Impaired empathy and physiological responses to social exclusion in chronic opioid users

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Introduction

- Opioid use disorder (OUD) is a rising public health concern worldwide[1]
- Social functioning may be impaired in OUD via changes to the endogenous opioid system. This could be due to factors preceding addiction (e.g. childhood trauma), and following addiction (increased social ostracism and marginalisation, and downregulation of opioid receptors)
- Impairments in empathy has been reported in OUD, particularly to 'emotional empathy' (the ability to vicariously experience others' emotional states)[2,3].
- There is also a heightened sensitivity to pain following chronic opioid use[4,5], and due to overlapping neural mechanisms[6] there may also be a heightened sensitivity to social pain

Aims

Aim 1: To assess whether emotional and cognitive empathy are affected by acute opioid intoxication in individuals with OUD.

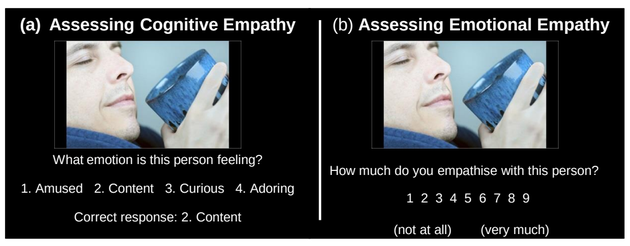
Aim 2: To assess whether there is a hyperalgesia to social exclusion ('social pain') in individuals with OUD who are not currently intoxicated, and whether this is alleviated by acute opioid intoxication.

Methods

Individuals on opioid substitution medication (OSM) were recruited into two groups:
1.'Intoxicated' users (taken OSM <4hrs), n=20
2.'Withdrawn' users (taken OSM >12hrs), n=20
3.Opioid naïve controls, n=24

To measure impaired empathy (hypothesis 1):

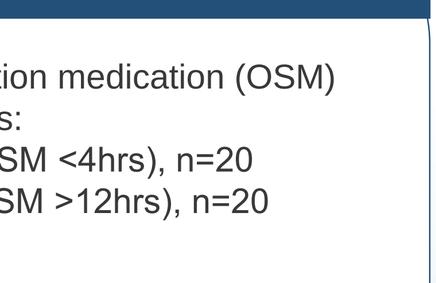
1. Multifaceted Empathy Test (MET):



2. Interpersonal Reactivity Index (IRI) (trait empathy)

To measure impaired responses to social exclusion (hypothesis 2):

The Cyberball Game – a computer task used to simulate social exclusion



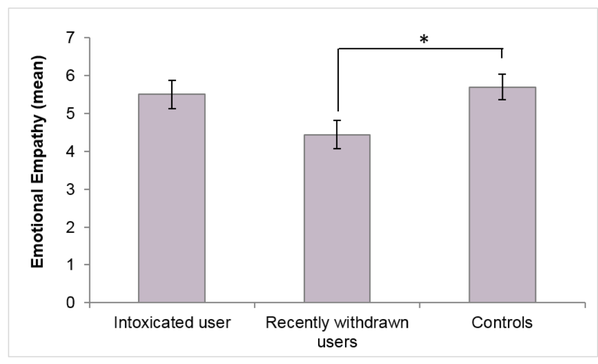
1 x inclusion game
2 x exclusion game

Outcome measures: Mood and psychological needs, salivary cortisol and heart rate (7 x over 2hrs).

Results

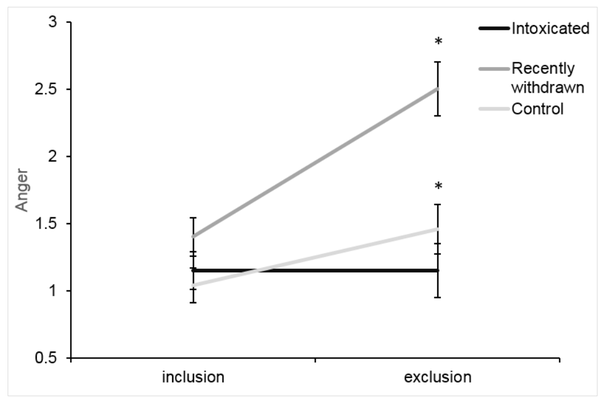
Hypothesis 1: Impaired empathy

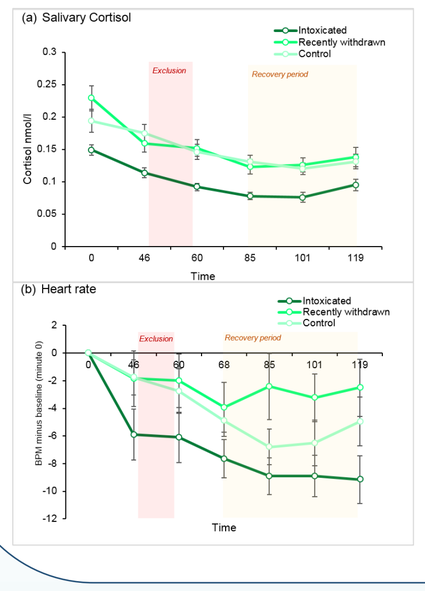
- MET: Emotional empathy was significantly lower in the Withdrawn group compared with Controls ($t(42)=2.64$, $p=.048$, $\eta^2=.14$)
- MET: Cognitive empathy did not differ between the three groups ($F(2,56)=1.76$, $p=.182$, $\eta^2=.04$)
- IRI: No group differences on emotional or cognitive trait empathy subscales



Hypothesis 2: Dysfunctional responses to social exclusion

- Significantly greater rates of anger following exclusion in the Withdrawn group ($p<.001$) and Controls ($p<.001$), whilst anger did not change in the Intoxicated group ($p=.561$)
- Significant reductions in mood, self-esteem, control and meaningful existence after exclusion, but no difference between the groups.





- Latent Growth Curve Models (LGCM) indicated lower cortisol responses at baseline and throughout social exclusion and recovery in the Intoxicated users ($b=-0.07$, $SE=0.03$, $p=.016$)
- LGCM's indicated lower heart rate at baseline for Intoxicated group ($b=-4.77$, $SE=2.17$, $p=.028$),
- Also there was less change in heart-rate over social exclusion and the recovery period.

Conclusions

- Impaired emotional empathy in withdrawn users could be due to increased rates of distress, where previous research has indicated that when individuals are dealing with their own distress they are less able to exert empathy[7]
- Crucially, this also highlighted that acutely intoxicated opioid users show intact emotional empathy compared to healthy controls.
- Blunted subjective anger in response to stress and lower cortisol and heart rate was observed in intoxicated users, partially supporting the notion that opioids could cause hyperalgesia to social pain.

Greater anger with impaired empathy suggests an overall impairment in both understanding and expressing one's own emotions in individuals who have chronically used opioids but are not acutely under the influence of them.

This could indicate that opioids are used to alleviate difficult emotional states such as anger, and heighten users' ability to tolerate social exclusion. As those with OUD frequently experience social ostracism and marginalisation, this could contribute to the use of opioids to cope with emotional distress.

References

[1] United Nations of Office on Drugs and Crime. World Drug Report 2018. 2018. [2] Tomei A, Besson J, Reber N, Rougemont-Bücking A, Grivel J. Personal distress and empathic concern in methadone-maintained patients. Journal of Substance Use. 2017;22(1):37-41. [3] Stange K, Krüger M, Janke E, Lichtinghagen R, Bleich S, Hillemacher T, et al. Positive association of personal distress with testosterone in opiate-addicted patients. Journal of Addictive Diseases. 2017:1-8. [4] Pud D, Cohen D, Lawental E, Eisenberg E. Opioids and abnormal pain perception: New evidence from a study of chronic opioid addicts and healthy subjects. Drug and alcohol dependence. 2006;82(3):218-23. [5] Higgins C, Smith B, Matthews K. Evidence of opioid-induced hyperalgesia in clinical populations after chronic opioid exposure: a systematic review and meta-analysis. British Journal of Anaesthesia. 2018. [6] Eisenberger NI. Social pain and the brain: controversies, questions, and where to go from here. Annu Rev Psychol. 2015;66:601-29. [7] Tangney JP, Stuewig J, Mashek DJ. Moral emotions and moral behavior. Annu Rev Psychol. 2007;58:345-72.

Declaration of Conflicts of Interests: CJA Morgan has consulted for Janssen, GlaxoSmithKline and Beckley canopy therapeutics. All other authors report no biomedical financial interests or potential conflicts of interest.