



## Morphine reduced perceived anger from neutral and implicit emotional expressions



Guro E. Løseth<sup>a,\*</sup>, Marie Eikemo<sup>b,c</sup>, Peder Isager<sup>a</sup>, Jostein Holmgren<sup>a</sup>, Bruno Laeng<sup>a</sup>, Vigdis Vindenes<sup>d</sup>, Trine Hjørnevik<sup>b</sup>, Siri Leknes<sup>a</sup>

<sup>a</sup> Department of Psychology, University of Oslo, Norway

<sup>b</sup> Department of Diagnostic Physics, Division of Radiology and Nuclear Medicine, Oslo University Hospital, Norway

<sup>c</sup> Division of Mental Health and Addiction, Oslo University Hospital, Norway

<sup>d</sup> Department of Forensic Medicine, Oslo University Hospital, Norway

### ARTICLE INFO

#### Keywords:

Opioid  
 μ-opioid  
 Emotion perception  
 Emotion recognition  
 Morphine  
 Social cognition  
 Autism traits

### ABSTRACT

The μ-opioid system modulates responses to pain and psychosocial stress and mediates non-social and social reward. In humans, the μ-opioid agonist morphine can increase overt attention to the eye-region and visual exploration of faces with neutral expressions. However, little is known about how the human μ-opioid system influences sensitivity to and appraisal of subtle and explicit cues of social threats and reward. Here, we examined the effects of selective μ-opioid stimulation on perception of anger and happiness in faces with explicit, neutral or implicit emotion expressions. Sixty-three healthy adults (32 females) attended two sessions where they received either placebo or 10 mg per oral morphine in randomised order under double-blind conditions. Based on the known μ-opioid reduction of pain and discomfort, as well as reports suggesting that the non-specific partial agonist buprenorphine or the non-specific antagonist naltrexone affect appraisal of social emotional stimuli, we hypothesised that morphine would reduce threat sensitivity and enhance perception of happy facial expressions. While overall perception of others' happiness was unaffected by morphine treatment, morphine reduced perception of anger in stimuli with neutral and implicit expressions without affecting perception of explicit anger. This effect was statistically unrelated to gender, subjective drug effects, mood and autism trait measures. The finding that a low dose of μ-agonist reduced the propensity to perceive anger in photos with subtle facial expressions is consistent with the notion that μ-opioids mediate social confidence and reduce sensitivity to threat cues.

### 1. Introduction

All social animals need to navigate an environment rich in social cues. Recognizing others' emotional expressions and successfully interpreting their intentions is necessary for adaptive social interactions. Accordingly, the brain devotes a large proportion of neurons to the processing of important social stimuli, such as the face and eyes of others (Itier and Batty, 2009). Inattention to social cues, as in autism spectrum disorder, is associated with poor social functioning (Chevallier et al., 2012). However, heightened vigilance to social signals could also be maladaptive. For instance, people with social anxiety display heightened sensitivity to subtle threat cues such as masked facial expressions of anger (Mogg and Bradley, 2002).

The emotional and motivational state of the individual affects which cues take priority and receive the most attention. The endogenous opioid system modulates both emotional-motivational state and

responses to appetitive and aversive stimuli across species. Activation of the μ-opioid receptors (MOR) is known to reduce pain and distress (Hsu et al., 2013; Leknes and Tracey, 2008; Lutz and Kieffer, 2013; Løseth et al., 2014). In the absence of aversive cues, MOR activation increases motivation and positive affective responses to rewards (Berridge and Kringelbach, 2013; Løseth et al., 2014). Rodent research has shown that the MOR system is also central for resolving conflicts between rewards and threats, e.g. dampening pain to enable approach of a valuable reward (Dum and Herz, 1984; Fields, 2006). In the social domain, MOR drugs enhance rodents' reward from social interaction (Trezza et al., 2011; Vanderschuren et al., 1996) and facilitate social encounters by dampening the normally occurring motivation to first explore new surroundings (Vanderschuren et al., 1995a,b), which could be linked to dampened anxiety or sensitivity to environmental threat cues (Panksepp et al., 1985).

Less is known about the μ-opioid system's role in the modulation of

\* Corresponding author at: Department of Psychology, University of Oslo, Postbox 1094 Blindern, Forskningsveien 3A, 0317 Oslo, Norway.  
 E-mail address: [g.e.loseth@psykologi.uio.no](mailto:g.e.loseth@psykologi.uio.no) (G.E. Løseth).

reactions to social cues in humans. The limited available evidence from human research points to similar MOR modulation of social interest and vulnerability to threat. For instance, a previous report from our laboratory (Chelnokova et al., 2014) showed that motivation to view pictures of attractive faces with neutral expressions increased after treatment with the MOR agonist morphine compared to the opioid antagonist naltrexone. The two drugs also oppositely modulated time spent looking at the eye region as well as visual exploration of these faces as a whole, consistent with  $\mu$ -opioid enhancement of social interest (Chelnokova et al., 2016). Since morphine shows high affinity only to MORs, we interpret these bidirectional drug effects as primarily MOR-mediated. Naltrexone is an opioid antagonist, primarily at the  $\mu$ - and  $\kappa$ -opioid receptors (KORs). Another commonly used drug in the human literature, buprenorphine, is a partial MOR agonist and KOR antagonist; accordingly, several related findings in the human literature may result from a combination of effects on MOR and KOR. Interestingly, animal studies suggest that KOR activation typically inhibits reward and promotes aversive states, whereas blocking KOR can dampen anxiety (Lutz and Kieffer, 2013).

A series of psychopharmacological studies using buprenorphine have yielded results consistent with *a*) increased sensitivity to positive social cues and *b*) reduced perception of threatening cues. For instance, compared to placebo buprenorphine improved short-term spatial memory for happy faces (Syal et al., 2015), increased ratings of positivity in response to pictures with social content and decreased perception of social rejection during a simulated social rejection task (Bershad et al., 2016). In addition, buprenorphine attenuated physiological stress responses to a psychosocial stress task (Bershad et al., 2015), selectively impaired recognition of fearful facial expressions in one study (Ipser et al., 2013), and reduced initial visual attention to fearful facial expressions in another (Bershad et al., 2016). The observed reduction in sensitivity and attention towards fear cues aligns well with evidence from other human studies using the MOR and KOR antagonists naloxone and naltrexone (but see Wardle et al., 2016). Indeed, naloxone enhanced acquisition of conditioned fear in humans (Eippert et al., 2008), a finding recently replicated and extended to fear conditioning induced solely through observation (social threat learning; Haaker et al., 2017). Another recent study measured implicit facial mimicry to happy faces and interpreted results as an indication of lowered interest in positive social interaction (Meier et al., 2016).

While fearful facial expressions can communicate impending threats from the environment, angry facial expressions can act as a specific threat cue, i.e. indicating that an individual might become dangerous or violent. Happy facial expressions on the other hand signal potential for rewarding interaction. In fact, just looking at pictures of happy faces can be rewarding in itself (Spreckelmeyer et al., 2009). In the present study, we examine the effects of the preferential MOR agonist morphine on perception of explicit and implicit expressions of happiness and anger. A low dose of morphine (10 mg per oral) was chosen to mimic endogenous MOR activation with minimal subjective side effects (as in Chelnokova et al., 2014; Eikemo et al., 2016). We hypothesised that morphine would dampen perception of anger and increase perception of happiness in the faces of others. We also tested the competing hypothesis that morphine would improve detection of implicit facial expressions regardless of valence. This was based on our previous finding that morphine increased visual exploration of faces and time spent looking at the eye-region (Chelnokova et al., 2016). The peptide oxytocin, which also increases gaze to the eyes, is found to consistently improve emotion recognition (Leppanen et al., 2017). Indeed, we have previously found (Leknes et al., 2013) that intranasal oxytocin improved sensitivity to implicit expressions of anger and happiness in the same set of face stimuli used in the present study. Consistent with the finding that oxytocin improved emotion recognition the most in people with autistic traits (Bartz et al., 2010), Leknes et al. (2013) also reported that the greatest oxytocin-related improvement in emotion perception occurred in participants with a lower ability to perceive

subtle emotional cues in the placebo condition. Based on this, as well as mounting evidence indicating that opioid dysregulation underpins the blunted social reward associated with autism (Pellissier et al., 2017), we explored whether morphine would enhance emotion perception more in participants with higher autistic traits.

## 2. Methods and materials

### 2.1. Study design

The within-subject, double-blind design consisted of two sessions where participants received 10 mg per oral morphine or placebo in counterbalanced order before completing tasks assessing reward responses and emotion perception. The ‘emotion perception’ task was part of a larger study investigating effects of enhanced  $\mu$ -opioid system activation on various behavioural reward measures and BOLD signal activity measured with fMRI (data to be reported elsewhere). The emotion perception task was completed outside of the MR-scanner at ~135 min after ingestion of drug/placebo.

### 2.2. Participants

Sixty-three healthy adult participants (32 females, 31 males) aged 19–45 years (mean age 27, SD = 5) completed testing with morphine and placebo in separate sessions. Sixty-eight participants were recruited through flyers and online advertisement and underwent a phone-assisted screening interview prior to inclusion. Exclusion criteria were ongoing or self-reported history of major psychiatric illness including depression and drug- or alcohol use disorder; no history of or ongoing prolonged pain condition; no current use of medication (antihistamines and contraceptives exempt), and no multiple complex allergies. Other exclusion criteria were pregnancy, a history of prolonged opioid medication, single- or repeated use of any strong opioids the last two years, and use of drugs containing codeine or other mild opioids during the last four months. All participants had normal or corrected-to-normal vision. Data from five participants was excluded: One participant received placebo both sessions; four were not able to return for their second session. See Table 1 for characteristics of the final sample of 63 participants.

Self-report data revealed that 23 of the 32 female participants used hormonal contraceptives. Of the remainder of the female sample, six confirmed that both test sessions fell within the same phase of the hormonal cycle; three were unable to estimate number of days since their last ovulation.

Self-reported recreational drug and alcohol was recorded as part of the pre-test screening using selected items from AUDIT and DUDIT (Alcohol/Drug Use Disorders Identification Test) (Berman et al., 2005; Saunders et al., 1993). See Table 2 for overview. Participants were instructed not to consume alcohol for 24 h before testing, to abstain from caffeine and tobacco for a minimum of one hour before the test session commenced, and advised not to drive or operate heavy machinery for six hours after drug administration. All participants were asked to eat a few hours or less before testing, and were offered a light meal or snack if they reported being hungry upon arrival.

Table 1  
Participant characteristics.<sup>a</sup>

	total n = 63	female n = 32	male n = 31
Age	27 ± 5.0	27 ± 3.7	27 ± 6.2
Weight (kg)	74 ± 11.7	66 ± 7.3	81 ± 10.5
Height (cm)	176 ± 9.1	170 ± 6.8	182 ± 6.4
BMI	24 ± 2.8	23 ± 2.5	24 ± 2.9

<sup>a</sup> All values are means ± standard deviation.

Download English Version:

<https://daneshyari.com/en/article/6817670>

Download Persian Version:

<https://daneshyari.com/article/6817670>

[Daneshyari.com](https://daneshyari.com)