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Just Gambling? Ethical Challenges Pertaining to Gambling Provision, Policy and Research

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Presentation

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The Effect of Regular Naltrexone Dosing on Disordered Gamblers: An Examination of Neural Activation, Gambling Urges, and Gambling Behaviour

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Disclaimer

- The views expressed in this presentation are my own and do not represent the views of the Alberta Gambling Research Institute, the University of Lethbridge, my co-investigators or their institutions.
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Gambling Disorder

- Disordered Gambling is a **psychiatric disorder**.
- Substance Use Disorder under the **'Behavioral Addiction'** sub-category.
- Similar cognitive, neurological, genetic, and behavioural symptoms and correlates as **substance dependence**.

Gambling Neurobiology

- Two somewhat **contradictory phenomena** (i.e., sensitivity and insensitivity) to gambling.
- Disordered gamblers are more likely to experience **greater electrophysiological responses to positive outcomes.**
- They are **more sensitive to gambling related cues** (e.g., stimuli associated with near-misses).
- Also more likely to engage in risky gambling **after they lose.**

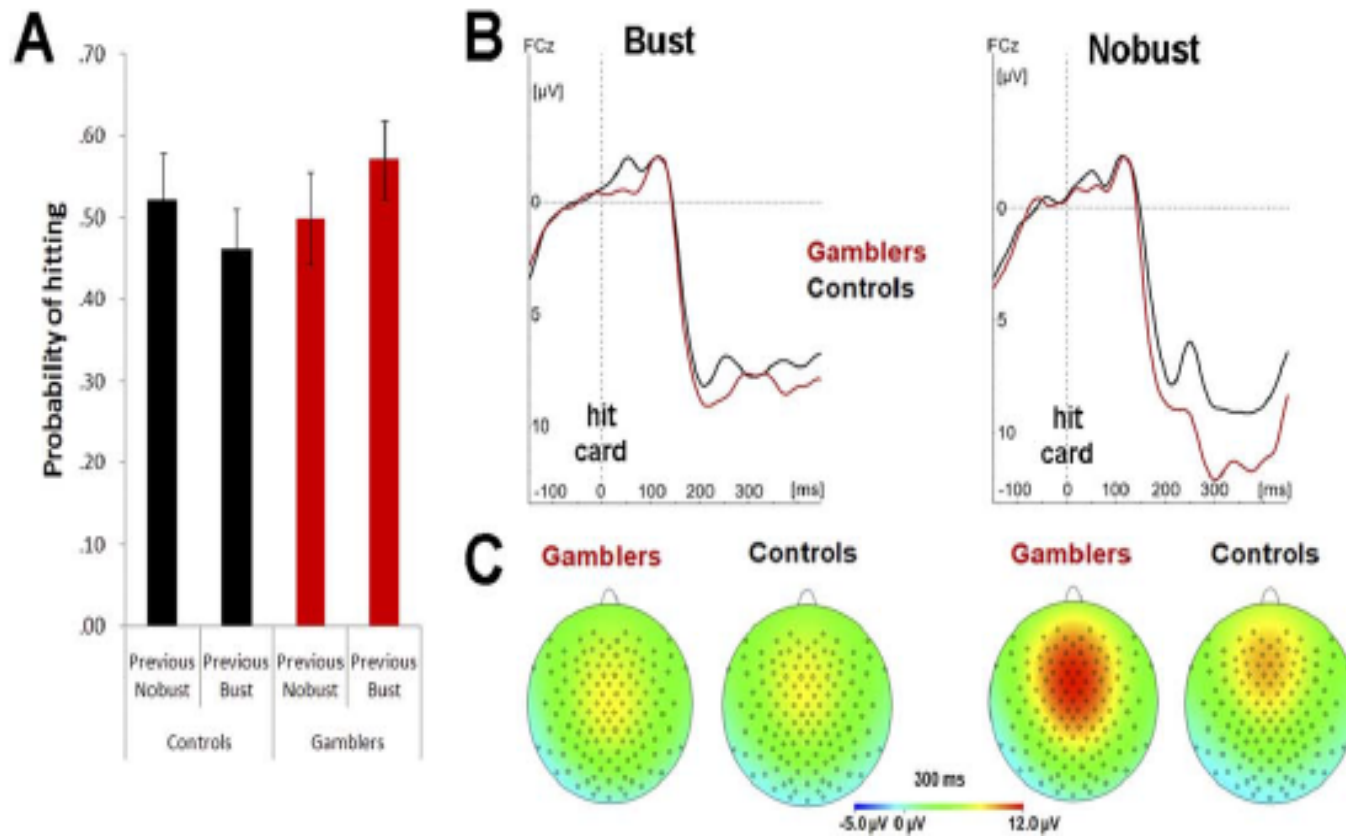
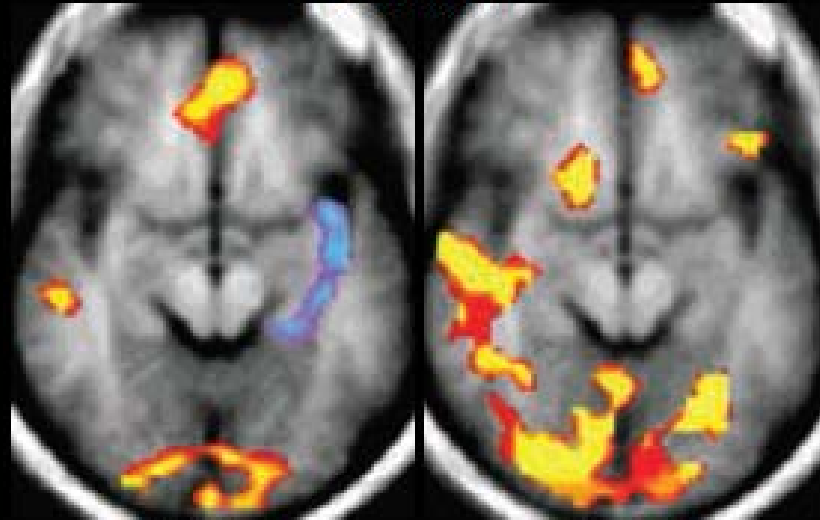


Figure 1. Behavior and electrophysiological responses of problem gamblers (gamblers) and normal control participants (controls) in a Black Jack task. **(A)** Probability of hitting (taking another card) at a point score of 16 after a previous “bust” or “no-bust” trial for the two groups. **(B)** Event-related brain potential responses from electrode FCz for hit trials at a point score of 16, which led to either a bust or no-bust. Time 0 represents the time at which the hit card was presented. **(C)** Topography of the scalp-recorded activity at 300 ms after presentation of the hit card for the two groups (gamblers and control participants) and the two outcomes (Bust and No-bust).

Gambling Neurobiology

- However, disordered gamblers are **less likely to activate brain regions** to gambling images, especially brain regions associated with **processing emotion**.
- Similar to **hypofrontality exhibited by substance users**.
- Suggesting a **conditioning and biological predisposition or consequence** to or from gambling.

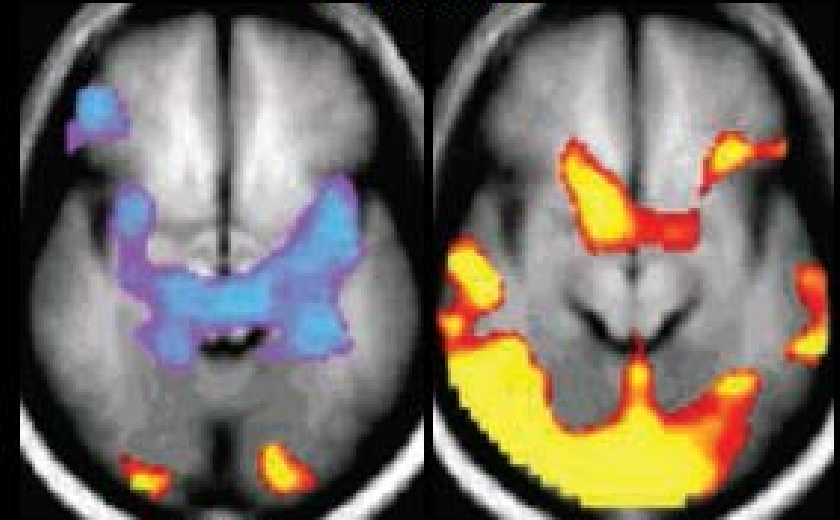
COCAINE



Addict

Control

GAMBLING



Addict

Control

Hooked. Brains of pathological gamblers watching a gambling video resemble those of cocaine addicts watching a cocaine video, with relatively less activation in regions implicated in judgment and motivation. Differences may reflect the toxic effects of cocaine exposure.

Why Pharmacology?

- Typically out-patient gambling clients **attend only a few sessions** and leave treatment early before recovering.
- Many clients often find counselling **difficult**. Some refuse to go.
- Pharmacological treatments offer the possibility of providing a **quick (1 hour to 13 hours) reduction** in gambling urge/craving-like symptoms.

Naltrexone

- Naltrexone is used as a treatment for **alcohol dependence** and **opioid dependence**.
- **Reduces cravings and pleasurable effects.**
- **Blocks** opioid receptor signals.
- Possibly modulates **dopamine** in the **mesolimbic** pathway.
- Hypothesis: gambling operates in a **similar** way to alcohol and opioids.

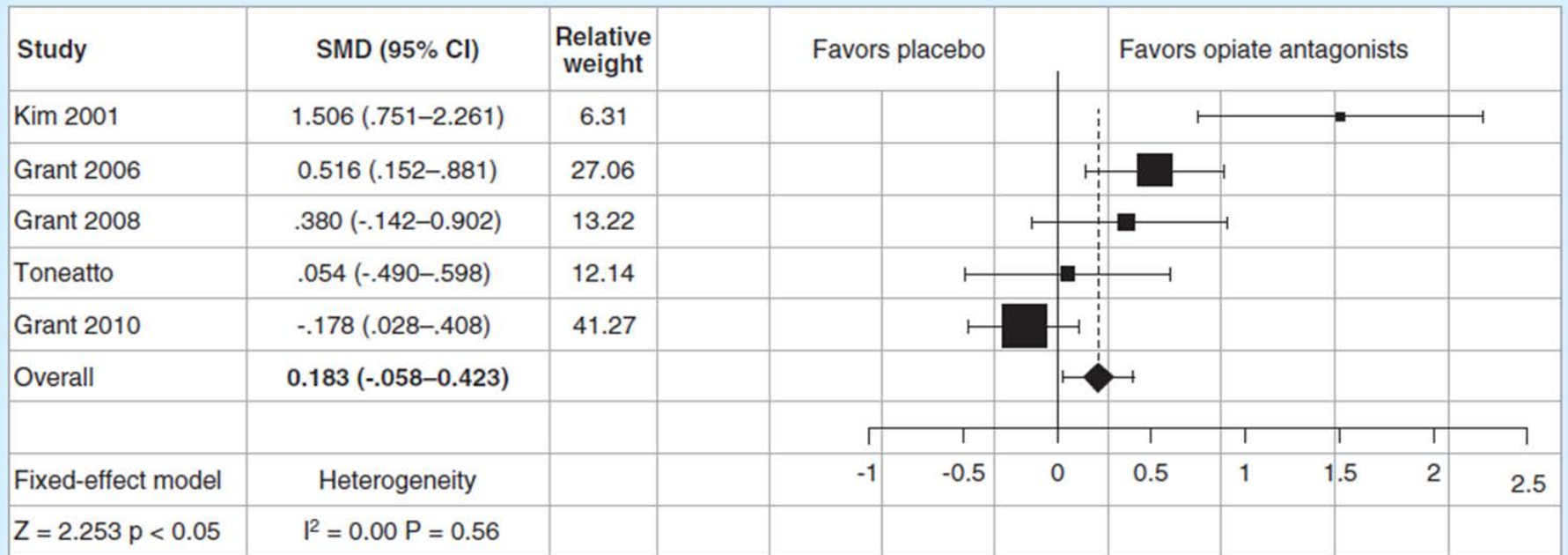


Figure 2. Opiate antagonist forest plot.

Source: Bartley & Bloch (2014).

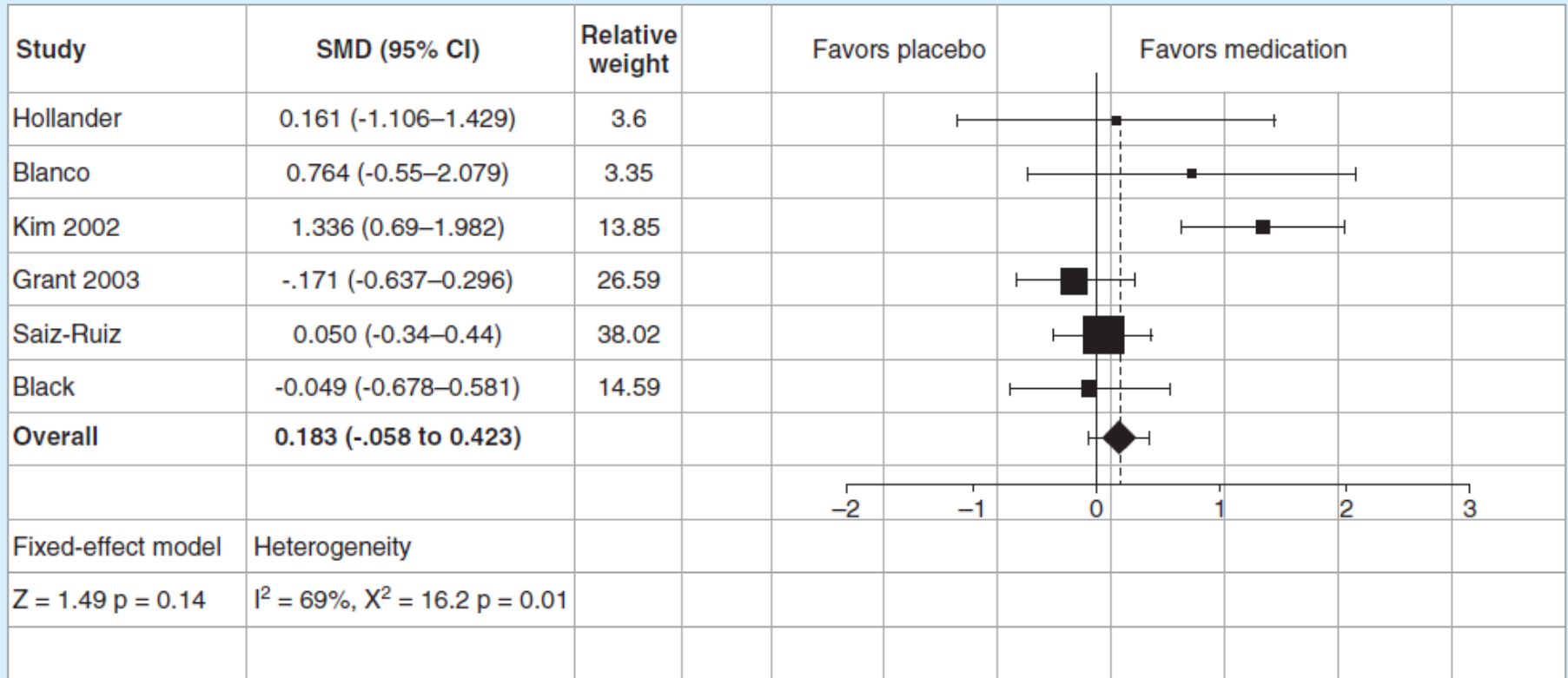


Figure 5. Antidepressant forest plot.

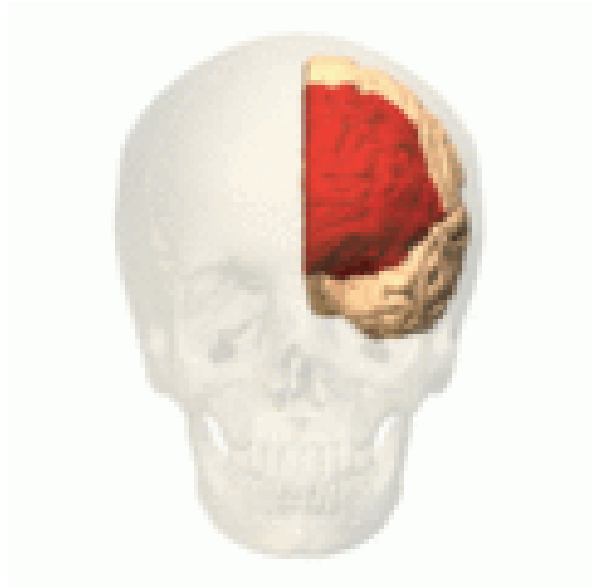
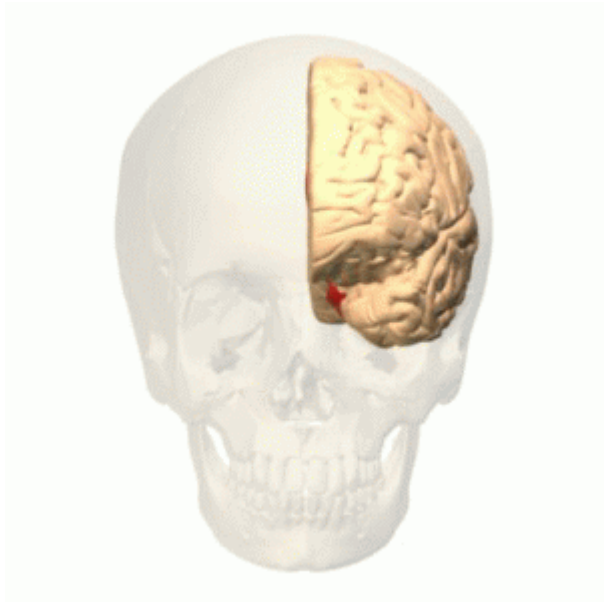
Source: Bartley & Bloch (2014).

Naltrexone Issues

- Naltrexone is **unsuitable** for those with **poor liver function** or are **using opioid-based medication** or illicit drugs.
- Therapeutic effects appear **dose- and treatment duration-related** (i.e., approximately 100/mg per day for 12 weeks).
- **Non-response issues.**
- Significant study effect **heterogeneity.**

Naltrexone-Imaging Study

- 55 Disordered Gamblers will receive 8-12 weeks of daily Naltrexone dosing.
- Assuming a 40% response rate (i.e., 1-month abstinence), and a large treatment effect-size, we expect to obtain **22 responders**.
- Participate in some form of regular **gambling counselling and support**.
- Test **pre- and post-treatment**.
- Changes in **gambling** and also **brain function**.
- Compare **responders vs. non-responders**.



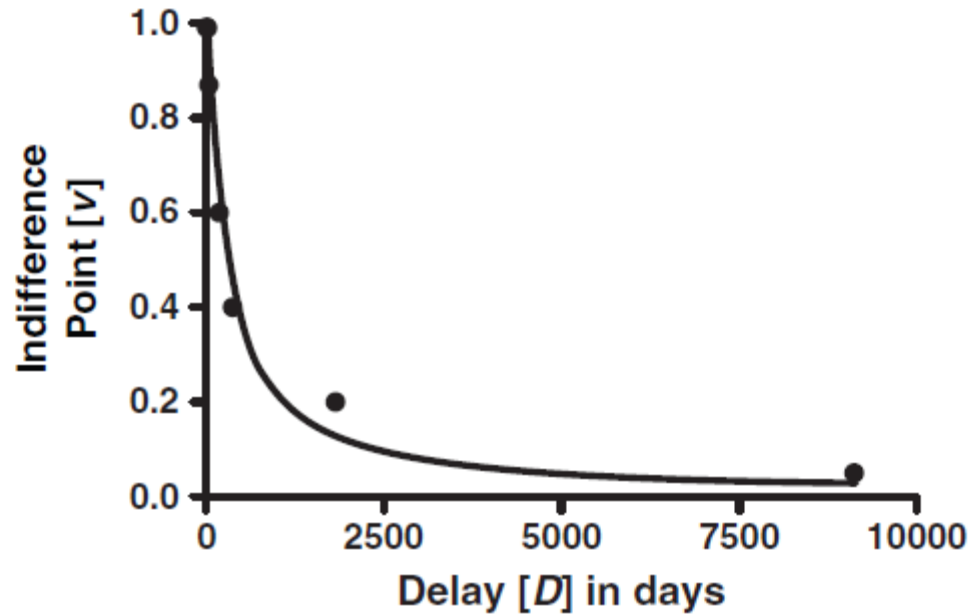
fMRI

- Our team are currently **scanning** gambling disordered people **pre-** and **post-treatment**.
- Measures include delay-discounting (**impulsivity**), stroop (**inhibition**), and gambling/scenic images (**craving/urge**).
- Resting state period.

Delay Discounting

- Hypothetical **choice** between a smaller amount of **money** (or any commodity) **now** and a larger amount of money (or any commodity) **later** (e.g., \$54 today or \$55 in one day).
- Typically, the delayed **alternative and magnitude of money is systematically varied** to achieve a curve of indifference points.
- Measure of **Impulsive choice**.

Fig. 3 Represents Mazur's (1987) hyperbolic delay discounting function. Solid dots represent estimated indifference points at each delay and the solid line represents the best fitting curve to those points



Source: Bickel et al. (2010).

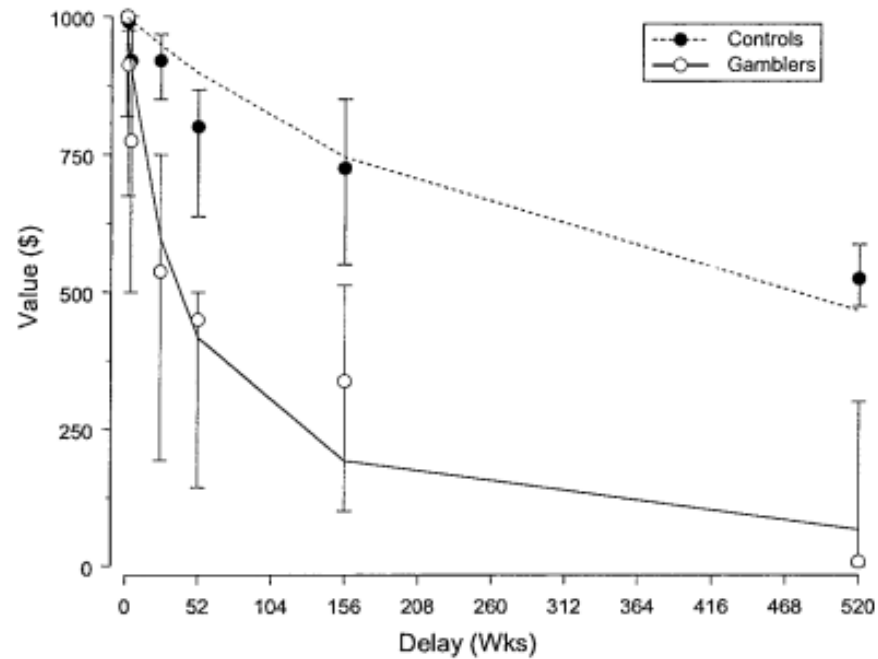


Figure 1. Aggregate indifference curves for gamblers and control participants. Data points show medians of the individual indifference points, and the error bars show the interquartile range of the individual indifference points at each of the seven delays. The solid reference line shows the best fit line for participants who gamble, and the dashed reference line shows the best fit line for control participants.

Source: Dixon et al. (2003).

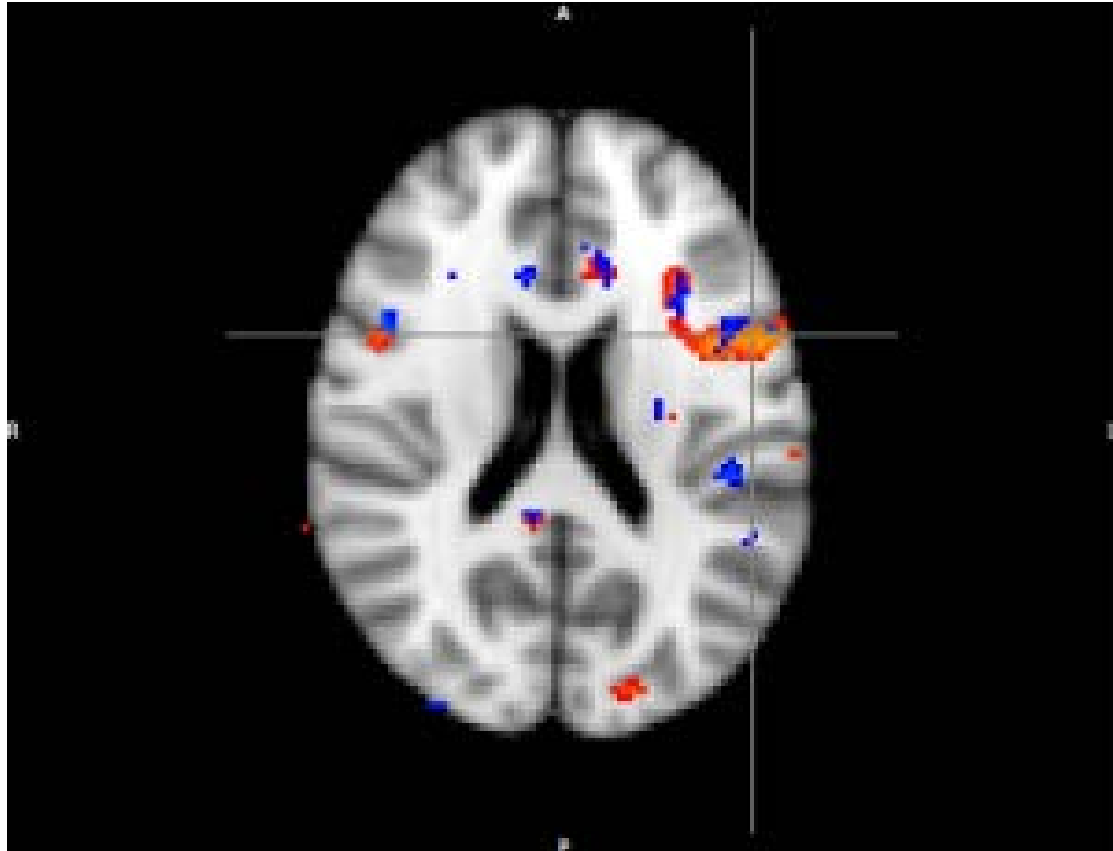
Results (so far)

- **N= 17 subjects;**
- 53 years,
- Female 47%,
- Length of Gambling Problem 18 years,
- Primarily EGM players,
- Time gambling 20 hours (two-weeks),
- Spend \$4105 (two weeks),
- DSM-V 7 'moderate'

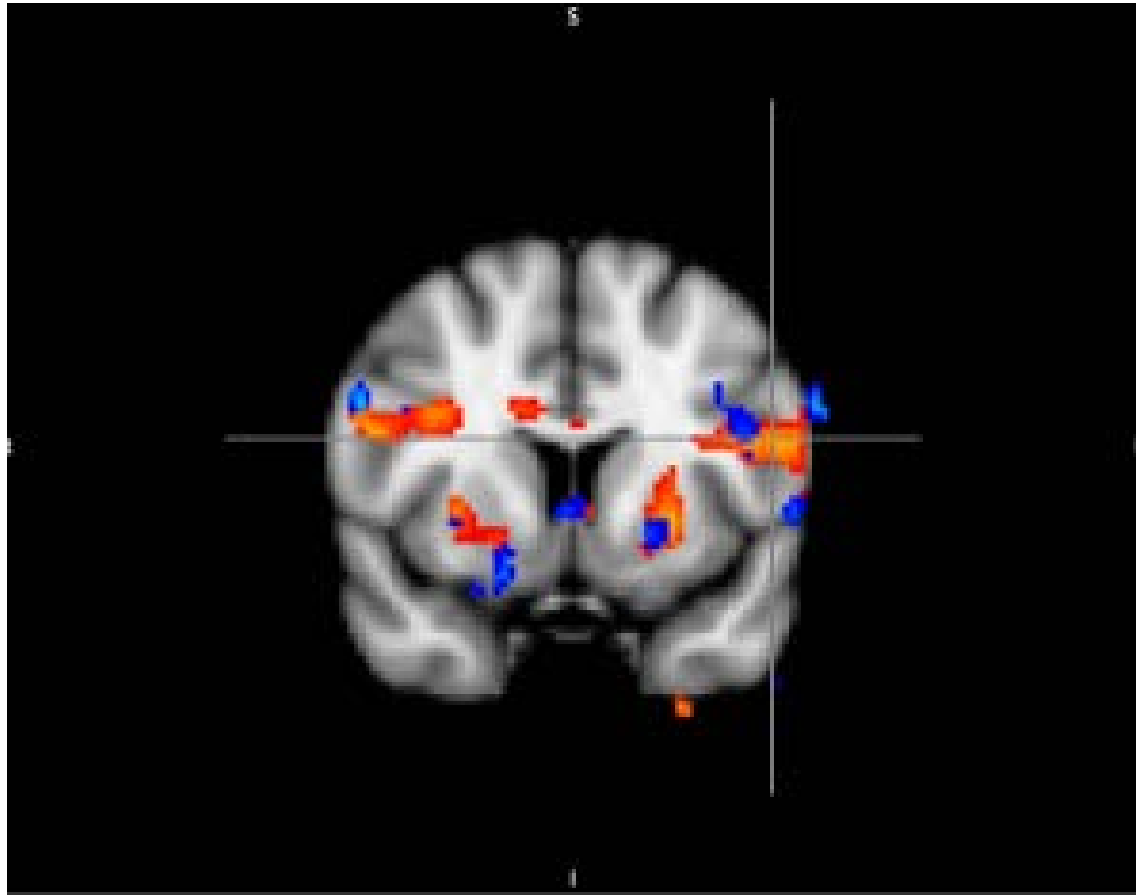
Results

- One subject entered the dosing stage.
- Dosage: **25mg per day.**
- Baseline Gambling Urges Score (Raylu and Oei, 2004); 42 (maximum)
- **Dropped out week 2;** Gambling Urge Score at week 2; 24
- Complaints of **dizziness, nausea, stomach upset.**
- **No gambling;** two-weeks.

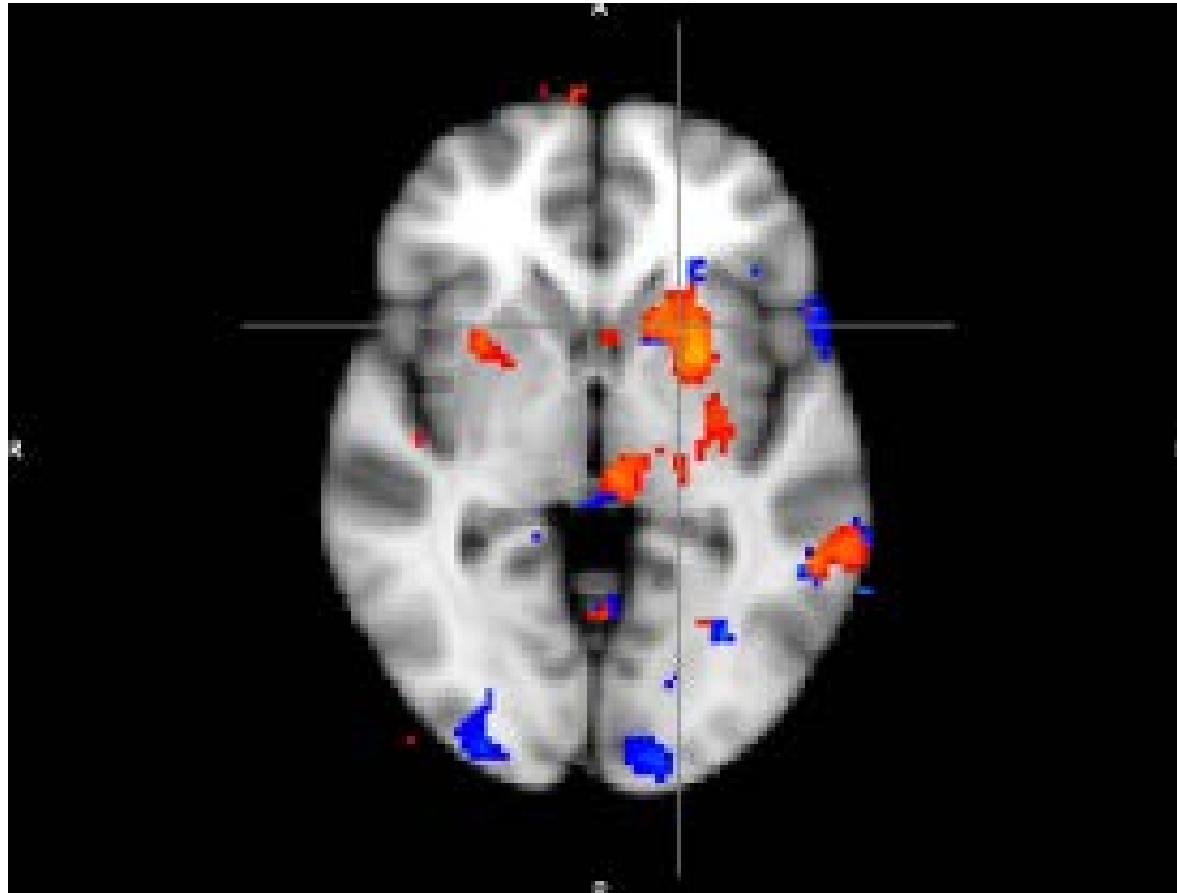
Gambling Disorder (n=3)



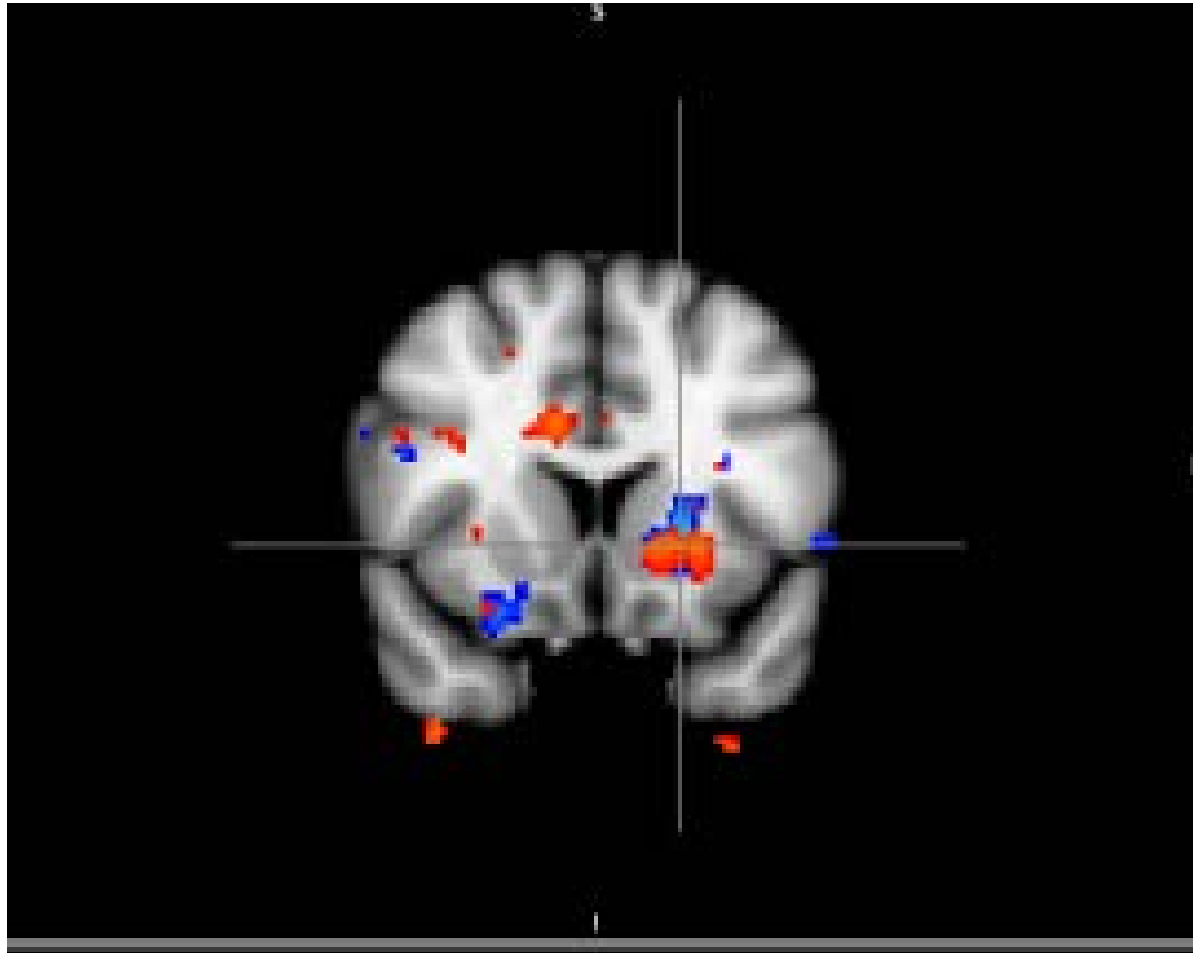
Gambling Disorder



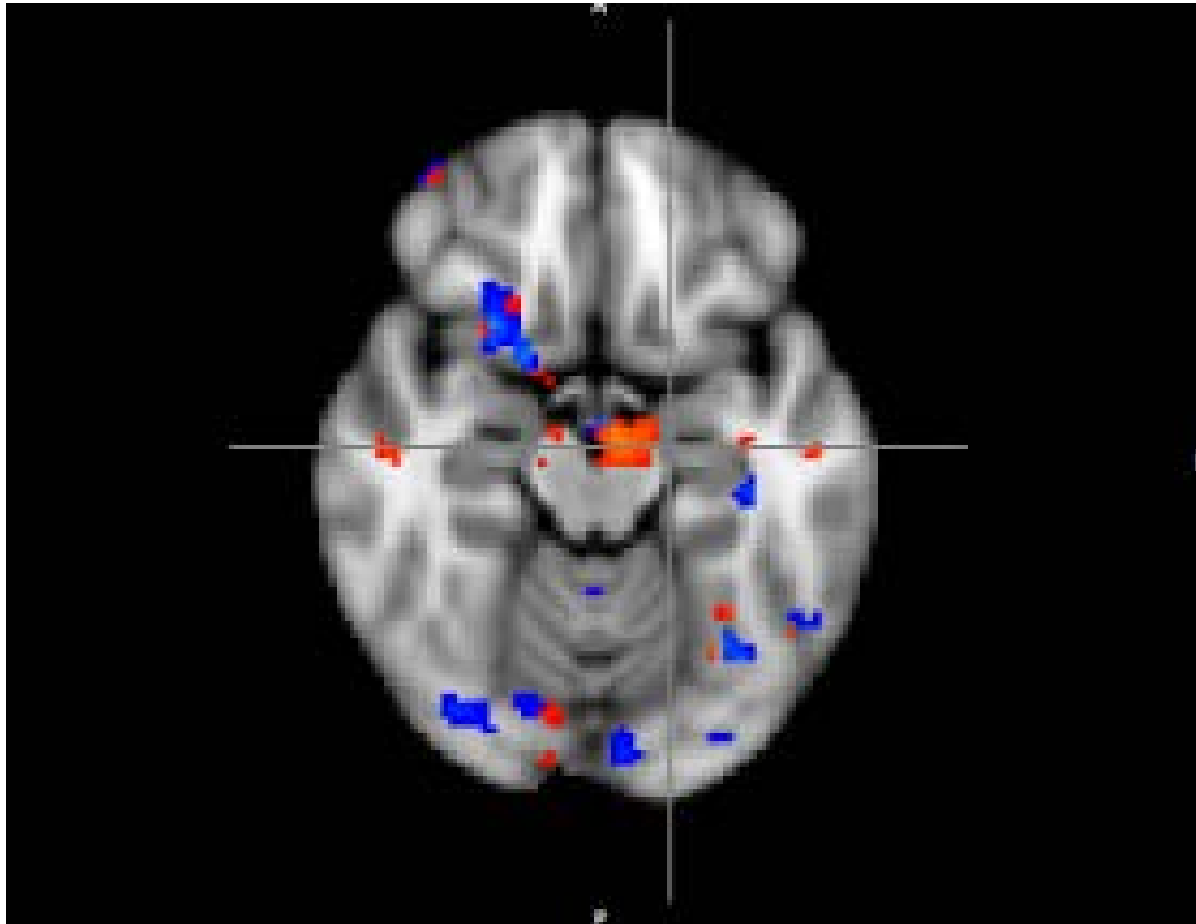
Gambling Disorder



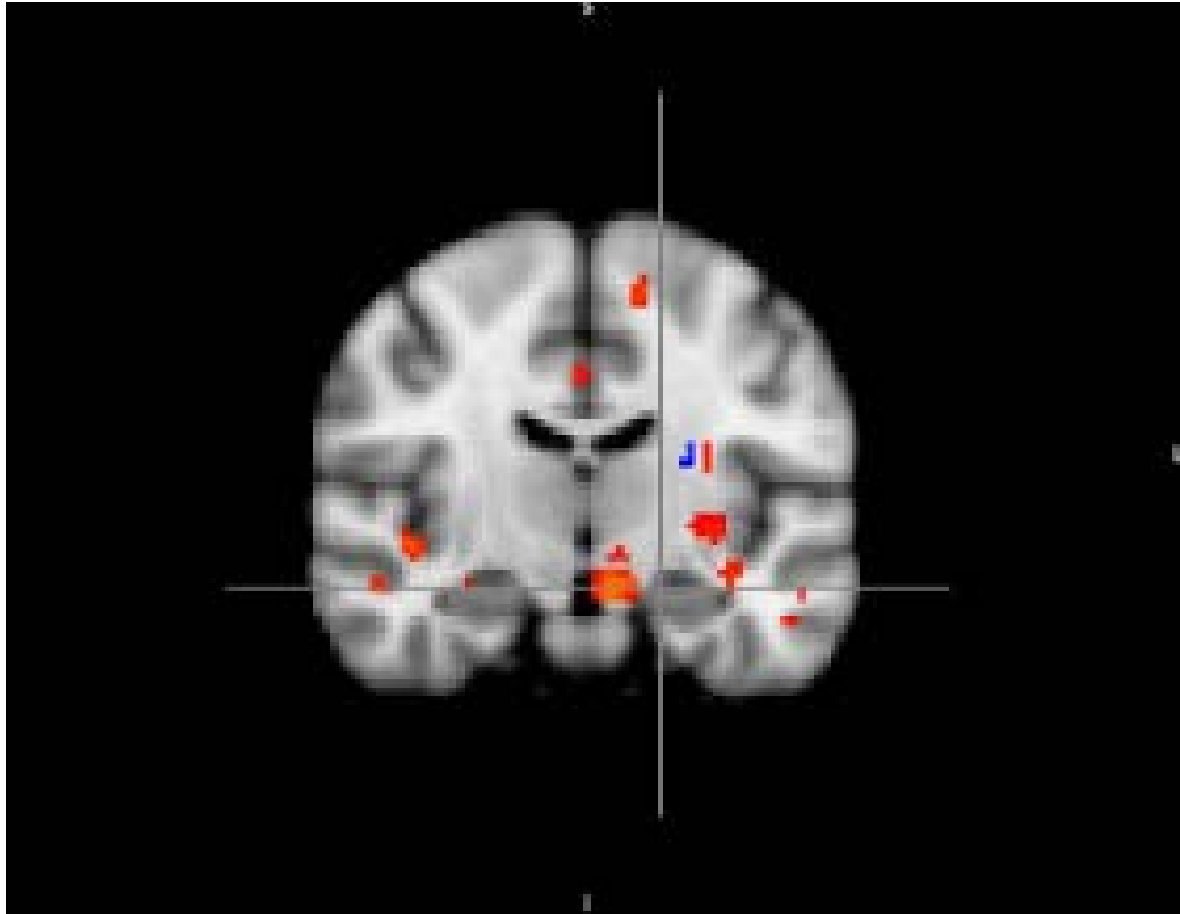
Gambling Disorder



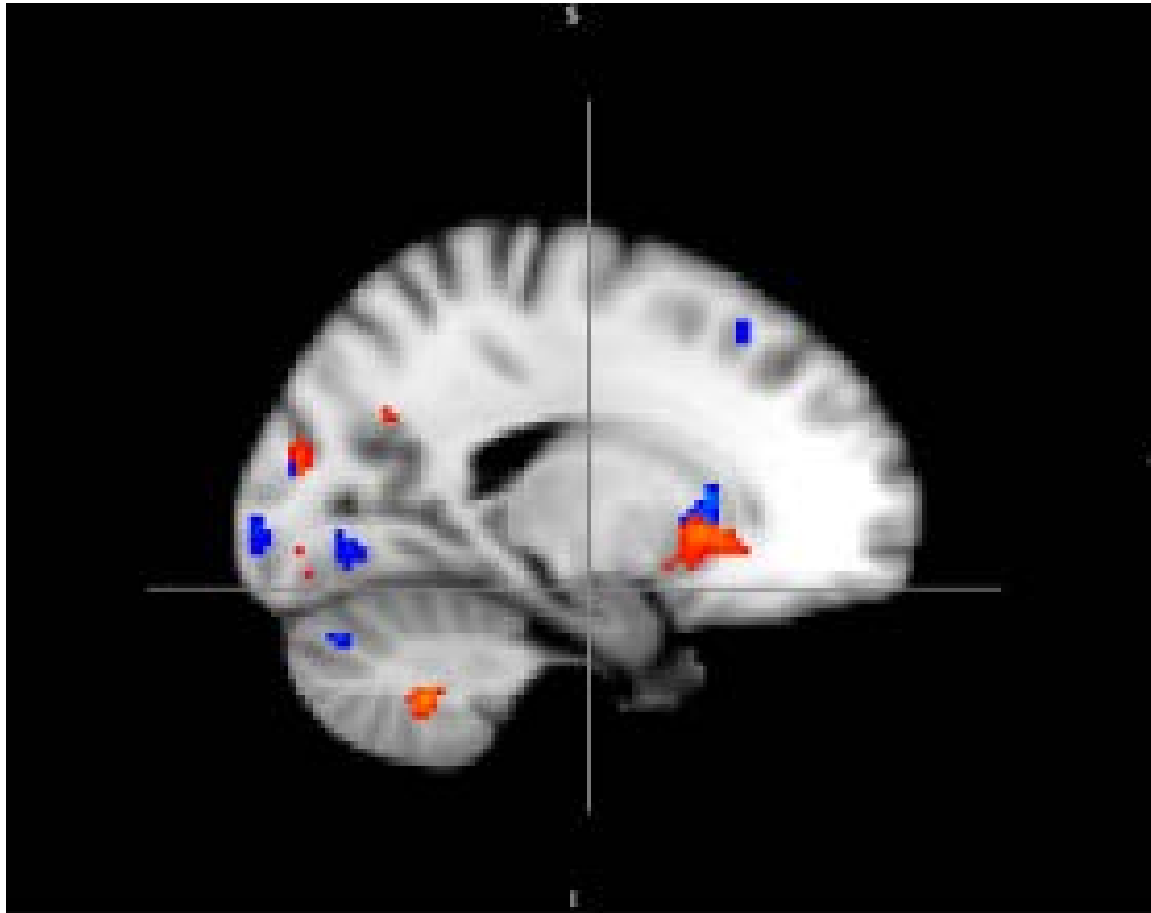
Gambling Disorder



Gambling Disorder



Gambling Disorder

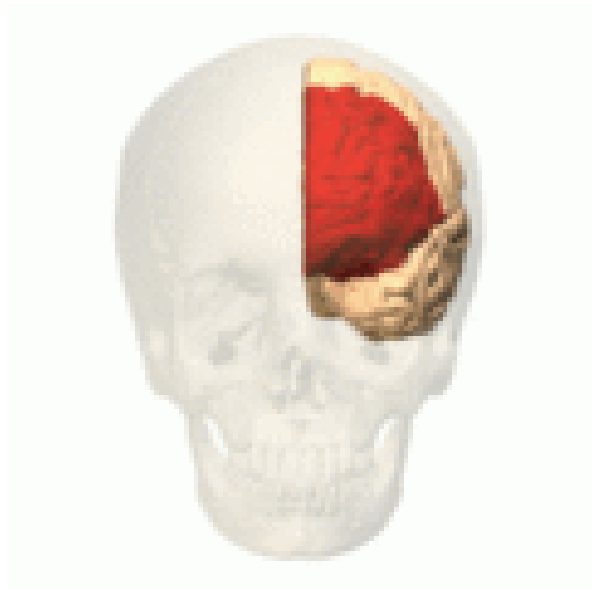
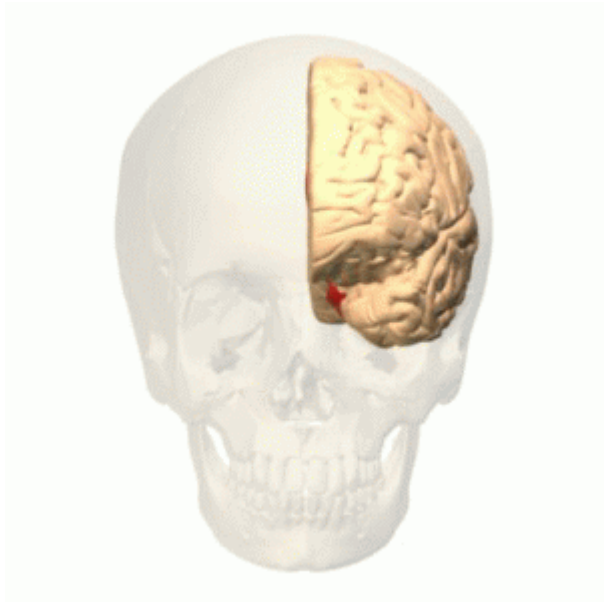


Interim Conclusions

- **Reduction in Gambling Urge** (for one participant) at a relatively low dosage level.
- **Significant side effects.**
- **Highly impulsive** behavioural responses. Participants chose almost exclusively immediate alternatives.

Interim Conclusions

- **Localised Activation** (especially for immediate choice) in the; Dorsal Later Prefrontal Cortex, Putamen, and Amygdala/Hippocampus.
- Suggestion delay discounting task at base-line activates brain regions associated with **cognition, reinforcement/learning, and emotion/memory.**
- Executive systems are **used at base-line.**



Three Systems Approach

- **Impulsive**; fast, automatic, automatic and habitual.
- **Reflective**; deliberative, forecasting the future consequences of a behaviour, inhibitory control, and self-awareness.
- **Interoceptive**; translating bottom-up somatic signals into a subjective state of craving.
(Brevers & Noel, 2013).

Three Systems Approach

- Suggestion that although **executive brain regions** were heavily involved in the delay-discounting task, these were **insufficient to overcome** their preference for immediate outcomes.
- **Two possibilities**; interoceptive systems give greater weight to emotional signals, and/or emotion signals are more powerful than executive signals.

Issues

- Interim analysis – **not definitive.**
- This study does not examine the **dopamine hypothesis.**

Implications

- Naltrexone can lower gambling **cravings**.
- Further evidence to support for **multiple brain regions in decision-making**.
- Naltrexone is problematic for those who are **sensitive to medication**.

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Thank You

Any Questions?