ENDOGENOUS OPIOID RELEASE IN PATHOLOGICAL GAMBLERS AFTER AN ORAL AMPHETAMINE CHALLENGE: A [^{11}C] CARFENTANIL PET STUDY

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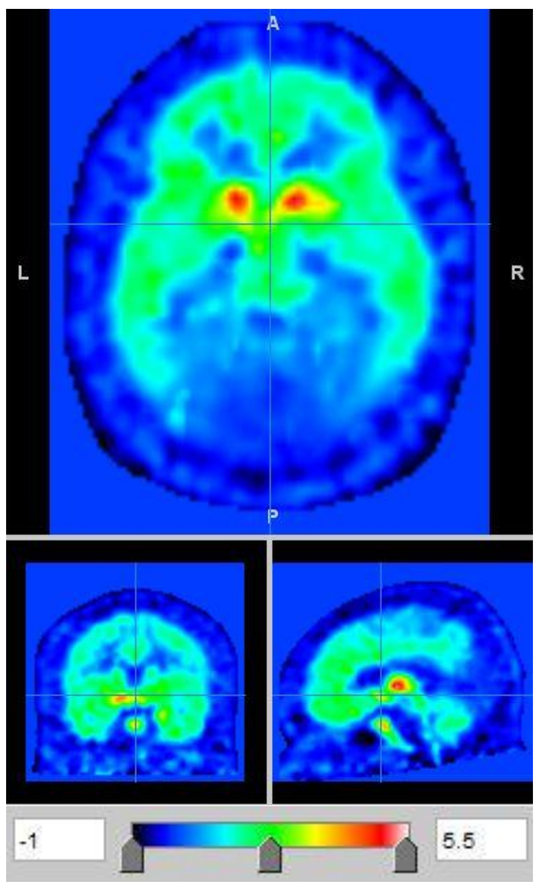
BACKGROUND

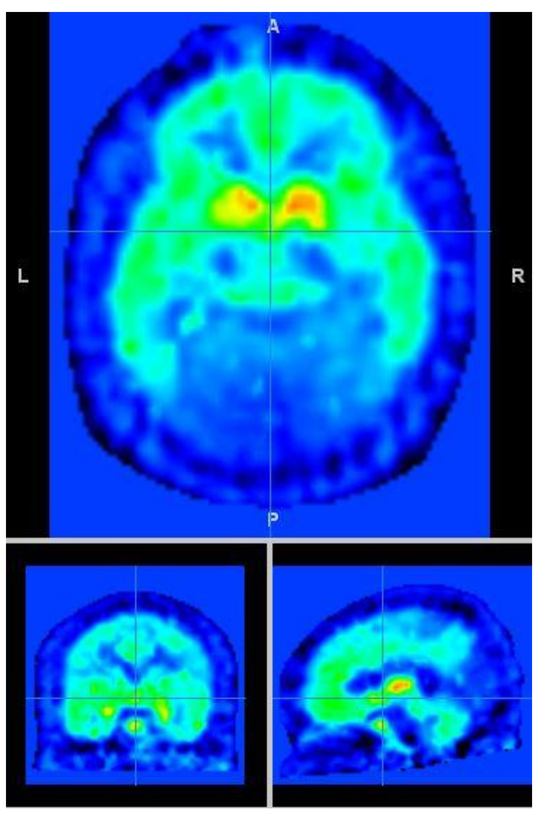
Gambling is a widespread behaviour that around 70% of the British population engage in at least occasionally. In some individuals, gambling spirals out of control and takes on the features of an addiction- **pathological gambling**. This condition has an **estimated prevalence of 0.5-3%** in Europe (Wardle, Sproston et al. 2007). The **opioid system** is involved in various aspects of human behaviour- pain, impulsivity, reward and **addiction**. Previous PET studies have shown **increased mu opioid receptor (MOR) availability** in alcohol-, cocaine- and opiate addiction (Williams, Daglish et al. 2007). Consistent with higher opioid levels is that **opiate antagonists**, e.g. naltrexone, nalmefene, are effective in treating addictive behaviour, including pathological gambling (PG). **[^{11}C]carfentanil** is a highly selective MOR agonist PET radioligand, which can be used to image MOR levels as well as the brain's release of endogenous opioids before and after administration of an oral endorphin releasing dose of amphetamine (Colasanti, Searle et al. 2012).

HYPOTHESES

Pathological gamblers (PG) will have:

a) higher baseline MOR availability and
b) blunted endogenous opioid release after an oral amphetamine challenge compared with healthy volunteers (HV).





Distribution of [^{11}C]carfentanil binding pre- and post amphetamine

METHODS

15 male HV, mean age 34.2, 2 smokers and **14 male PG**, mean age 33.9, 3 smokers underwent **2 [^{11}C]carfentanil PET scans**, one before and one after an **oral amphetamine challenge (0.5mg/kg)**. We followed our previous PET protocol (Colasanti, Searle et al. 2012).

Outcome parameter: ΔBP_{ND}= (BP_{ND} pre-amph – BP_{ND} post-amph)/BP_{ND} pre-amph

Regions of interest: caudate, putamen, thalamus, cerebellum, frontal lobe, nucleus accumbens, anterior cingulate, amygdala and insula cortices

Subjective responses to the amphetamine administration were measured using the simplified version of the **amphetamine interview self-rated scale (**SAIRS; **euphoria**, restlessness, alertness, anxiety)- visual analogue scale ranging from 0 (least ever felt) to 10 (most ever felt).

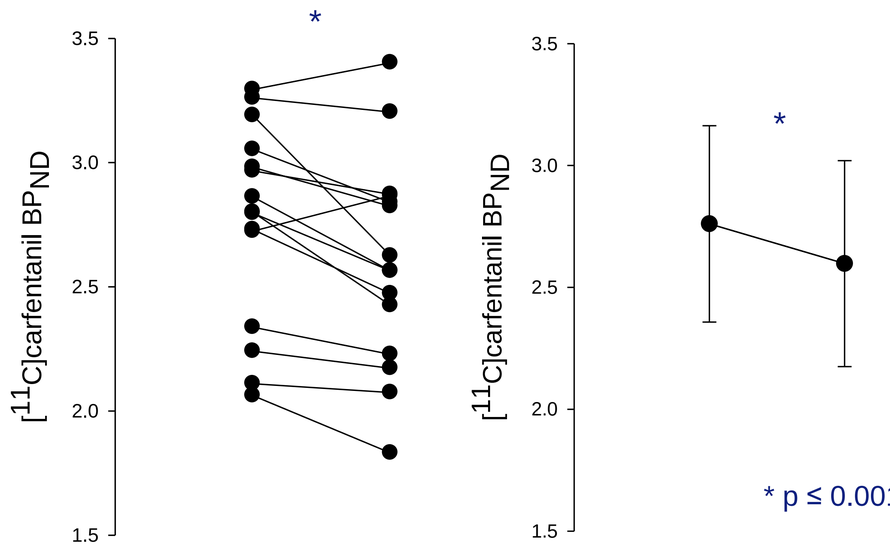
RESULTS

There were **no differences in baseline** availability of mu opioid receptors.

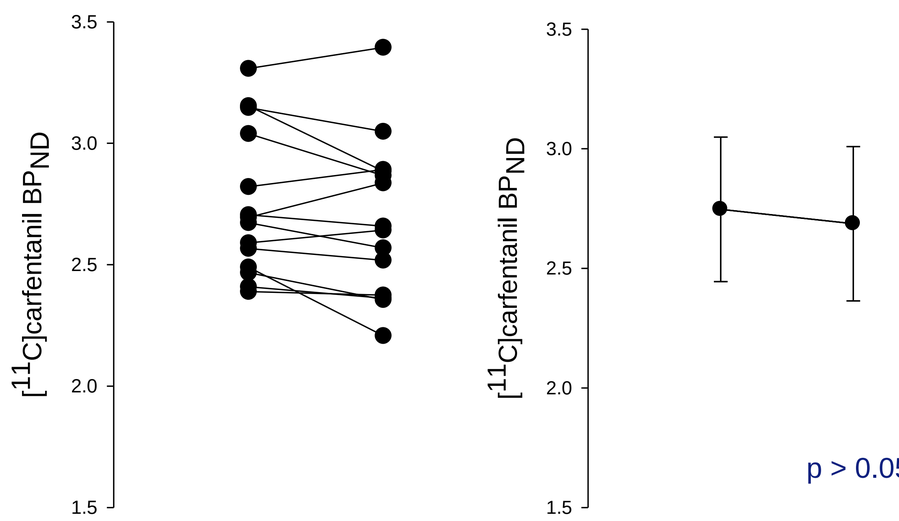
HV: significant reduction in [^{11}C]carfentanil binding after amphetamine challenge in
8/9 ROI (caudate, putamen, thalamus, cerebellum, frontal lobe, nucleus accumens, anterior cingulate, and insula cortices)
$\%\Delta BP_{ND}$ decrease of min 5%, **no increase**.

PG: significant reduction in [^{11}C]carfentanil binding after amphetamine challenge in
2/9 ROI (putamen, thalamus)
$\%\Delta BP_{ND}$ decrease of max 2.6%, **increase in 5/9 ROI** (caudate, cerebellum, frontal lobe, anterior cingulate and insula cortices).

Subjective responses: limited,
HV: mean change in euphoria scores +1.2 ± 1.42, max change +3
PG: mean change in euphoria scores +1.1 ± 0.95, max change +3
No correlations between changes in **euphoria scores** and regional percentage **[^{11}C]carfentanil binding**.



HV: Nucleus accumbens; left panel- individual [^{11}C]carfentanil binding pre- and post- amphetamine, right panel- mean and SD of [^{11}C]carfentanil binding



PG: Nucleus accumbens; left panel- individual [^{11}C]carfentanil binding pre- and post- amphetamine, right panel- mean and SD of [^{11}C]carfentanil binding

CONCLUSIONS

Whilst **no higher baseline MOR availability was evident in PG** compared with HV, following the amphetamine challenge, a **smaller increase in endogenous opioid levels was detected in PG** compared with HV. This blunted endogenous opioid release suggests **opioid dysregulation in PG**. Our PET protocol is able to detect changes in [^{11}C]carfentanil binding without participants experiencing an adverse 'high', evidenced in the lack of significant euphoria score changes. It provides a robust method to probe the opioid system in the living human brain.

ACKNOWLEDGEMENT

This study is funded by the Medical Research Council.

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