

Forskerlinjen

Project description

Are the stress-relieving effects of acute social support mediated by the human mu-opioid system?

Introduction:

This psychopharmacological project uses an opioid antagonist drug (naltrexone) or placebo and a lab-based stress task together with social support from a friend to test the hypothesis that benefiting from social support relies on the brain's endogenous opioid system.

Background:

The proposal is motivated by two findings. **First**, epidemiological studies have long connected vulnerability to addiction with social stressors and a poor social support network (Stone et al., 2012). More recently, clinical studies highlight a similar role of distress in driving opioid misuse in chronic pain patients (Martel et al., 2014; McHugh et al., 2016). **Second**, several lines of evidence from non-human animals link social distress with opioid addiction at the level of brain mechanisms (Burkett and Young, 2012). Social support, like opioid drugs, activates μ -opioid receptors (MORs) (Vanderschuren et al., 1995), and relies on MOR mechanisms to produce relief of both physical pain (D'Amato and Pavone, 2012) and social distress (Machin and Dunbar, 2011). MOR knockout mice reveal that μ -opioid signalling is necessary for both social bonding (Moles et al., 2004) and drug reward (Charbogne et al., 2014).

After receiving a non-sedative dose of an opioid drug, animals that had been socially isolated sought out less social support (Machin and Dunbar, 2011; Løseth et al., 2014), consistent with the notion that addictive drugs can replace the need for social contact. In other words, opioid drugs could lead to addiction because they act on – or hijack – the powerful mechanisms that ensure lasting social bonds (Nelson and Panksepp, 1998). Surprisingly however, the hypothesis that opioid drugs relieve distress by 'hijacking' brain pathways intended to support social bonds (Nelson and Panksepp, 1998) has never been tested in humans.

Research questions:

Does pharmacological blockade of endogenous opioid receptors inhibit stress relief from social support in healthy humans?

Objectives and method:

What is the goal of the project? The goal is to test the effects of pharmacological opioid blockade on benefits conferred by speaking with a friend after stress induction.

Which statistical methods to use as well as software: Mixed models using R

Student assignments:

Contributing to data collection in the lab. Measures: ratings of affective state, heart rate and heart rate variability, cortisol levels, possibility for fMRI or other physiological lab data.

Additional behavioural task measures include fear induced by watching scary film clips together or alone, see e.g. (Tedeschi et al., 2021).

About the research environment:

Who collaborates on the project? Leknes Affective Brain lab (LABlab) members, especially project leader group: Marie Eikemo, Guro Løseth, Siri Leknes

Frequency of professional meetings / lab meetings. LABlab holds weekly lab meetings and organises an international virtual seminar series.

Supervision:

Who will act as main and assistant supervisor? Main: Siri Leknes, co-supervisor: Guro Løseth

Structure and focus in the supervision. Biweekly supervisory meetings. Hands-on supervision during data collection and data analysis.

Ethical approvals and data:

Describe the data sources and whether the data is available as of today. Data will be collected. Final N to be determined based on power analysis simulations and/or Bayesian stopping rule; minimum effect size of interest is estimated to $d=0.3$.

Describe whether the ethical approvals are available. The project is approved by the Regional Ethics Committee.

Tentative article:

Are the stress-relieving effects of acute social support mediated by the human mu-opioid system?

Contact:

Siri Leknes siri.leknes@psykologi.uio.no

References:

Burkett JP, Young LJ (2012) The behavioral, anatomical and pharmacological parallels between social attachment, love and addiction. *Psychopharmacology (Berl)* 224:1–26.

Charbogne P, Kieffer BL, Befort K (2014) 15 years of genetic approaches in vivo for addiction research: Opioid receptor and peptide gene knockout in mouse models of drug abuse. *Neuropharmacology* 76 Pt B:204–217.

D'Amato F, Pavone F (2012) Modulation of nociception by social factors in rodents: contribution of the opioid system. *Psychopharmacology (Berl)* 224:189–200.

Løseth GE, Ellingsen D-M, Leknes S (2014) State-dependent μ -opioid Modulation of Social Motivation – a model. *Front Behav Neurosci* 8.

Machin AJ, Dunbar RIM (2011) The brain opioid theory of social attachment: a review of the evidence. *Behaviour* 148:985–1025.

- Martel MO, Dolman AJ, Edwards RR, Jamison RN, Wasan AD (2014) The association between negative affect and prescription opioid misuse in patients with chronic pain: The mediating role of opioid craving. *The Journal of Pain* 15:10.1016/j.jpain.2013.09.014.
- McHugh RK, Weiss RD, Cornelius M, Martel MO, Jamison RN, Edwards RR (2016) Distress Intolerance and Prescription Opioid Misuse among Patients with Chronic Pain. *The Journal of Pain* 17:806–814.
- Moles A, Kieffer BL, D'Amato FR (2004) Deficit in attachment behavior in mice lacking the mu-opioid receptor gene. *Science* 304:1983–1986.
- Nelson EE, Panksepp J (1998) Brain substrates of infant-mother attachment: contributions of opioids, oxytocin, and norepinephrine. *Neurosci Biobehav Rev* 22:437–452.
- Stone AL, Becker LG, Huber AM, Catalano RF (2012) Review of risk and protective factors of substance use and problem use in emerging adulthood. *Addict Behav*.
- Tedeschi E, Armand S, Buyalskaya A, Silston B, Mobbs D (2021) Fear in groups: Increasing group size reduces perceptions of danger. *Emotion* 21:1499–1510.
- Vanderschuren LJ, Stein EA, Wiegant VM, Van Ree JM (1995) Social play alters regional brain opioid receptor binding in juvenile rats. *Brain Res* 680:148–156.