from diabetes, lactose intolerance, lesions or skin disease on the left forearm and if they were free of psychiatric or neurological disorders. Furthermore, their sexuality was checked to avoid sexual rewards during the experiment. Therefore, male experimenters tested male participants and same applied to the opposite sex. The age was limited from eighteen to thirty five to avoid great differences in variances because of age variety. For the whole experiment the participants needed to have an adequate understanding of the German language.

They had to agree to drawing blood- and urine samples and taking Naltrexone, Amisulpride or a placebo. Further they should be clear about the procedure and that they undergo facial electromyography. They had to sign an informed consent.
If they passed the online questionnaire they were invited to the experiment.
There were two sessions. In the first session their blood levels and an electrocardiography were taken by a medical doctor. The BMI should lie between 17 and 35kg/m². The hearing and seeing abilities (with glasses or lenses) of the participants should be normal. With female participants a pregnancy test was administered.
If the participants met all the criteria, an appointment for the second session was made.
There again urine was tested for pregnancy and drug abuse. Then the participants got either Solian®, Dependex® or Mannitol. Solian® provides 400mg Amisulprid, Dependex® provides 50mg Naltrexone and Mannipol is the placebo. The capsules were administered orally in a randomized, double-blind manner.
The pill was already capsuled and neither the experimenters nor the participants knew which substrate was administered. After two hours the preferences for milk or cacao drinks respectively were evaluated. Additionally, the maximum voluntary contraction using a hand dynamometer (HD-BTA, Vernier Software & Technology, USA) with the right hand was processed squeezing three times for three seconds. After a short break the participants were prepared for the facial electromyography and the sensors were adapted. Three hours after taking the pill the main experiment exploring “wanting” and “liking” was started. In another study giving Amisulpride and Naltrexone participants had to wait three hours before starting the tasks (Weber et al., 2016).
At the beginning participants were seated at a table and comfortably rested their left forearm on a pillow. They sat down in front of a monitor (19 inch monitor, with 1.440 x 900pixels) and received detailed instructions. Then their view of their forearm was blocked by a curtain. This was important for the social condition, so that participants could better concentrate on the caresses (see below) and this independently from the experimenter. Then they accomplished some training trials for each condition with further instructions displayed on the monitor. They did four trials for the “food condition” and another four for the “social condition”. In the “food condition” the participants got three different mixes of milk respectively cacao drinks with the same

amount on calories as rewards: milk, chocolate milk, and a 4:1 mix of milk and chocolate milk. Between the trials tap water was served to cancel the taste of the reward before. We used computer-controlled pumps (PHD Ultra pumps, Harvard Apparatus) attached to plastic tubes (internal ø 1,6 mm; external ø 3,2 mm; Tygon tubing, U.S. Plastic Corp.) to deliver the rewards and the tap water. The tubes were positioned with an adjustable arm that the participant can easily receive the liquids and swallow easily.

In the “social condition” they received caresses on the forearm in three different speeds. The caresses were applied along a previously marked area of nine centimetres reaching from the wrist towards the elbow. The three different velocities of six cm/s, 21 cm/s and 27 cm/s for each six seconds were chosen based on pilot testing.

There were four blocks (two social and two food blocks) counterbalanced like ABAB or BABA for all participants. For each block participants had to do twenty trials. Figure 4 presents the main elements of one trial.

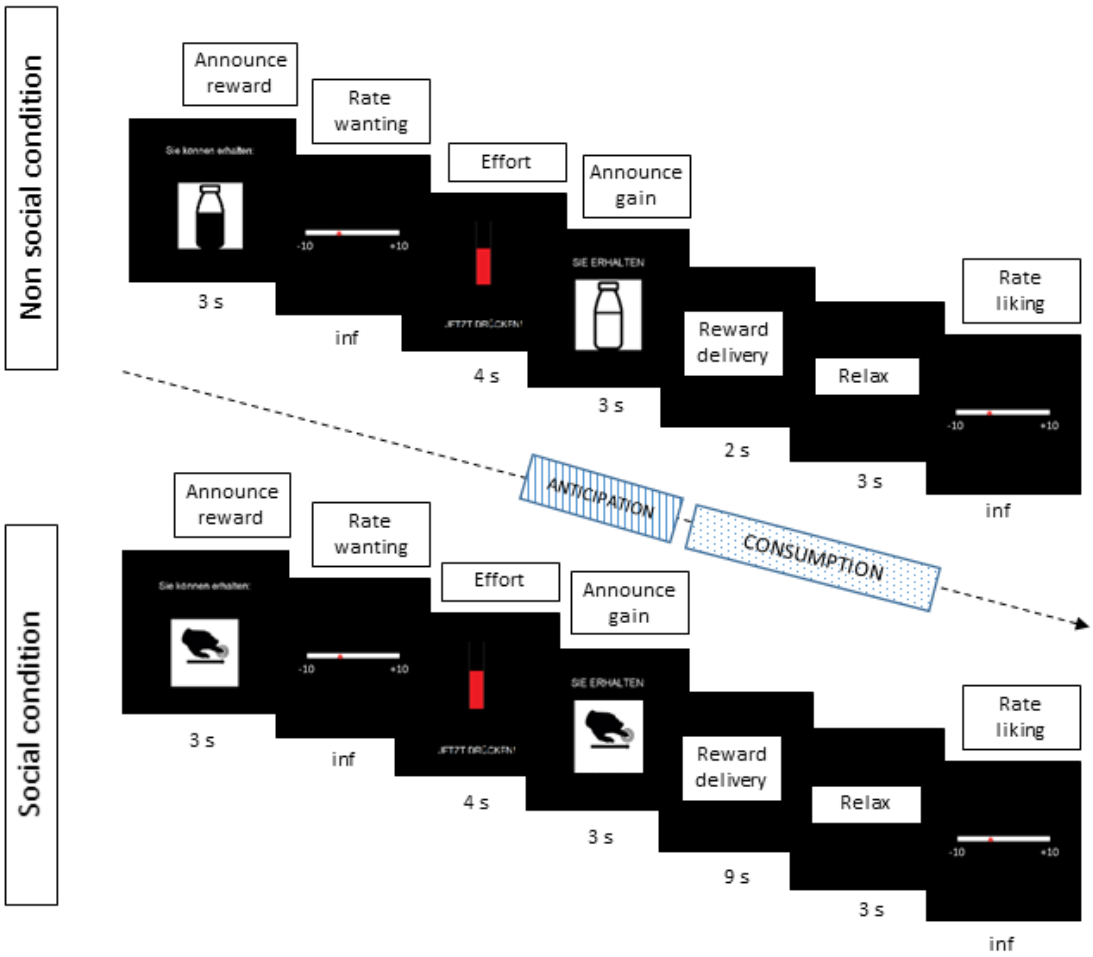

FIG.4. Main elements of each trial for the social and non-social conditions. fEMG analyses were carried out during reward anticipation (3 seconds) and reward consumption (3 seconds of relax).

First a picture of the first or second preference of reward (food or social reward) was shown. Then participants rated how much they “want” the award announced.
After that, the participants had to squeeze a dynamometer and got a visual feedback showing their contraction (see Fig. 3.).

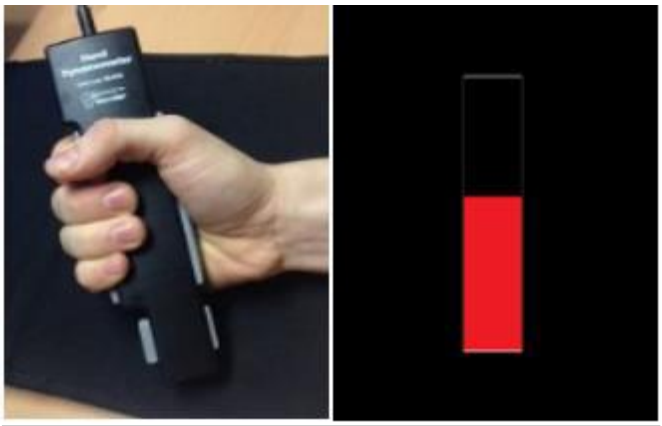

FIG. 3. Hand dynamometer (Vernier HD-BTA) and visual feedback

When squeezing the amount of force determined the probability to receive the reward announced. Afterwards a picture of the reward they earned was shown for 3 seconds. We defined this period as the anticipation period. This could be the award announced (1st or 2nd preference) or the 3rd preference chosen. The higher the contraction, the higher the probability to receive the reward announced. Then the reward obtained was delivered. In the “food condition” participants were instructed to lean back and swallow the reward delivered. After the swallowing we installed a relaxation phase of 3 seconds, the consumption period. Then the participants rated how much they “liked” the reward obtained. In the “food condition” participants got tap water from the tubes to cleanse the oral cavity. Both conditions ended with a blank screen. Between each block was a short break, where the experimenters checked if the participant is still fine. Afterwards the participants did go on with further tasks for the project.

Measures “liking”

fEMG

Using fEMG we expected to collect data for hedonic pleasure or “liking” respectively. Several studies indicate that orofacial affective expressions are reliable measures for “liking”. (Berridge, 2000; Tibboel et al., 2015).
Because of the affective compound in “liking” the two muscles in the face which express emotions were recorded. In emotion research mainly the measures of the activity from the zygomaticus major, which is activated during smiling, and the corrugator supercilii, which is activated during frowning, are of interest (Larsen, Norris & Cacioppo, 2003).
Therefore, particular face areas of the participants where first cleaned with alcohol. Then we used an abrasive paste to improve the signal. Before attaching the electrodes, areas were cleaned with water. We attached six electrodes bipolar to the face. According to the guidelines (Fridlund & Cacioppo, 1986) two electrodes were attached on the left corrugator supercilii and two electrodes on the left zygomaticus major. Additionally, a ground and a reference electrode were attached. The ground electrode was attached on the participant’s forehead and the reference electrode on the left mastoid.
For measurement a g.USBamp amplifier (g.tec Medical Engineering GmbH) was used. For processing Matlab R2014b (www.themathworks.com) and partly the EEGLAB toolbox (Delorme & Makeig, 2004) were used. The fEMG signal was sampled at 1200Hz with impedances below 10kOHM. A 20 to 400 Hz bandpass filter was applied, then data were rectified and smoothed with a 40 Hz low-pass filter. Epochs were extracted focusing on periods of reward anticipation and reward consumption. For the analyses we excluded recordings of the swallowing. EMG data was averaged over time-windows of one second.

Subjective ratings “liking”

In addition to the fEMG we implemented subjective ratings which took place after the consumption period. On a continuous scale they rated how much they “liked” the reward. The scale ranged from “not at all” (translated “gar nicht”) to “very much” (translated “sehr”). The midpoint represented “neutral”.

Measures “wanting”

Hand dynamometer

During each trial participants had to squeeze a hand dynamometer (Vernier Software & Technology) with their right hand. The amount of force determined the probability to get a reward more or less liked. This method is used to obtain objective data for the motivational compound “wanting”. This kind of measurement was already used in studies with primary (Ziauddeen et al., 2012) and monetary rewards (Pessiglione et al., 2007). There it was shown that participants squeezed harder to receive rewards high rated. Previous studies show that speed, performance and long persistence on a task are objective indicators for “wanting” (Bargh, Lee-Chai, Barndollar, Gollwitzer, & Trötschel, 2001; Carver & Scheier, 1998; Kivetz, Urminsky, & Zheng, 2006).
To calibrate the dynamometer participants were asked to press the dynamometer for three times for 3 seconds as hard as they could before and after the main task. The overall maximum value was taken as the maximum voluntary contraction (MVC).
For the data of the hand dynamometer we extracted a sliding average of one second as percentage of the MVC.

Subjective ratings “wanting”

In addition to the hand dynamometer a subjective rating scale for “wanting” was used. Before each trial participants were asked how much they “wanted” the reward announced. The scale ranged like the rating scale for “liking” from “not at all” to “very much”. Participants used a keypad to adjust the marker for the scale.

Analysis

Statistical analysis was computed in IBM SPSS Version 20. Data was analysed with mixed ANOVAS. Several variables were not distributed normally. For this study we assumed that the ANOVA offers a robust procedure against the requirement of normal distribution (Glass, Peckham, & Sanders, 1972; Harwell, Rubinstein, Hayes, & Olds, 1992; Salkind, 2010).

Results

Subjective ratings

First Subjective ratings of "**wanting"** and "**liking",** and "**effort"** (force of hand dynamometer) were analysed.
For answering the hypothesis several mixed-design ANOVAs, including the "drug group" (Naltrexone or placebo) as a between-subjects factor and the "reward level" as a within-subject factor, was conducted. The data was split into two levels above and below the median of "wanting", "liking" and "effort". We decided to divide the data by the median because initial reward preferences changed during the experiment.

Results from subjective ratings "wanting"

The values of the continuous scale after the announcement of the reward were computed to receive data for "subjective wanting".
The behavioural analyses on ratings of the dependent variable "**wanting"** resulted in no significant main effect for the interaction between "drug group" and "reward level". That means that intervention groups did not differ significantly, $F(1, 41) = .047$, $p = .830$, partial $\eta^2 = .001$. As we analysed main effects of "reward level" (above or below the median) we revealed a significant effect $F(1, 41) = 126.566$, $p < .001$, partial $\eta^2 = .760$. The means were M = 5,41 (SD = 3.56) (above) and M = -,68 (SD = 4.01) (below).

Results from subjective ratings "liking"

The behavioural analyses of the dependent variable "**liking**" delivered similar results. Here the subjective ratings for "liking" after the delivery of the reward were taken into account. For the analysis of the interaction between "drug group" and "reward level" we could not find a significant main effect either. There was no significant difference between participants receiving Naltrexone or the placebo respectively,
$F(1, 41) = .183$, $p = .671$, partial $\eta^2 = .005$. Again we found a significant effect for the factor "reward level" $F(1, 41) = 155.190$, $p < .001$, partial $\eta^2 = .795$. The means were M = 5,13 (SD = 2.99) (above) and M = -1,39 (SD = 3.32) (below).

Results from subjective ratings "effort" (hand dynamometer)

Here we analyzed the data of the hand dynamometer. We defined "wanting" as the dependent variable, measured through the pressing of the dynamometer. The ANOVA contained the factor "drug group" and the factor "reward level".
We could not find a significant main effect for the interaction between "drug group" and "reward level". There was no significant difference between the two groups. Regarding the values we saw a trend $F(1, 41) = 3.217$, $p = .080$, partial $\eta^2 = .074$. We found that the mean for effort was higher in the placebo group M = 207,84 (SD = 73.80) for the rewards rated above the median than in the Naltrexone group M = 181,75 (SD = 65.65). For the rewards valued below the median the means were M = 122,17 (SD = 47.67) (Naltrexone) and M = 170,88 (SD = 73.72) (placebo).
Additionally we revealed a significant effect within the factor "reward level" $F(1, 41) = 58.613$, $p < .001$, partial $\eta^2 = .594$. The means were M = 194,79 (SD = 70.24) (above) and M = 146,53 (SD = 66.08) (below).

To summarise, we could not find any main effects on the interaction between "drug group" and "reward level" neither on the ratings of "wanting", "liking" nor "effort". We found a trend for "effort" showing that participants receiving a placebo squeezed harder for rewards high and lower rated than participants from the Naltrexone group. Further, "reward levels" differed significantly from each other.

Results facial EMG

To measure "liking" the data of the fEMG was analysed. We recorded the muscle activity of each muscle separately. For each muscle we used the data again split into above and below the median based on the median of "wanting", "liking" and "effort" (instead of splitting the data by the type of reward in high/low reward or $1^{st}/2^{nd}$ preference respectively). We computed several ANOVAs adding an additional within-subject factor "time". The factor "time" represented the time-windows of one second of the fEMG.
For the data of the zygomaticus major and the corrugator supercilii mixed-design ANOVAs, including the factors "drug group" (Naltrexone or placebo), "reward level" (above and below the median) and "time", were calculated. We computed the same ANOVAs for the anticipation and the consumption period.

Anticipation – Zygomaticus Major (ZM)

As we analysed the data of ZM using the **median of "wanting"**, we had no significant main effects for interactions between "drug group", "reward level" and "time". For the following sections the term "overall" defines the interaction between "drug group", "reward level" and "time".

There was no significant difference in the interaction between the "drug group" and the "reward level", $F(1, 41) = .039$, $p = .844$, partial $\eta^2 = .001$ or the "time" $F(2, 40) = .851$, $p = .431$, partial $\eta^2 = .021$ and "overall" $F(2, 40) = .286$, $p = .752$, partial $\eta^2 = .007$.

Then the data was split into above and below the **median of "liking"**. But again there was no significant difference in interactions between "reward level" and "drug group" and between "time" and "drug group". Interactions between "reward level" $F(1, 41) = 0.763$, $p = .388$, partial $\eta^2 = .019$ and "drug group" were not significant. The interactions between "time" and "drug group" $F(2, 40) = 0.751$, $p = .475$, partial $\eta^2 = .018$ and "overall" $F(2, 40) = 1.328$, $p = .271$, partial $\eta^2 = .032$ were not significant.

Additionally, the data was split into above and below the **median of "effort"**. There was no significant effect in the interaction between "drug group" and "reward level", $F(1, 41) = 2.866$, $p = .098$, partial $\eta^2 = .067$. There was no significant effect in the interaction between "drug group" and "time", $F(2, 40) = 0.760$, $p = .471$, partial $\eta^2 = .019$. And there was no significant interaction between "drug group", "reward level" and "time" $F(2, 40) = 1.122$, $p = .331$, partial $\eta^2 = .027$.

Consumption – Zygomaticus Major (ZM)

Then the analyses were run again for the consumption period of 5 seconds.

As we split the data into above and below the **median of "wanting"** there was no significant effect for interactions between"drug group" and "reward level" and "time" or "overall". For "reward level" the values were $F(1, 41) = 1.524$, $p = .224$, partial $\eta^2 = .037$. For "time" the values were $F(4, 37) = .662$, $p = .619$, partial $\eta^2 = .006$. And the "overall" values were $F(4, 37) = .110$, $p = .979$, partial $\eta^2 = .003$.

Conducting the ANOVA with the data split into above and below the **median of "liking"** we got a significant main effect within the factor "drug group" $F(1, 41) = 5.749$, $p = .021$, partial $\eta^2 = .126$. Analysing simple main effects indicated that the mean score did not differ significantly in the "drug group". Neither at the high "reward level" (above the median of "liking") $F(1, 41) = 1.827$, $p = 1.84$, partial $\eta^2 = .044$ nor at the low "reward level" (below the median of "liking") $F(1, 41) = .662$, $p = .421$, partial $\eta^2 = .016$.
A significant effect occurred within the "reward level" of the placebo group. There the mean scores differed significantly $F(1, 41) = 4.508$, $p = .040$, partial $\eta^2 = .101$. At the high level the mean (M = 236.80, SD = 18.45) was significantly higher than the mean of the low level (M = 200.453, SD = 19.81).

Then we split the data into above and below the **median of "effort".** We could not find a significant effect in the "reward level", "time" or "overall". Regarding the ZM according to the "reward level" we got $F(1, 41) = .915$, $p = .345$, partial $\eta^2 = .022$. As we looked at the "time" $F(4, 37) = .571$, $p = .648$, partial $\eta^2 = .014$. Analysing the "overall" effects they showed $F(1, 41) = .915$, $p = .345$, partial $\eta^2 = .022$

To summarise, for the ZM we only had a significant effect regarding the data split into above and below of the median of "liking". There we found that the mean values for the **ZM** at the **high level** (M = 236.80, SD = 18.45) was significantly higher than the mean of the **low level** (M = 200.453, SD = 19.81) **within the placebo group**.

Anticipation Corrugator Supercilii (CS)

Running ANOVAs for CS with data was split into above and below the **median of "wanting"** we found no significant effect. Regarding the "reward level" we got $F(1, 41) = .146$, $p = .704$, partial $\eta^2 = .004$, for "time" we got $F(2, 40) = .580$, $p = .562$, partial $\eta^2 = .014$ and "overall" $F(2, 40) = .169$, $p = .844$, partial $\eta^2 = .004$.

Then we split the data into above and below the **median of "liking".** There was no significant difference between the "drug groups". The values for "reward levels" were $F(1, 41) = .283$, $p = .589$, partial $\eta^2 = .007$, for "time" $F(2, 40) = .467$, $p = .628$, partial $\eta^2 = .012$ and for "overall" $F(2, 40) = .094$, $p = .910$, partial $\eta^2 = .002$.

As we split the data into above and below the **median of "effort"**, we got $F(1, 41) = .638$, $p = .429$, partial $\eta^2 = .016$ for the "reward levels", $F(2, 40) = .637$, $p = .532$, partial $\eta^2 = .016$ for "time" and "overall" $F(2, 40) = .045$, $p = .956$, partial $\eta^2 = .001$. That means there was no significant effect for "drug group".

Consumption – Corrugator Supercilii (CS)

Again the data was split into above and below the median of "**wanting", "liking" and "effort"**.

Conducting the ANOVA with the data split into above and below the **median of "wanting"** there was no significant effect. The interaction between the "reward level" and "drug group" was not significant $F(1, 41) = .001$, $p = .973$, partial $\eta^2 = .000$. The interaction between "time" and "drug group" $F(4, 37) = .713$, $p = .584$ was not significant, partial $\eta^2 = .018$. And the "overall" interaction $F(4, 37) = 1.935$, $p = .107$, partial $\eta^2 = .046$ was not significant.

Then we split the data into above and below the **median of "liking"**. Again we could not find a significant effect within the "drug group", neither for the "reward level" $F(1, 41) = .510$, $p = .479$, partial $\eta^2 = .013$, "time" $F(4, 37) = .740$, $p = .566$, partial $\eta^2 = .018$, nor "overall" $F(4, 37) = 1.674$, $p = .159$, partial $\eta^2 = .040$.

Additionally, we split the data into above and below the **median of "effort".** There the values for the interaction between the "reward level" and the "drug group" was $F(1, 41) = .245$, $p = .623$, partial $\eta^2 = .006$. Regarding the time windows of the EMG we got $F(4, 37) = .674$, $p = .611$, partial $\eta^2 = .017$. The "overall" values were $F(4, 37) = 2.055$, $p = .089$, partial $\eta^2 = .049$. That means we had no significant differences in the interactions between "reward level" and "drug group", "time" and "drug group" and "overall".

Summary Results

Several mixed-design ANOVAs were conducted to compare the effects between a Naltrexone and a placebo group. Data from fEMG and subjective ratings were computed. We could not find a significant effect in the factor "drug group" except of one condition.

There was a significant effect in the interaction between the “drug group” and the “reward level” at p<.05 level concerning the zygomaticus major during the consumption period F(1, 41) = 5.749, p = .021, partial η² = .126. Analysing simple main effects indicated that the mean score did not differ significantly between the Naltrexone and the placebo group. Neither at the high “reward level” (above the median of “liking”) F(1, 41) = 1.827, p = 1.84, partial η² = .044 nor at the low “reward level” (below the median of “liking”) F(1, 41) = .662, p = .421, partial η² = .016.
The significant effect occurred in the factor “reward level” of the placebo group. The mean scores differed significantly F(1, 41) = 4.508, p = .040, partial η² = .101. At the high level the mean (M = 236.80, SD = 18.45) was significantly higher than the mean of the low level (M = 200.453, SD = 19.81) (see Fig.5.).

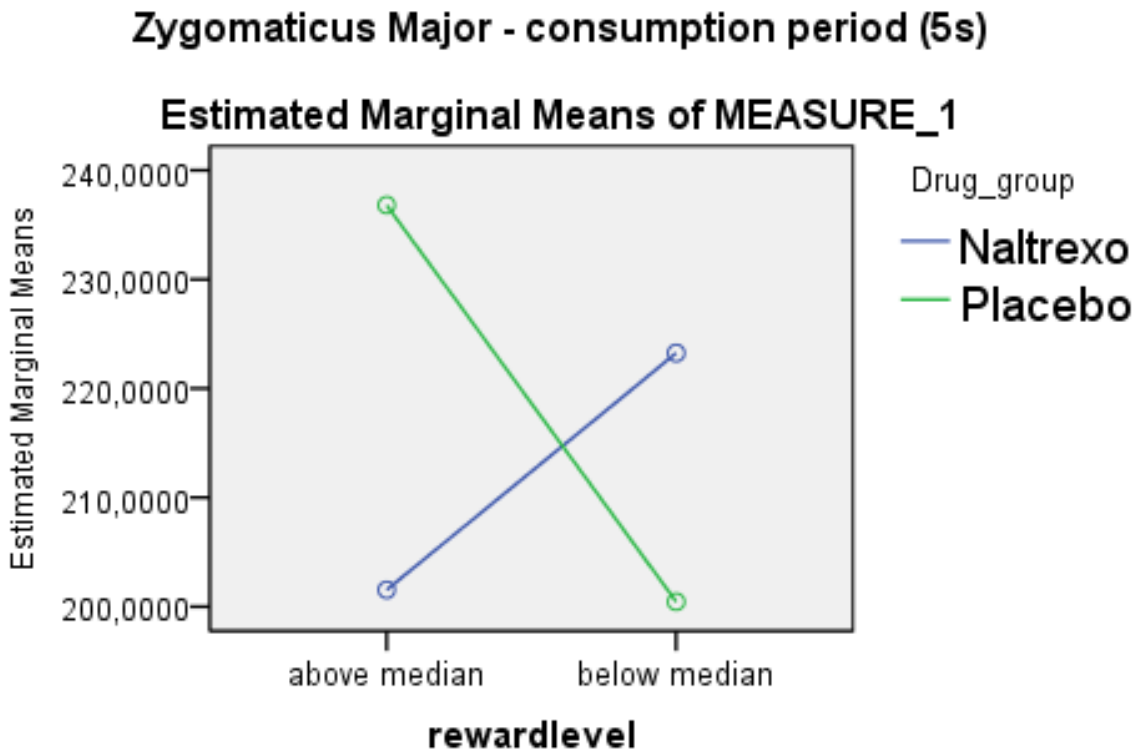

Fig. 5. significant effect within the placebo group.
F(1, 41) = 4.508, p < .040, partial η² = .101. Above median (M = 236.80, SD = 18.45) and below median (M = 200.453, SD = 19.81) for the placebo group.

For a better overview of the results tables including all values are attached.

Discussion

In a double-blind real effort task giving Naltrexone I explored the opioid related changes in “wanting” and “liking” rewarding with food rewards. In animal research the processes of “wanting” and “liking" are well explored (Wyvell & Berridge, 2000; Peciña, Cagniard, Berridge, Aldridge, & Zhuang, 2003).

For exploring opioid receptors modulating effects on hedonic pleasure especially animal studies are conducted (Trezza, Baarendse, & Vanderschuren, 2010). Here we explored “wanting” and “liking” receiving food rewards in humans. The processes of “wanting” and “liking” rely on the opioid- and dopamine-system (Berridge & Kringelbach, 2015). I compared subjective ratings and behavioural data from two groups receiving either Naltrexone or a placebo. One of the most important opioid receptors in processing “wanting” and “liking” is the μ-opioid receptor (Loseth, Ellingsen, & Leknes, 2014). Currently there is no specific μ-opioid receptor antagonist which is licensed from the Austrian BASG (Bundesamt für Sicherheit im Gesundheitswesen). That is why we chose Dependex® providing 50 mg Naltrexone. It has a high affinity to the μ-opioid receptor (Loseth, Ellingsen, & Leknes, 2014) and is well tolerated (Miotto et al. 2002; Yeomans & Gray, 2002). 50 mg per oral Naltrexone as a standard dosage is shown to block most of the opioid receptors in the brain (Lee et al. 1988). Ko et al. (1988) argue that Naltrexone is a strong antagonist for the μ-opioid receptor at least in monkeys. Here blocking opioid receptors giving Naltrexone was expected to result in lower “liking” and lower “wanting” to a lesser extent. For proof we collected data from subjective ratings, a hand dynamometer and fEMG. Subjective ratings were computed from two continuous scales. One scale measured “subjective wanting” and the other one measured “subjective liking”. For statistical analyses a mixed-design ANOVA was conducted in SPSS. Neither for “subjective wanting” nor “subjective liking” we got a significant effect. There are some possible reasons for these results. Rating the degree of “wanting” or “liking” stimuli is a form of decision making. Laurent, Morse & Balleine (2015) argue that the opioid system not only plays a role in the motivational and hedonic aspects of reward processing but even in decision making. They suggest that the μ-opioid receptor plays a functional role and, therefore, by blocking it could affect the subjective ratings. It may have resulted in the low ratings in the extreme parts of the continuous scale and more ratings around the centre, resulting in no significant effect. Modulating opioid receptors exploring distinct aspects of

decision making will be a topic for future research (Laurent, Morse, & Balleine, 2015). In addition Naltrexone treatment is shown to result in a reduction of reward responsiveness (Eikemo, Biele, Willoch, Thomsen, & Leknes, 2017). Studies with rodents show that blocking opioid receptors decreases preferences for rewards like sucrose, fat or sex cues (Mahler & Berridge, 2012).

During the experiment another interesting phenomenon occurred. We gave milk or cacao drinks respectively as rewards. In a pre-survey we evaluated the preferences for these drinks. We did that to generate two levels of reward to explore changes in "wanting" and "linking" between these two levels. It turned out that initial preferences were not stable across the experiment and changed during testing. Therefore, we split the data into above and below the median of "wanting", "liking" or "effort". We could not find a significant effect in "subjective liking" in the "drug group" which goes in line with other studies (Scinska et al., 2000; Yeomans and Gray, 2002). They report that opioid antagonism has no effect on the subjective quality of foods.

Concerning the subjective ratings we could not find a significant effect in "wanting" between the Naltrexone and the placebo group which goes in line with Murray et al. (2014). Differences to other studies may occur because of different types or amounts of rewards and the time of rewarding (one up to several days) (Murray et al., 2014). Further on such effects need more than subjective ratings to explore this kind of processes (Berridge & Robinson, 2003; Barbano & Cador, 2007).

Other studies try to assess the value of a reward through the analysis of orofacial reactions and the microstructure of the licking responses as a result of liquid intake (Davis & Smith, 1992; Smith, 2001; Berridge, 2009; Johnson et al., 2010).

In this project we had human participants and such methods would go beyond our hypotheses. That is why we chose to collect data from a hand dynamometer (Vernier software) as addition to the subjective ratings with a continuous scale.

Several studies show that humans change their degree of effort with regard to the expected value of the reward (Robbins & Everitt, 1996; Schultz, 2005; Berridge, 2004). Studies indicate that manipulating the effort required to obtain a reward seems to be an efficient method to dissociate the processes of "wanting" and "liking" (Waugh & Gotlib, 2008).

In this project we did not change the effort required. Instead the more you press, the higher the chance to get the most-"liked" reward increases. Here we used this method to explore differences in "wanting" in a real effort task. We could not find a

significant difference in the means of “effort” achieved to earn a reward more or less preferred between the experimental and the control group. We found a trend showing that participants receiving Naltrexone did press lower than participants from the control group. This would be in line with our hypothesis that Naltrexone suppresses “wanting”. Participants put in more effort for rewards higher valued. Giesen, Havermans, Nederkoorn, Strafaci, & Jansen (2009) demonstrate that participants even work harder to get more snack foods although they want to eat less. In this project this should not be the case because we assumed that participants of our project started hungry into the experiment because of two hours without eating before coming to the laboratory and three hours waiting after a small snack before starting the experiment. Therefore, we expected them to be hungry and that participants wanted the rewards.

We expected by blocking opioid receptors with Naltrexone this would reduce “liking” to a higher extent than “wanting”. Studies show that processes of “liking” rely more on the opioid systems as against the processes of “wanting” which rely more on the dopamine system (Davis et al., 2009, Peciña, 2008). This may have led to finding no significant effect between Naltrexone and the placebo group in the effort task with the hand dynamometer. In another study participants rate the pleasantness of food on a scale to assess “liking” either and use a forced choice methodology to gain data for “wanting” (Finlayson, King, and Blundell, 2007). In their study participants prefer high-fat savoury foods over low-fat savoury foods with no effects on “liking” and the participants like high fat sweet foods more than low-fat sweet foods with no difference in “wanting”. Finlayson, King & Blundell (2008) could not replicate these results and conclude that the force choice method effects both reward processes. Epstein, Truesdale, Wojcik, Paluch & Raynor (2003) demonstrate that food-deprived participants work longer (and thus much harder) to obtain food rewards than participants who are already fed up with no effect on subjective ratings of “liking”.

We did not find a significant effect for Naltrexone altering “wanting” and ”liking” (rating scales and effort task) which goes in line with (Scińska et al., 2000). They find no effects of Naltrexone on intensity and pleasantness of sucrose, quinine, citric acid, sodium chloride, and ethanol taste. Additionally, they cannot find an effect on ratings of olfactory stimuli (Scińska et al., 2000). In addition we found significant main effects concerning the “reward level” for the subjective ratings and the pressing of the hand

dynamometer. We expected that because we split the data into above and below the median based on the median of “wanting”, “liking” and “effort”.

The main part of our project was the collection of data from facial electromyography (fEMG). EMG is an experimental method to record and analyse myoelectric signals (Basmajian & De Luca, 1985). Horio (2003) shows that EMG is able to measure facial muscle signals according to taste. He indicates that most facial and chewing muscles of adults show greater responses to tastes disliked than to those preferred or less preferred.

Hu et al. (1999) recommend EMG because it is a physiological method to receive quantitative data. It is possible to minimize human errors and you can easily code facial muscle patterns. They also come to similar results like Horio (2003) suggesting that face muscles show greater activation to stimuli disliked.

In our study we took fEMG data from two muscles during two periods.

We installed an anticipation and a consumption period. The anticipation period lasted 3 seconds and took place after announcing the reward which could be obtained. That means we measured fEMG before the consumption and, therefore, fEMG data could represent the effects of expecting the value of the reward. Balleine (2005) argues that such a method measures “expected pleasantness” rather than “liking”. It contains predictions of the reward and, therefore, underlies cognitive desires. In animal studies this represents a distinct motivational control system of reward processing (Berridge and Aldridge, 2008; Berridge and O’Doherty, 2014; Dickinson and Balleine, 1994; Wassum et al., 2011b).

This may explain the following results of the anticipation period. Activation of the CS did not differ significantly between the two “drug groups”. We analysed the data split into above and below the median of “wanting”, “liking” and “effort” (pressing of hand dynamometer).

For the ZM we did not find a significant difference between the two groups either. The lack of ZM activation goes in line with prior research. These studies indicate that ZM does not reflect hedonic pleasure but CS activation seems to correspond with disgust (Booth et al., 2010; Horio, 2003; Hu et al., 1999).

Data of the consumption period was taken after swallowing. During this period we found a significant effect which occurred within the different “reward levels” in the placebo group. The ZM activation was higher for the rewards valued above the median of “liking” than for the rewards valued below. This indicates that participants

of the placebo group “liked” rewards higher valued more than rewards lower valued. For swallowing we decided a time period of 2 seconds. It is possible that participants took more time for rewards “liked” and, therefore, we found a higher activation of the lower face muscles. Future investigations need to improve EMG recording to better distinguish facial processing and to facilitate reliable interpretations of such results. Analysing the CS activation during the consumption period we could not find a difference in the interaction between the “drug group” and “reward level”, between “drug group” and “time” and between “drug group” and “overall”. Differences to other studies may emerge due to different methods of stimulus input (e.g. Bertino, Beauchamp, & Engelman, 1991). Animal studies show that regulation of facial expression is likely to be assessed with a distributed multifocal processing system for exploring lower and upper facial muscles (Morecraft, Louie, Herrick, & Stilwell-Morecraft, 2001; Morecraft, Stilwell–Morecraft, & Rossing, 2004).

Conclusion

We found no relevant differences between a placebo group and an experimental group receiving Naltrexone. We explored changes in “wanting” and “liking” using subjective ratings, data from a hand dynamometer and facial EMG. We gave a single dose of Naltrexone 50mg, which seems to have no significant effect on “wanting” and “liking” receiving food rewards. Our results go in line with other studies finding no differences in the subjective sensory quality of food (Scinska et al., 2000; Yeomans and Gray, 2002).

Murry et al., (2014) describe a similar pattern of ratings on the intensity of pleasant and unpleasant rewards. Other studies show that blocking opioid receptors has no effects on subjective pleasantness (Rabiner et al., 2011; Petrovic et al., 2008). Opioid antagonism has effects on neural responses to aversive food stimuli (Murray et al., 2014). Aversive food stimuli used in exploring “wanting” and “liking” could be an interesting aspect for future research, especially when using fEMG (Booth et al., 2010; Horio, 2003; Hu et al., 1999).

Havermans (2011; 2012) argues not to distinguish between “wanting” and “liking” exploring food rewards because they are intrinsically related and cannot be considered as two different components. Colleagues will have a look on food rewards giving Amisulpride as a dopamine antagonist. We may compare and combine these results in the course of our project. Future research should explore changes in

“wanting” and “liking” blocking opioid and dopamine receptors to find out more about the complex composition of reward processing.

For this thesis I did not explore gender differences in “wanting” and “liking”. There are indications that these processes differ in men and women even in the olfaction domain (Triscoli, Croy, Olausson, & Sailer, 2014). Studies of sexual behavior find gender differences as well (Dewitte, 2015). A fMRI study shows differences in anticipation of monetary and social rewards (Spreckelmeyer et al., 2009). Future theses could have a look on the gender differences regarding primary food rewards.

References

Abulof, U. (2017). Introduction: Why We Need Maslow in the Twenty-First Century. *Society*, *54*(6), 508–509. https://doi.org/10.1007/s12115-017-0198-6.

Anton, R. F., Moak, D. H., Waid, L. R., Latham, P. K., Malcolm, R. J., & Dias, J. K. (1999). Naltrexone and Cognitive Behavioral Therapy for the Treatment of Outpatient Alcoholics: Results of a Placebo-Controlled Trial. *American Journal of Psychiatry*, *156*(11), 1758–1764. https://doi.org/10.1176/ajp.156.11.1758.

Baldo, B. A., & Kelley, A. E. (2007). Discrete neurochemical coding of distinguishable motivational processes: insights from nucleus accumbens control of feeding. *Psychopharmacology*, *191*(3), 439–459. https://doi.org/10.1007/s00213-007-0741-z.

Bakshi, V. P., & Kelley, A. E. (1993). Feeding induced by opioid stimulation of the ventral striatum: Role of opiate receptor subtypes. *The Journal of Pharmacology and Experimental Therapeutics*, *265*(3), 1253–1260.

Basmajian, J. V., & Luca, C. J. de. (1985). *Muscles Alive: their functions revealed by electromyography*. Baltimore: Williams & Wilkins.

Barbano, M. F., & Cador, M. (2007). Opioids for hedonic experience and dopamine to get ready for it. *Psychopharmacology*, *191*(3), 497–506. https://doi.org/10.1007/s00213-006-0521-1.

Bargh, J. A., Lee-Chai, A., Barndollar, K., Gollwitzer, P. M., & Trötschel, R. (2001). The automated will: Nonconscious activation and pursuit of behavioral goals. *Journal of Personality and Social Psychology*, *81*(6), 1014–1027. https://doi.org/10.1037//0022-3514.81.6.1014.

Barch, D. M., Treadway, M. T., & Schoen, N. (2014). Effort, anhedonia, and function in schizophrenia: Reduced effort allocation predicts a motivation and functional impairment. *Journal of Abnormal Psychology*, *123*(2), 387–397. https://doi.org/10.1037/a0036299.

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. https://doi.org/10.1037/0033-2909.117.3.497.

Berns, G. S., McClure, S. M., Pagnoni, G., & Montague, P. R. (2001). Predictability Modulates Human Brain Response to Reward. *Journal of Neuroscience*, *21*(8), 2793–2798. https://doi.org/10.1523/JNEUROSCI.21-08-02793.2001.

Bertino, M., Beauchamp, G. K., & Engelman, K. (1991). Naltrexone, an opioid blocker, alters taste perception and nutrient intake in humans. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, *261*(1), R59–R63. https://doi.org/10.1152/ajpregu.1991.261.1.R59.

Berridge, K. C. (1996). Food reward: Brain substrates of wanting and liking. *Neuroscience & Biobehavioral Reviews*, *20*(1), 1–25. https://doi.org/10.1016/0149-7634(95)00033-B.

Berridge, K. C. (2004). Motivation concepts in behavioral neuroscience. *Physiology & Behavior*, *81*(2), 179–209. https://doi.org/10.1016/j.physbeh.2004.02.004.

Berridge, K. C. (2009). 'Liking' and 'wanting' food rewards: Brain substrates and roles in eating disorders. *Physiology & Behavior*, *97*(5), 537–550. https://doi.org/10.1016/j.physbeh.2009.02.044.

Berridge, K. C., & Aldridge, J. W. (2008). Decision Utility, the Brain, and Pursuit of Hedonic Goals. *Social Cognition; New York*, *26*(5), 621–646. http://dx-doi-org.uaccess.univie.ac.at/10.1521/soco.2008.26.5.621.

Berridge, K. C., & Kringelbach, M. L. (2008). Affective neuroscience of pleasure: reward in humans and animals. *Psychopharmacology*, *199*(3), 457–480. https://doi.org/10.1007/s00213-008-1099-6.

Berridge, K. C., & O'Doherty, J. P. (2014). Chapter 18 - From Experienced Utility to Decision Utility. In P. W. Glimcher & E. Fehr (Eds.), *Neuroeconomics (Second*

Edition), 335–351. San Diego: Academic Press. https://doi.org/10.1016/B978-0-12-416008-8.00018-8.

Berridge, K. C., & Robinson, T. E. (1998). What is the role of dopamine in reward: hedonic impact, reward learning, or incentive salience? *Brain Research Reviews*, *28*(3), 309–369. https://doi.org/10.1016/S0165-0173(98)00019-8.

Berridge, K. C., & Robinson, T. E. (2003). Parsing reward. *Trends in Neurosciences*, *26*(9), 507–513. https://doi.org/10.1016/S0166-2236(03)00233-9.

Berridge, K. C., Robinson, T. E., & Aldridge, J. W. (2009). Dissecting components of reward: 'liking', 'wanting', and learning. *Current Opinion in Pharmacology*, *9*(1), 65–73. https://doi.org/10.1016/j.coph.2008.12.014.

Bindra, D. (1974). A motivational view of learning, performance, and behavior modification. *Psychological Review*, *81*(3), 199–213. https://doi.org/10.1037/h0036330.

Blood, A. J., Zatorre, R. J., Bermudez, P., & Evans, A. C. (1999). Emotional responses to pleasant and unpleasant music correlate with activity in paralimbic brain regions. *Nature Neuroscience*, *2*(4), 382. https://doi.org/10.1038/7299.

Bodnar, R. J. (2004). Endogenous opioids and feeding behavior: a 30-year historical perspective. *Peptides*, *25*(4), 697–725. https://doi.org/10.1016/j.peptides.2004.01.006.

Bolles, R. C. (1972). Reinforcement, expectancy, and learning. *Psychological Review*, *79*(5), 394–409. https://doi.org/10.1037/h0033120.

Boyle, A. E. L., Stewart, R. B., Macenski, M. J., Spiga, R., Johnson, B. A., & Meisch, R. A. (1998). Effects of Acute and Chronic Doses of Naltrexone on Ethanol Self-Administration in Rhesus Monkeys. *Alcoholism: Clinical and Experimental Research*, *22*(2), 359–366. https://doi.org/10.1111/j.1530-0277.1998.tb03661.x.

Burattini, C., Burbassi, S., Aicardi, G., & Cervo, L. (2008). Effects of naltrexone on cocaine- and sucrose-seeking behaviour in response to associated stimuli in rats. *International Journal of Neuropsychopharmacology*, *11*(1), 103–109. https://doi.org/10.1017/S1461145707007705.

Cabanac, M. (1979). Sensory Pleasure. *The Quarterly Review of Biology*, *54*(1), 1–29. https://doi.org/10.1086/410981.

Cabanac, M. (1992). Pleasure: the common currency. *Journal of Theoretical Biology*, *155*(2), 173–200.

Carver, C. S., & Scheier, M. F. (1998). *On the serf-regulation of behavior*. New York, NY: Cambridge University Press.

Chikazoe, J., Lee, D. H., Kriegeskorte, N., & Anderson, A. K. (2014). Population coding of affect across stimuli, modalities and individuals. *Nature Neuroscience*, *17*(8), 1114. https://doi.org/10.1038/nn.3749.

Ciccocioppo, R., Martin-Fardon, R., & Weiss, F. (2002). Effect of Selective Blockade of μ1 or δ Opioid Receptors on Reinstatement of Alcohol-Seeking Behavior by Drug-Associated Stimuli in Rats. *Neuropsychopharmacology*, *27*(3), 391–399. https://doi.org/10.1016/S0893-133X(02)00302-0.

Ciccocioppo, R., Lin, D., Martin-Fardon, R., & Weiss, F. (2003). Reinstatement of ethanol-seeking behavior by drug cues following single versus multiple ethanol intoxication in the rat: effects of naltrexone. *Psychopharmacology*, *168*(1), 208–215. https://doi.org/10.1007/s00213-002-1380-z.

Curran, M. P., & Perry, C. M. (2001). Amisulpride. *Drugs*, *61*(14), 2123–2150. https://doi.org/10.2165/00003495-200161140-00014.

Davidson, D., Palfai, T., Bird, C., & Swift, R. (1999). Effects of Naltrexone on Alcohol Self-Administration in Heavy Drinkers. *Alcoholism: Clinical and Experimental Research*, *23*(2), 195–203. https://doi.org/10.1111/j.1530-0277.1999.tb04099.x.

Davis, C. A., Levitan, R. D., Reid, C., Carter, J. C., Kaplan, A. S., Patte, K. A., … Kennedy, J. L. (2009). Dopamine for “Wanting” and Opioids for “Liking”: A Comparison of Obese Adults With and Without Binge Eating. *Obesity*, *17*(6), 1220–1225. https://doi.org/10.1038/oby.2009.52.

Davis, J. D., & Smith, G. P. (1992). Analysis of the microstructure of the rhythmic tongue movements of rats ingesting maltose and sucrose solutions. *Behavioral Neuroscience*, *106*(1), 217–228. https://doi.org/10.1037/0735-7044.106.1.217.

Delorme, A., & Makeig, S. (2004). EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of Neuroscience Methods*, *134*(1), 9–21. https://doi.org/10.1016/j.jneumeth.2003.10.009.

Dewitte, M. (2015). Gender Differences in Liking and Wanting Sex: Examining the Role of Motivational Context and Implicit Versus Explicit Processing. *Archives of Sexual Behavior*, *44*(6), 1663–1674. https://doi.org/10.1007/s10508-014-0419-7.

Dickinson, A., & Balleine, B. (1994). Motivational control of goal-directed action. *Animal Learning & Behavior*, *22*(1), 1–18. https://doi.org/10.3758/BF03199951.

Eikemo, M., Biele, G., Willoch, F., Thomsen, L., & Leknes, S. (2017). Opioid Modulation of Value-Based Decision-Making in Healthy Humans. *Neuropsychopharmacology*, *42*(9), 1833–1840. https://doi.org/10.1038/npp.2017.58.

Eikemo, M., Løseth, G. E., Johnstone, T., Gjerstad, J., Willoch, F., & Leknes, S. (2016). Sweet taste pleasantness is modulated by morphine and naltrexone. *Psychopharmacology*, *233*(21), 3711–3723. https://doi.org/10.1007/s00213-016-4403-x.

Ekman, P., & Friesen, W. V. (1971). Constants across cultures in the face and emotion. *Journal of Personality and Social Psychology*, *17*(2), 124–129. https://doi.org/10.1037/h0030377.

Everitt, B. J., & Robbins, T. W. (2005). Neural systems of reinforcement for drug addiction: from actions to habits to compulsion. *Nature Neuroscience*, *8*(11), 1481. https://doi.org/10.1038/nn1579.

Finlayson, G., King, N., & Blundell, J. E. (2007). Is it possible to dissociate 'liking' and 'wanting' for foods in humans? A novel experimental procedure. *Physiology & Behavior*, *90*(1), 36–42. https://doi.org/10.1016/j.physbeh.2006.08.020.

Finlayson, G., King, N., & Blundell, J. (2008). The role of implicit wanting in relation to explicit liking and wanting for food: Implications for appetite control. *Appetite*, *50*(1), 120–127. https://doi.org/10.1016/j.appet.2007.06.007.

Francis, S., Rolls, E., Bowtell, R., McGlone, F., O'Doherty, J., Browning, A., … Smith, E. (1999). The representation of pleasant touch in the brain and its relationship with taste and olfactory areas. *Neuroreport*, *10*(3), 453–459.

Franzen, J., & Brinkmann, K. (2016). Wanting and liking in dysphoria: Cardiovascular and facial EMG responses during incentive processing. *Biological Psychology*, *121*, 19–29. https://doi.org/10.1016/j.biopsycho.2016.07.018.

Fridlund, A. J., & Cacioppo, J. T. (1986). Guidelines for Human Electromyographic Research. *Psychophysiology*, *23*(5), 567–589. https://doi.org/10.1111/j.1469-8986.1986.tb00676.x.

Fridlund, A. J., & Izard, C. E. (1982). Electromyographic studies of facial expressions of emotions and patterns of emotions. In J. T. Cacioppo & R. E. Petty (Eds.), *Social psychophysiology: A sourcebook*, 243–286. New York: Guilford Press.

Giesen, J. C. A. H., Havermans, R. C., Nederkoorn, C., Strafaci, S., & Jansen, A. (2009). Working harder to obtain more snack foods when wanting to eat less. *Behaviour Research and Therapy*, *47*(1), 13–17. https://doi.org/10.1016/j.brat.2008.09.007.

Giraudo, S. Q., Grace, M. K., Welch, C. C., Billington, C. J., & Levine, A. S. (1993). Naloxone's anorectic effect is dependent upon the relative palatability of food. *Pharmacology, Biochemistry, and Behavior*, *46*(4), 917–921.

Glass, G. V., Peckham, P. D., & Sanders, J. R. (1972). Consequences of Failure to Meet Assumptions Underlying the Fixed Effects Analyses of Variance and Covariance. *Review of Educational Research*, 42(3), 237–288. https://doi.org/10.3102/00346543042003237.

Harwell, M. R., Rubinstein, E. N., Hayes, W. S., & Olds, C. C. (1992). Summarizing Monte Carlo Results in Methodological Research: The One- and Two-Factor Fixed Effects ANOVA Cases. *Journal of Educational and Behavioral Statistics*, 17(4), 315–339. https://doi.org/10.3102/10769986017004315.

Havermans, R. C. (2011). "You Say it's Liking, I Say it's Wanting …". On the difficulty of disentangling food reward in man. *Appetite*, *57*(1), 286–294. https://doi.org/10.1016/j.appet.2011.05.310.

Havermans, R. C. (2012). How to tell where 'liking' ends and 'wanting' begins. *Appetite*, *58*(1), 252–255. https://doi.org/10.1016/j.appet.2011.10.013.

Heidbreder, C. (2005). Recent Advances in the Pharmacotherapeutic Management of Drug Dependence and Addiction. *Current Psychiatry Reviews*, *1*(1), 45–67. https://doi.org/10.2174/1573400052953538.

Hernandez-Avila, C. A., Song, C., Kuo, L., Tennen, H., Armeli, S., & Kranzler, H. R. (2006). Targeted Versus Daily Naltrexone: Secondary Analysis of Effects on Average Daily Drinking. *Alcoholism: Clinical and Experimental Research*, *30*(5), 860–865. https://doi.org/10.1111/j.1530-0277.2006.00101.x.

Hetherington, M. M., Vervaet, N., Blass, E., & Rolls, B. J. (1991). Failure of naltrexone to affect the pleasantness or intake of food. *Pharmacology Biochemistry and Behavior*, *40*(1), 185–190. https://doi.org/10.1016/0091-3057(91)90343-Z.

Horio, T. (2003). EMG Activities of Facial and Chewing Muscles of Human Adults in Response to Taste Stimuli, *Percept. Mot. Skills* 97**,** 289–298.

Hortsjö, C. H. (1970). *Man's Face and Mimic Language*. Malmö: Nordens Boktrycheri.

Hu, S., Player, K. A., Mcchesney, K. A., Dalistan, M. D., Tyner, C. A., & Scozzafava, J. E. (1999). Facial EMG as an indicator of palatability in humans. *Physiology & Behavior*, *68*(1), 31–35. https://doi.org/10.1016/S0031-9384(99)00143-2.

Hull, C. L. (1943). Principles of Behavior: An Introduction to Behavior Theory. In *The Journal of Abnormal and Social Psychology, 39*, 377–380. https://doi.org/10.1037/h0051597.

Izard, C. E. (1992). Basic emotions, relations among emotions, and emotion-cognition relations. *Psychological Review*, *99*(3), 561–565. https://doi.org/10.1037/0033-295X.99.3.561.

Johnson, A. W., Sherwood, A., Smith, D. R., Wosiski-Kuhn, M., Gallagher, M., & Holland, P. C. (2010). An analysis of licking microstructure in three strains of mice. *Appetite*, *54*(2), 320–330. https://doi.org/10.1016/j.appet.2009.12.007.

Kelley, A. E., Bless, E. P., & Swanson, C. J. (1996). Investigation of the effects of opiate antagonists infused into the nucleus accumbens on feeding and sucrose drinking in rats. *The Journal of Pharmacology and Experimental Therapeutics*, *278*(3), 1499–1507.

Kivetz, R., Urminsky, O., & Zheng, Y. (2006). The Goal-Gradient Hypothesis Resurrected: Purchase Acceleration, Illusionary Goal Progress, and Customer Retention. *Journal of Marketing Research*, *43*(1), 39–58. https://doi.org/10.1509/jmkr.43.1.39.

Ko, M.-C., Butelman, E. R., Traynor, J. R., & Woods, J. H. (1998). Differentiation of Kappa Opioid Agonist-Induced Antinociception by Naltrexone Apparent pA2 Analysis

in Rhesus Monkeys. *The Journal of pharmacology and experimental therapeutics*, *285*(2), 518–526.

Kringelbach, M. L. (2004). Food for thought: hedonic experience beyond homeostasis in the human brain. *Neuroscience*, *126*(4), 807–819. https://doi.org/10.1016/j.neuroscience.2004.04.035.

Larsen, J. T., Norris, C. J., & Cacioppo, J. T. (2003). Effects of positive and negative affect on electromyographic activity over zygomaticus major and corrugator supercilii. *Psychophysiology*, *40*(5), 776–785. https://doi.org/10.1111/1469-8986.00078.

Lau, C.-I., Wang, H.-C., Hsu, J.-L., & Liu, M.-E. (2013). Does the dopamine hypothesis explain schizophrenia? *Reviews in the Neurosciences*, *24*(4). https://doi.org/10.1515/revneuro-2013-0011.

Laurent, V., Morse, A. K., & Balleine, B. W. (2015). The role of opioid processes in reward and decision-making. *British Journal of Pharmacology*, *172*(2), 449–459. https://doi.org/10.1111/bph.12818.

Lee, M. C., Wagner, H. N., Tanada, S., Frost, J. J., Bice, A. N., & Dannals, R. F. (1988). Duration of Occupancy of Opiate Receptors by Naltrexone. *Journal of Nuclear Medicine*, *29*(7), 1207–1211.

Liu, X., & Weiss, F. (2002). Additive Effect of Stress and Drug Cues on Reinstatement of Ethanol Seeking: Exacerbation by History of Dependence and Role of Concurrent Activation of Corticotropin-Releasing Factor and Opioid Mechanisms. *Journal of Neuroscience*, *22*(18), 7856–7861. https://doi.org/10.1523/JNEUROSCI.22-18-07856.2002.

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

Mahler, S. V., & Berridge, K. C. (2012). What and when to “want”? Amygdala-based focusing of incentive salience upon sugar and sex. *Psychopharmacology*, *221*(3), 407–426. https://doi.org/10.1007/s00213-011-2588-6.

Maslow, A. H. (1943). A theory of human motivation. *Psychological Review*, *50*(4), 370–396.

Mason, W. A., Saxon, S. V., & Sharpe, L. G. (1963). Preferential responses of young chimpanzees to food and social rewards. *The Psychological Record*, *13*(3), 341–345. https://doi.org/10.1007/BF03393535.

McCabe, C., Huber, A., Harmer, C. J., & Cowen, P. J. (2011). The D2 antagonist sulpiride modulates the neural processing of both rewarding and aversive stimuli in healthy volunteers. *Psychopharmacology*, *217*(2), 271. https://doi.org/10.1007/s00213-011-2278-4.

McKeage, K., & Plosker, G. L. (2004). Amisulpride. *CNS Drugs*, *18*(13), 933–956. https://doi.org/10.2165/00023210-200418130-00007.

Meyer, M. C., Straughn, A. B., Lo, M. W., Schary, W. L., & Whitney, C. C. (1984). Bioequivalence, dose-proportionality, and pharmacokinetics of naltrexone after oral administration. *The Journal of Clinical Psychiatry*, *45*(9 Pt 2), 15–19.

Miotto, K., McCann, M., Basch, J., Rawson, R., & Ling, W. (2002). Naltrexone and Dysphoria: Fact or Myth? *The American Journal on Addictions*, *11*(2), 151–160. https://doi.org/10.1080/10550490290087929.

Monti, P. M., Rohsenow, D. J., Hutchison, K. E., Swift, R. M., Mueller, T. I., Colby, S. M., … Abrams, D. B. (1999). Naltrexone’s Effect on Cue-Elicited Craving Among Alcoholics in Treatment. *Alcoholism: Clinical and Experimental Research*, *23*(8), 1386–1394. https://doi.org/10.1111/j.1530-0277.1999.tb04361.x.

Morecraft, R. J., Louie, J. L., Herrick, J. L., & Stilwell-Morecraft, K. S. (2001). Cortical innervation of the facial nucleus in the non-human primate: A new interpretation of

the effects of stroke and related subtotal brain trauma on the muscles of facial expression. *Brain*, *124*(1), 176–208. https://doi.org/10.1093/brain/124.1.176.

Morecraft, R. J., Stilwell–Morecraft, K. S., & Rossing, W. R. (2004). The Motor Cortex and Facial Expression: New Insights From Neuroscience. *The Neurologist*, *10*(5), 235. https://doi.org/10.1097/01.nrl.0000138734.45742.8d.

Murray, E., Brouwer, S., McCutcheon, R., Harmer, C. J., Cowen, P. J., & McCabe, C. (2014). Opposing neural effects of naltrexone on food reward and aversion: implications for the treatment of obesity. *Psychopharmacology*, *231*(22), 4323–4335. https://doi.org/10.1007/s00213-014-3573-7.

Nathan, P. J., O'Neill, B. V., Bush, M. A., Koch, A., Tao, W. X., Maltby, K., … Bullmore, E. T. (2012). Opioid Receptor Modulation of Hedonic Taste Preference and Food Intake: A Single-Dose Safety, Pharmacokinetic, and Pharmacodynamic Investigation With GSK1521498, a Novel μ-Opioid Receptor Inverse Agonist. *The Journal of Clinical Pharmacology*, *52*(4), 464–474. https://doi.org/10.1177/0091270011399577.

O'Brien, C. P., Volpicelli, L. A., & Volpicelli, J. R. (1996). Naltrexone in the treatment of alcoholism: A clinical review. *Alcohol*, *13*(1), 35–39. https://doi.org/10.1016/0741-8329(95)02038-1.

O'Malley, S. S., Krishnan-Sarin, S., Farren, C., Sinha, R., & Kreek, M. (2002). Naltrexone decreases craving and alcohol self-administration in alcohol-dependent subjects and activates the hypothalamo–pituitary–adrenocortical axis. *Psychopharmacology*, *160*(1), 19–29. https://doi.org/10.1007/s002130100919.

Peciña, S. (2008). Opioid reward 'liking' and 'wanting' in the nucleus accumbens. *Physiology & Behavior*, *94*(5), 675–680. https://doi.org/10.1016/j.physbeh.2008.04.006.

Peciña, S., & Berridge, K. C. (2005). Hedonic Hot Spot in Nucleus Accumbens Shell: Where Do μ-Opioids Cause Increased Hedonic Impact of Sweetness? *Journal of*

Neuroscience, *25*(50), 11777–11786. https://doi.org/10.1523/JNEUROSCI.2329-05.2005.

Peciña, S., Cagniard, B., Berridge, K. C., Aldridge, J. W., & Zhuang, X. (2003). Hyperdopaminergic Mutant Mice Have Higher “Wanting” But Not “Liking” for Sweet Rewards. *The Journal of Neuroscience*, *23*(28), 9395–9402. https://doi.org/10.1523/JNEUROSCI.23-28-09395.2003.

Perrault, G., Depoortere, R., Morel, E., Sanger, D. J., & Scatton, B. (1997). Psychopharmacological Profile of Amisulpride: An Antipsychotic Drug with Presynaptic D2/D3 Dopamine Receptor Antagonist Activity and Limbic Selectivity. *Journal of Pharmacology and Experimental Therapeutics*, *280*(1), 73–82.

Pessiglione, M., Schmidt, L., Draganski, B., Kalisch, R., Lau, H., Dolan, R. J., & Frith, C. D. (2007). How the Brain Translates Money into Force: A Neuroimaging Study of Subliminal Motivation. *Science*, *316*(5826), 904–906. https://doi.org/10.1126/science.1140459.

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. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, *28*(42), 10509–10516. https://doi.org/10.1523/JNEUROSCI.2807-08.2008.

Pool, E., Sennwald, V., Delplanque, S., Brosch, T., & Sander, D. (2016). Measuring wanting and liking from animals to humans: A systematic review. *Neuroscience & Biobehavioral Reviews*, *63*, 124–142. https://doi.org/10.1016/j.neubiorev.2016.01.006.

Rabiner, E. A., Beaver, J., Makwana, A., Searle, G., Long, C., Nathan, P. J., … Bullmore, E. T. (2011). Pharmacological differentiation of opioid receptor antagonists by molecular and functional imaging of target occupancy and food reward-related brain activation in humans. *Molecular Psychiatry*, *16*(8), 826–835. https://doi.org/10.1038/mp.2011.29.

Robinson, T. E., & Berridge, K. C. (2003). Addiction. *Annual Review of Psychology; Palo Alto*, *54*, 25–53.

Robbins, T. W., & Everitt, B. J. (1992). Functions of dopamine in the dorsal and ventral striatum. *Seminars in Neuroscience*, *4*(2), 119–127. https://doi.org/10.1016/1044-5765(92)90010-Y.

Robbins, T. W., & Everitt, B. J. (1996). Neurobehavioural mechanisms of reward and motivation. *Current Opinion in Neurobiology*, *6*(2), 228–236. https://doi.org/10.1016/S0959-4388(96)80077-8.

Rohsenow, D. J., & Monti, P. M. (o. J.). *Naltrexone's Effects on Reactivity to Alcohol Cues Among Alcoholic Men*. 5.

Rosenzweig, P., Canal, M., Patat, A., Bergougnan, L., Zieleniuk, I., & Bianchetti, G. (2002). A review of the pharmacokinetics, tolerability and pharmacodynamics of amisulpride in healthy volunteers. *Human Psychopharmacology: Clinical and Experimental*, *17*(1), 1–13. https://doi.org/10.1002/hup.320.

Rozin, P. (1999). Preadaptation and the puzzles and properties of pleasure. In *Well-being: The foundations of hedonic psychology,* 109–133. New York, NY, US: Russell Sage Foundation.

Salkind, N. J. (2010). *Encyclopedia of Research Design* (Vol. 2). Los Angeles: Sage.

Schoemaker, H., Claustre, Y., Fage, D., Rouquier, L., Chergui, K., Curet, O., … Scatton, B. (1997). Neurochemical Characteristics of Amisulpride, an Atypical Dopamine D2/D3 Receptor Antagonist with Both Presynaptic and Limbic Selectivity. *Journal of Pharmacology and Experimental Therapeutics*, *280*(1), 83–97.

Schultz, W. (2005). Behavioral Theories and the Neurophysiology of Reward. *Annual Review of Psychology*, *57*(1), 87–115. https://doi.org/10.1146/annurev.psych.56.091103.070229.

Schultz, W. (2015). Neuronal Reward and Decision Signals: From Theories to Data. *Physiological Reviews*, *95*(3), 853–951. https://doi.org/10.1152/physrev.00023.2014.

Schwartz, G. E., Fair, P. L., Salt, P., Mandel, M. R., & Klerman, G. L. (1976). Facial muscle patterning to affective imagery in depressed and nondepressed subjects. *Science*, *192*, 489–491.

Scińska, A., Koroś, E., Polanowska, E., Kukwa, A., Bogucka-Bonikowska, A., Kostowski, W., … Bieńkowski, P. (2000). An opioid receptor antagonist, naltrexone, does not alter taste and smell responses in humans. *Polish Journal of Pharmacology*, *52*(5), 397–402.

Skinner, B. F. (1950). Are theories of learning necessary? *Psychological Review, 57,* 193-216.

Small, D. M., Zatorre, R. J., Dagher, A., Evans, A. C., & Jones-Gotman, M. (2001). Changes in brain activity related to eating chocolate - From pleasure to aversion. *Brain*, *124*(9), 1720–1733. https://doi.org/10.1093/brain/124.9.1720.

Smith, G. P. (2001). John Davis and the meanings of licking. *Appetite*, *36*(1), 84–92. https://doi.org/10.1006/appe.2000.0371.

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. https://doi.org/10.1093/scan/nsn051.

Steiner, J. E. (1979). Human Facial Expressions in Response to Taste and Smell Stimulation. In H. W. Reese & L. P. Lipsitt (Hrsg.), *Advances in Child Development and Behavior*, *13*, 257–295. https://doi.org/10.1016/S0065-2407(08)60349-3.

Steiner, J. E., Glaser, D., Hawilo, M. E., & Berridge, K. C. (2001). Comparative expression of hedonic impact: affective reactions to taste by human infants and other

primates. *Neuroscience & Biobehavioral Reviews*, *25*(1), 53–74. https://doi.org/10.1016/S0149-7634(00)00051-8.

Stromberg, M. F., Casale, M., Volpicelli, L., Volpicelli, J. R., & O'brien, C. P. (1998). A Comparison of the Effects of the Opioid Antagonists Naltrexone, Naltrindole, and β-Funaltrexamine on Ethanol Consumption in the Rat. *Alcohol*, *15*(4), 281–289. https://doi.org/10.1016/S0741-8329(97)00131-6.

Thut, G., Schultz, W., Roelcke, U., Nienhusmeier, M., Missimer, J., Maguire, R. P., & Leenders, K. L. (1997). Activation of the human brain by monetary reward. *NeuroReport*, *8*(5), 1225.

Tibboel, H., De Houwer, J., Spruyt, A., Brevers, D., Roy, E., & Noël, X. (2015). Heavy social drinkers score higher on implicit wanting and liking for alcohol than alcohol-dependent patients and light social drinkers. *Journal of Behavior Therapy and Experimental Psychiatry*, *48*, 185–191. https://doi.org/10.1016/j.jbtep.2015.04.003.

Tassinary, L. G., & Cacioppo, J. T. (1992). Unobservable facial actions and emotion. *Psychological Science, 3*(1), 28–33.

Trezza, V., Baarendse, P. J. J., & Vanderschuren, L. J. M. J. (2010). The pleasures of play: pharmacological insights into social reward mechanisms. *Trends in Pharmacological Sciences*, *31*(10), 463–469. https://doi.org/10.1016/j.tips.2010.06.008.

Triscoli, C., Croy, I., Olausson, H., & Sailer, U. (2014). Liking and wanting pleasant odors: Different effects of repetitive exposure in men and women. *Frontiers in Psychology*, *5*. https://doi.org/10.3389/fpsyg.2014.00526.

Verebey, K., Volavka, J., Mulé, S. J., & Resnick, R. B. (1976). Naltrexone: disposition, metabolism, and effects after acute and chronic dosing. *Clinical Pharmacology and Therapeutics*, *20*(3), 315–328.

Wassum, K. M., Ostlund, S. B., Balleine, B. W., & Maidment, N. T. (2011). Differential dependence of Pavlovian incentive motivation and instrumental incentive learning processes on dopamine signaling. *Learning & Memory*, *18*(7), 475–483. https://doi.org/10.1101/lm.2229311.

Waugh, C. E., & Gotlib, I. H. (2008). Motivation for reward as a function of required effort: Dissociating the 'liking' from the 'wanting' system in humans. *Motivation and Emotion*, *32*(4), 323–330. https://doi.org/10.1007/s11031-008-9104-2.

Weerts, E. M., McCaul, M. E., Kuwabara, H., Yang, X., Xu, X., Dannals, R. F., … Wand, G. S. (2013). Influence of OPRM1 Asn^{40} Asp variant (A118G) on [^{11}C] carfentanil binding potential: preliminary findings in human subjects. *The International Journal of Neuropsychopharmacology*, *16*(1), 47–53. https://doi.org/10.1017/S146114571200017X.

Weber, S. C., Beck-Schimmer, B., Kajdi, M.-E., Müller, D., Tobler, P. N., & Quednow, B. B. (2016). Dopamine D2/3- and μ-opioid receptor antagonists reduce cue-induced responding and reward impulsivity in humans. *Translational Psychiatry*, *6*(7), 850. https://doi.org/10.1038/tp.2016.113.

World Medical Association (2013). World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA 310,* 2191–2194.

Wyvell, C. L., & Berridge, K. C. (2000). Intra-Accumbens Amphetamine Increases the Conditioned Incentive Salience of Sucrose Reward: Enhancement of Reward "Wanting" without Enhanced "Liking" or Response Reinforcement. *Journal of Neuroscience*, *20*(21), 8122–8130. https://doi.org/10.1523/JNEUROSCI.20-21-08122.2000.

Yeomans, M. R., & Gray, R. W. (1996). Selective effects of naltrexone on food pleasantness and intake. *Physiology & Behavior*, *60*(2), 439–446.

Yeomans, M. R., & Gray, R. W. (2002). Opioid peptides and the control of human ingestive behaviour. *Neuroscience & Biobehavioral Reviews*, *26*(6), 713–728. https://doi.org/10.1016/S0149-7634(02)00041-6.

Zald, D. H., Lee, J. T., Fluegel, K. W., & Pardo, J. V. (1998). Aversive gustatory stimulation activates limbic circuits in humans. *Brain, 121*, 1143–1154.

Zald, D. H., & Pardo, J. V. (1997). Emotion, olfaction, and the human amygdala: Amygdala activation during aversive olfactory stimulation. *Proceedings of the National Academy of Sciences of the United States of America, 94*(8), 4119–4124.

Abstract (ENG)

Reward processing plays a big part in addiction research and clinical disorders. We already know from animal and human studies that there are two reward processes. “Wanting” comprises the motivational role whereas “liking” reflects the hedonic aspects of reward processing. In this study we explore “wanting” and “liking” of food rewards by blocking opioid receptors. During a within-subject design explicit measures (ratings scales, real effort) and implicit measure (facial electromyography) were analysed. During this double-blind experiment 42 healthy voluntary participants got either 50mg of Naltrexone or a placebo. Through blocking opioid receptors with Naltrexone we expected a reduction of “liking”, leading to lower results in the subjective ratings and lower activation of the corrugator supercilii measured via facial EMG. For measuring “wanting” with the hand dynamometer (real effort) we expected a reduction to a lesser extent than for “liking”.

We did not find any significant differences between the experimental and the control group. A significant effect occurred within the placebo group during the consumption period concerning the zygomaticus major. The conclusion of the study is that blocking opioid receptors with naltrexone do not change “wanting” and “liking” to a significant extent when receiving food rewards.

Keywords

Primary rewards; Food; facial EMG; Real effort task; opioid antagonism

Abstract (GER)

Die Verarbeitung von Belohnungen spielt eine große Rolle in der Suchttherapie und bei klinischen Erkrankungen. Durch Studien an Tieren und Menschen sind die zwei Gehirnprozesse „wanting“ und „liking“ bereits etabliert. “Wanting” stellt die motivationale Komponente dar, während “liking” den hedonischen Aspekt der Belohnungsverarbeitung umfasst.

In dieser Studie untersuchten wir die Unterschiede zwischen “wanting” und “liking” bei primären Belohnungen (Milch- bzw. Kakaogetränke) durch Blockieren von Opioid-Rezeptoren beim Menschen.

Während eines Within-Subject Designs wurden explizite (Bewertungsskalen, Kraftaufwand) und implizite Messungen (Gesichtselektromyographie, fEMG) ausgewertet und analysiert.

In dieser doppel-blinden Studie erhielten 42 gesunde Freiwillige entweder 50mg Naltrexon oder ein Placebo. Durch das Blockieren von Opioid-Rezeptoren durch Naltrexon erwarteten wir eine Reduktion des „liking“. Dies würde sich in den subjektiven Bewertungsskalen und in der Reduktion der Aktivierung des Corrugator Superciliis zeigen. Für die Messungen von „wanting“ durch den Kraftaufwand mit dem Hand-Dynamometer erwarteten wir eine geringere Reduktion als beim „liking“. Wir fanden keinen signifikanten Unterschied zwischen der Experimental- und der Kontrollgruppe. Einzig in der Placebogruppe trat während des Konsums der Belohnung ein statistisch nachweisbarer Effekt des Zygomaticus Majors auf.

In der Studie kommen wir zu dem Schluss, dass durch die Blockierung von Opioid-Rezeptoren mit Naltrexon sich „wanting“ und „liking“, bei Erhalt von primären Belohnungen, nicht nachweislich verändern.

Keywords

Primäre Belohnungen; Essen; Gesichtselektromyographie; Kraftaufwand; Motivation; Opioid Rezeptoren

Supplementary material:

Table of Figures

List of Abbreviations

fEMG……..……..……facial Electromyography
MVC…..……..…….Maximum Voluntary Contraction
NAcc…….……...Nucleus Accumbens
VPa……..Ventral Pallidum
ZM……...Zygomaticus Major
CS…….Corrugator Supercilii

Description of all elements in a trial

Each trial included (See Fig. S1) the following steps:
1) a fixation cross (2 seconds),
2) a picture announcing the highest possible reward for 3 seconds (high or low),
3) a continuous scale ranging from ‘not at all’ to ‘very much’ to rate “wanting”,
4) a 2 seconds period to announce the squeezing of the hand dynamometer,
5) a 4 seconds period of squeezing, where participants determined the probability to obtain the reward announced. During this period they received visual feedback showing their contraction (sliding average of 1 second, as percentage of the MVC),
6) a picture announcing the reward obtained (3 seconds), which could be high, low, or very low,
7) a phase of 3 seconds to prepare for the reward obtained (3 seconds in the non-social, 4 seconds in the social condition),
8) reward delivering for 2 seconds in the non-social and 9 seconds in the social condition
– we defined this time periods to enable sufficiently long tactile stimulation and

keeping the overall trial duration similar across the two conditions,
– only in the non-social condition we showed instructions to lean back and swallow the reward delivered (duration of 3 seconds),
9) a relaxation phase of 5 seconds duration,
10) a continuous scale ranging from ‘not at all’ to ‘very much’ to rate the “liking”,

Afterwards participants received water to cancel the taste of the reward obtained before, in the same way like receiving milk or cacao drinks respectively (but only in the non-social condition).
In both conditions a blank screen was shown for 3 to 4 seconds at the end of each trial.

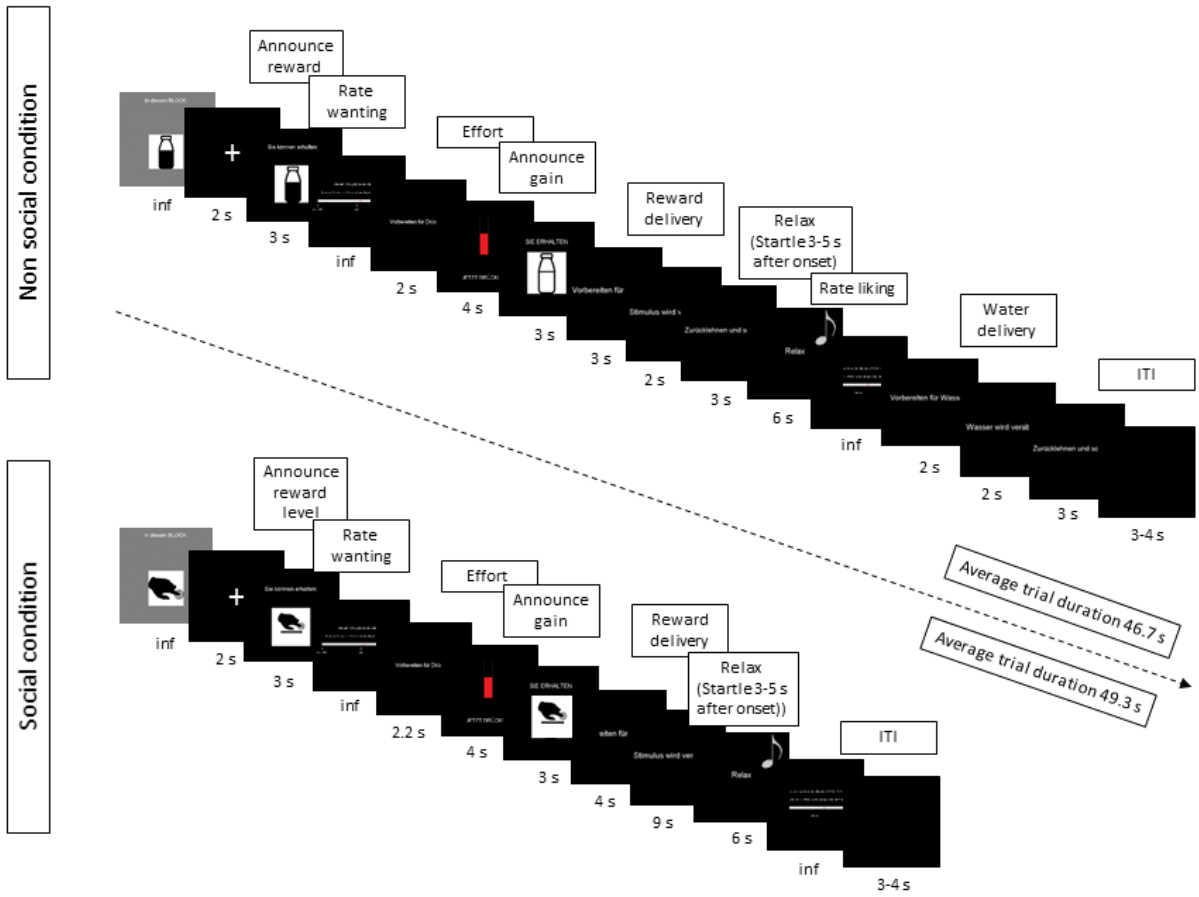

Fig. S1: Trial examples for the social and non-social conditions, including all screens.

Overview of all results

Subjective Ratings "wanting"

	F- values	p- values	Partial η²
Drug group*reward level	*F*(1, 41) = .047	*p* = .830	partial η² = .001
Reward level	*F*(1, 41) = .183	*p* < .001	partial η² = .005

Sign. Main Effect	Means	Standard Deviations
Reward level – above	M = 5,41	SD = 3.56
Reward level - below	M = -,68	SD = 4.01

Subjective Ratings "liking"

	F- values	p- values	Partial η²
Drug group*reward level	*F*(1, 41) = .047	*p* = .830	partial η² = .001
Reward level	*F*(1, 41) = .183	*p* < .001	partial η² = .005

Sign. Main Effect	Means	Standard Deviations
Reward level – above	M = 5,13	SD = 2.99
Reward level - below	M = -1,39	SD = 3.32

Subjective Ratings "effort" (Hand Dynamometer)

	F- values	p- values	Partial η²
Drug group*reward level	*F*(1, 41) = .047	*p* = .830	partial η² = .001
Reward level	*F*(1, 41) = .183	*p* < .001	partial η² = .005

Sign. Main Effect	Means	Standard Deviations
Reward level – above	M = 194,79	SD = 70.24
Reward level - below	M = 146,53	SD = 66.08

fEMG:

Anticipation Period - Zygomaticus major

Median split **by wanting:**

	F- values	**p- values**	**Partial η²**
Reward level	*F*(1, 41) = .039	*p* = .844	partial η² = .001
Time	*F*(2, 40) = .851	*p* = .431	partial η² = .021
Overall	*F*(2, 40) = .286	*p* = .752	partial η² = .007

Median split **by liking**:

	F- values	**p- values**	**Partial η²**
Reward level	*F*(1, 41) = .763	*p* = .388	partial η² = .019
Time	*F*(2, 40) = .751	*p* = .475	partial η² = .018
Overall	*F*(2, 40) = 1.328	*p* = .271	partial η² = .032

Median split **by effort:**

	F- values	**p- values**	**Partial η²**
Reward level	*F*(1, 41) = 2.866	*p* = .098	partial η² = .067
Time	*F*(2, 40) = .760	*p* = .471	partial η² = .019
Overall	*F*(2, 40) = 1.122	*p* = .331	partial η² = .027

Consumption Period - Zygomaticus Major

Median split **by wanting**

	F- values	**p- values**	**Partial η²**
Reward level	*F*(1, 41) = 1.524	*p* = .224	partial η² = .037
time	*F*(4, 37) = .662	*p* = .619	partial η² = .016
overall	*F*(4, 37) = .110	*p* = .979	partial η² = .003

Median split **by effort**

	F- values	**p- values**	**Partial η²**
Reward level	*F*(1, 41) = .915	*p* = .345	partial η² = .022
time	*F*(4, 37) = .571	*p* = .648	partial η² = .014
overall	*F*(4, 37) = .691	*p* = .599	partial η² = .017

Median split by liking > significant effect

	F- values	**p- values**	**Partial η²**
Reward level	*F(1, 41) = 5.749*	***p* = .021**	partial η² = .126
time	*F*(4, 37) = .555	*p* = .695	partial η² = .014
overall	*F*(4, 37) = .368	*p* = .831	partial η² = .009

Estimates

Measure: MEASURE_1

Drug_group	rewardlevel	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
Naltrexone	1	201,542	18,447	164,260	238,825
	2	223,245	19,805	183,217	263,272
Placebo	1	**236,804**	18,447	199,521	274,087
	2	**200,453**	19,805	160,426	240,480

Pairwise Comparisons

Measure: MEASURE_1

Drug_group	(I) rewardlevel	(J) rewardlevel	Mean Difference (I-J)	Std. Error	Sig.[b]	95% Confidence Interval for Difference[b]	
						Lower Bound	Upper Bound
Naltrexone	1	2	-21,702	17,121	,212	-56,305	12,900
	2	1	21,702	17,121	,212	-12,900	56,305
Placebo	1	2	36,351*	17,121	,040	1,749	70,953
	2	1	-36,351*	17,121	,040	-70,953	-1,749

Based on estimated marginal means

*. The mean difference is significant at the ,05 level.

b. Adjustment for multiple comparisons: Least Significant Difference (equivalent to no adjustments).

Multivariate Tests

Drug_group		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared
Naltrexone	Pillai's trace	,039	1,607[a]	1,000	40,000	,212	,039
	Wilks' lambda	,961	1,607[a]	1,000	40,000	,212	,039
	Hotelling's trace	,040	1,607[a]	1,000	40,000	,212	,039
	Roy's largest root	,040	1,607[a]	1,000	40,000	,212	,039
Placebo	Pillai's trace	,101	4,508[a]	1,000	40,000	,040	,101
	Wilks' lambda	,899	4,508[a]	1,000	40,000	,040	,101
	Hotelling's trace	,113	4,508[a]	1,000	40,000	,040	,101
	Roy's largest root	,113	4,508[a]	1,000	40,000	,040	,101

Each F tests the multivariate simple effects of rewardlevel within ech level combination of the other effects shown. These tests are based on the linearly independent pairwise comparisons among the estimated marginal means.

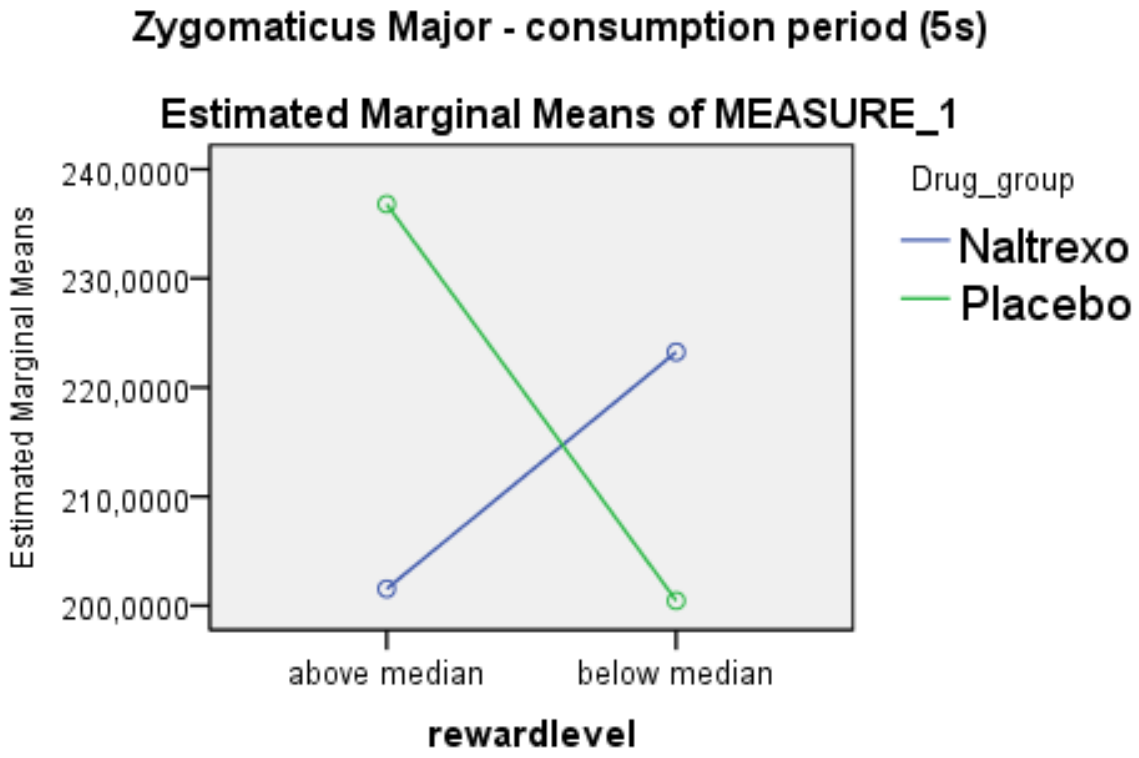

Fig. 5. significant effect within the placebo group. $F(1, 41) = 4.508$, $p < .040$, partial $\eta^2 = .101$. Above median ($M = 236.80$, $SD = 18.45$) and below median ($M = 200.453$, $SD = 19.81$) for the placebo group.

Anticipation Period - Corrugator Supercilii

Median split **by wanting**

	F- values	**p- values**	**Partial η²**
Reward level	*F*(1, 41) = .146	*p* = .704	partial η² = .004
time	*F*(2, 40) = .580	*p* = .562	partial η² = .014
overall	*F*(2, 40) = .169	*p* = .844	partial η² = .004

Median split **by liking**

	F- values	**p- values**	**Partial η²**
Reward level	*F*(1, 41) = .283	*p* = .589	partial η² = .007
time	*F*(2, 40) = .467	*p* = .628	partial η² = .012
overall	*F*(2, 40) = .094	*p* = .910	partial η² = .002

Median split **by effort**

	F- values	**p- values**	**Partial η²**
Reward level	*F*(1, 41) = .638	*p* = .429	partial η² = .016
time	*F*(2, 40) = .637	*p* = .532	partial η² = .016
overall	*F*(2, 40) = .045	*p* = .956	partial η² = .001

Consumption Period - Corrugator Supercilii

Median split **by wanting**

	F- values	**p- values**	**Partial η²**
Reward level	*F*(1, 41) = .001	*p* = .973	partial η² = .000
time	*F*(4, 37) = .713	*p* = .584	partial η² = .018
overall	*F*(4, 37) = 1.935	*p* = .107	partial η² = .046

Median split **by liking**

	F- values	**p- values**	**Partial η²**
Reward level	*F*(1, 41) = .510	*p* = .479	partial η² = .013
time	*F*(4, 37) = .740	*p* = .566	partial η² = .018
overall	*F*(4, 37) = 1.674	*p* = .159	partial η² = .040

Median split **by effort**

	F- values	**p- values**	**Partial η²**
Reward level	*F*(1, 41) = .245	*p* = .623	partial η² = .006
time	*F*(4, 37) = .674	*p* = .611	partial η² = .017
overall	*F*(4, 37) = 2.055	*p* = .089	partial η² = .049