CENTRE for GAMBLING RESEARCH at UBC

Neuroscience of Gambling Addiction

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Alberta Gambling Research Institute, Banff

a place of mind
THE UNIVERSITY OF BRITISH COLUMBIA
Department of Psychology

Overview

- Endogenous opioid function in pathological gamblers: understanding the mechanism of naltrexone action?
- Gambling-related cognitive distortions and the effects in insula damage: the gambler's fallacy and the near-miss effect

Disclosure

The Centre for Gambling Research at UBC is supported by the British Columbia Lottery Corporation and the Province of BC government.

Gambling in British Columbia

- Past year gambling involvement: 72.5%
- Most popular forms of gambling: lottery (44%), charity raffle (16%), casino incl. slot machines (11%), private games (11%), sports betting (3%)
- Prevalence of problem gambling (PGSI 3+): 3.3% (0.7% for PGSI 8+)
- Forms most associated with PG: casino incl. slot machines (42%), private games (39%), stocks & shares (27%), bingo (14%), internet gambling (13%)
- Estimated % of total revenue from PGs: 26%

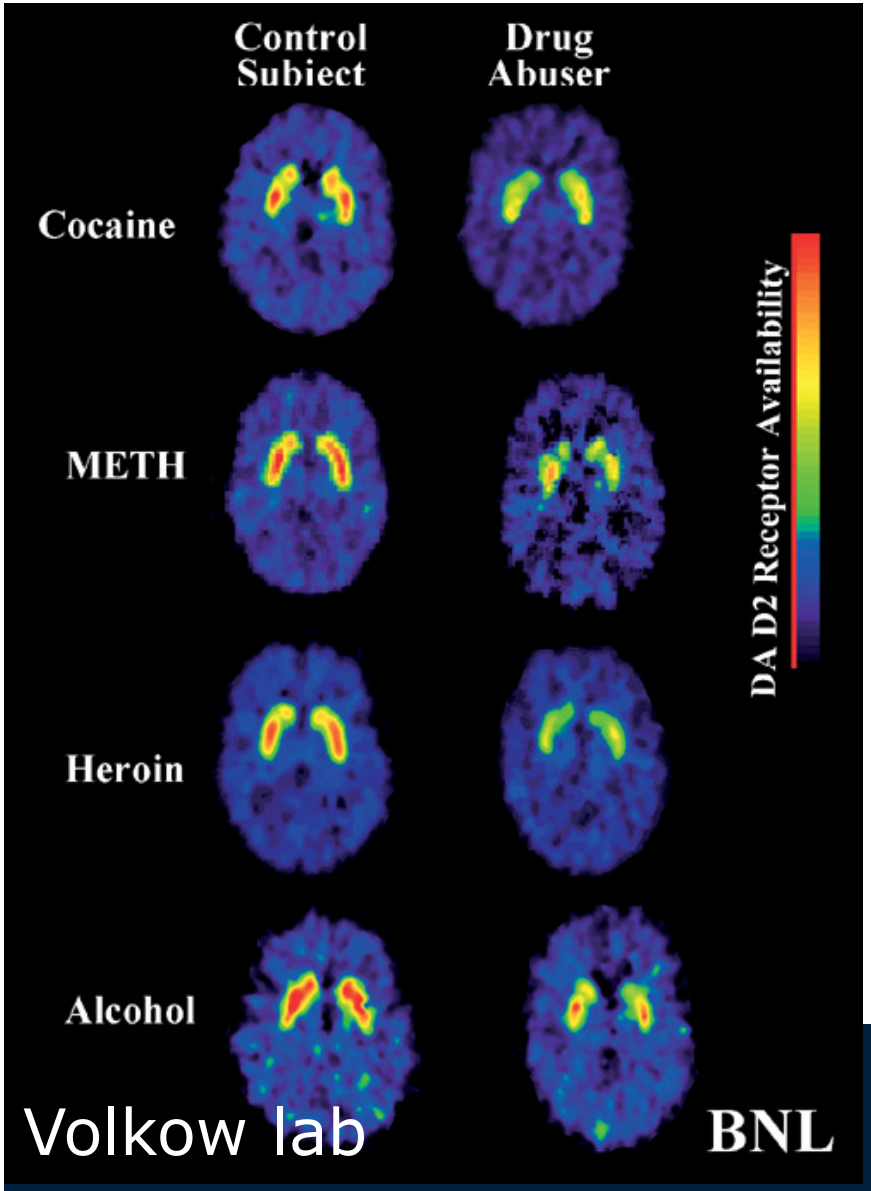
PHO report 'Lowering the Stakes' 2012, BC Prevalence Survey 2014

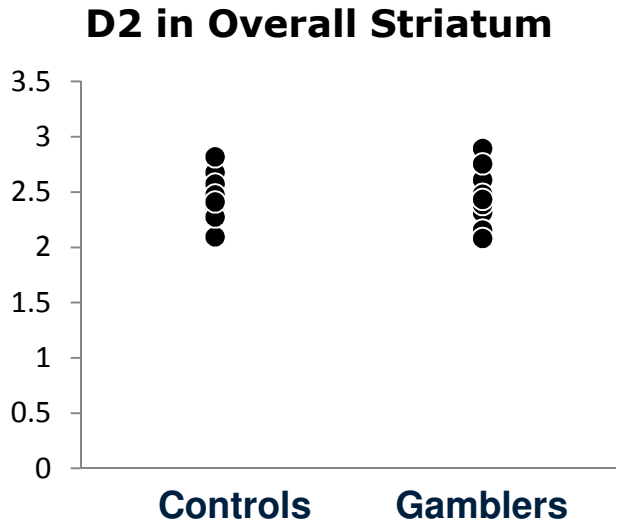
Neurochemistry of Gambling Disorder

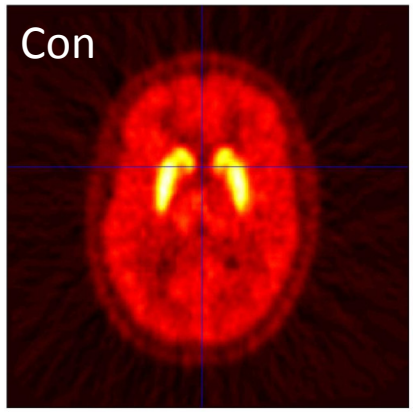
- Neuroscience models of addiction emphasize pathophysiology in the dopamine system (Volkow, Wise): reduced D2 receptors, reduced DA release

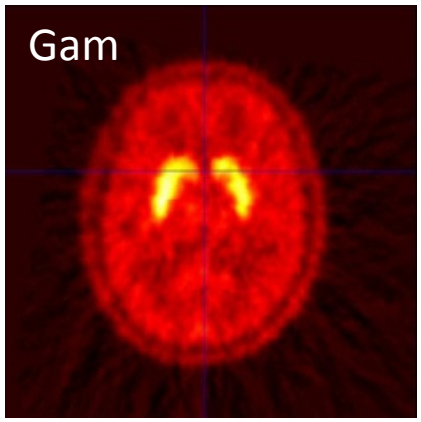
- A number of small PET studies in PG have indicated no change in D2 receptors (Clark et al 2012); possibly increased DA release (Boileau et al 2014)

Dopamine









Clark et al (2012 NeuroImage)
See also: Linnet et al 2011
Joutsa et al 2012
Boileau et al 2013

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Neurochemistry of Gambling Disorder

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Pharmacotherapy for PG

	Dose (mg per day)	Number of participants	Response rate for drug	Response rate for placebo
Naltrexone	50-150	122	61.8%	34·2%
Nalmefene	20-100	414	51·8%	46%
Fluvoxamine	50-250	47	72%	48%
Paroxetine	10-60	121	62·9%	39·7%
Sertraline	50-150	60	68%	66%
Bupropion	75-375	39	35·7%	47·1%
Olanzapine	2.5-15	63	66·7%	71·4%

Hodgins et al (2011 Lancet)

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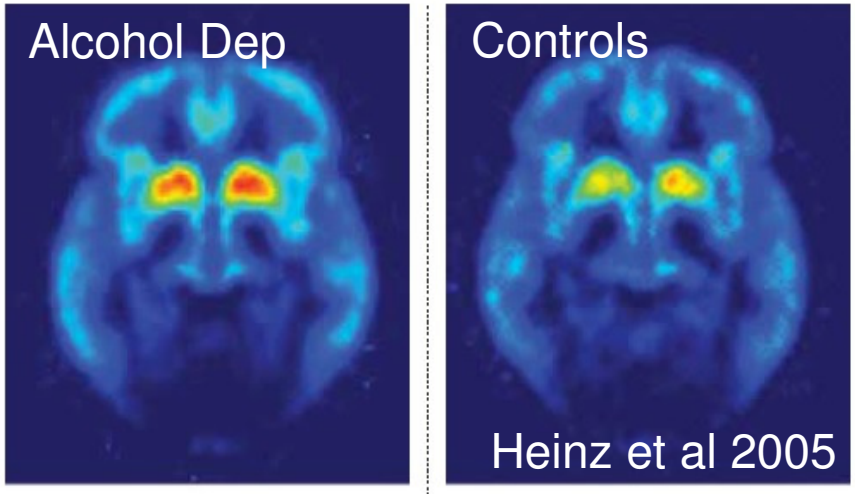
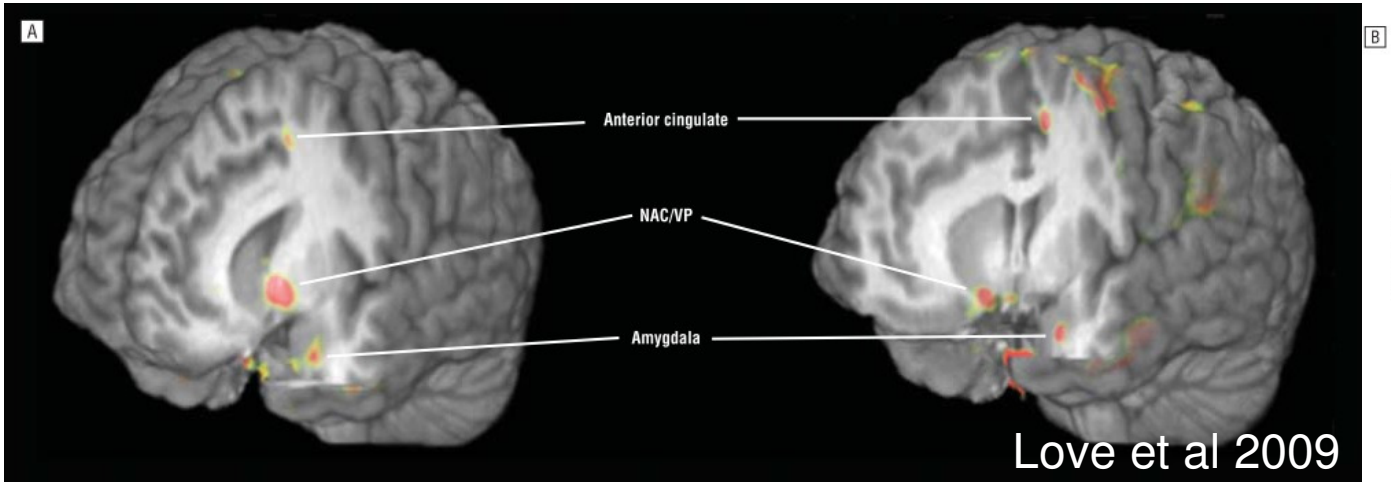
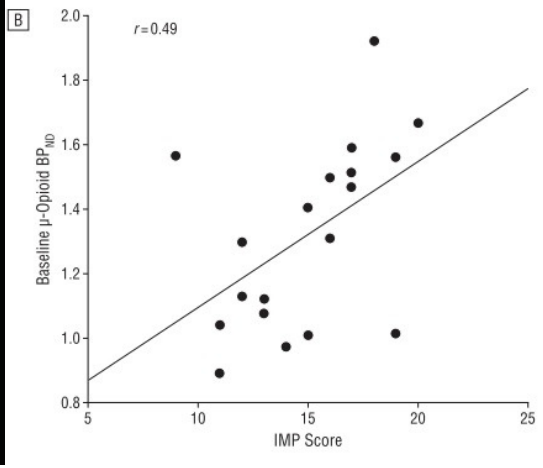
- Gambling (pachinko) associated with elevated β–endorphin (Shinohara et al 1999)
- No data on integrity of the opioid system in Gambling Disorder

Opioid Binding in Substance Use Disorders

3 receptors: mu, delta & kappa
Carfentanil is a mu selective PET tracer
Carf binding is increased in SUD, and +ively correlated with craving & impulsivity







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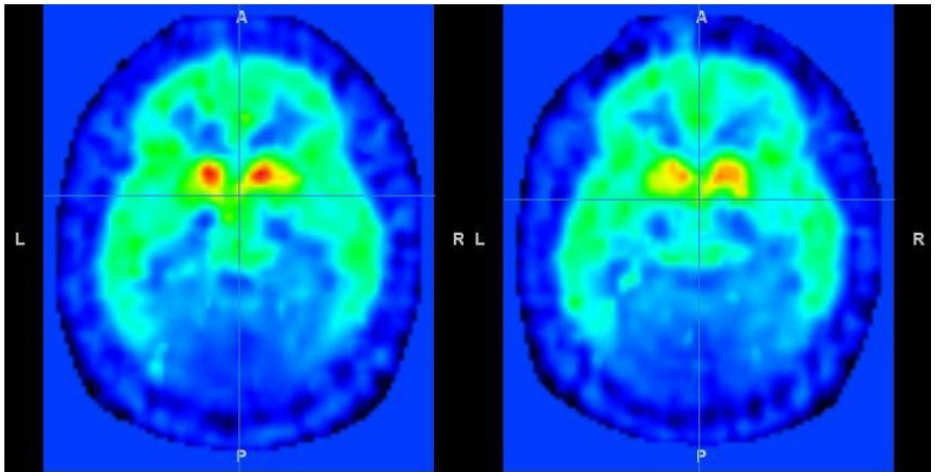
Methods: Carfentanil PET imaging of mu-opioid receptors and opioid release



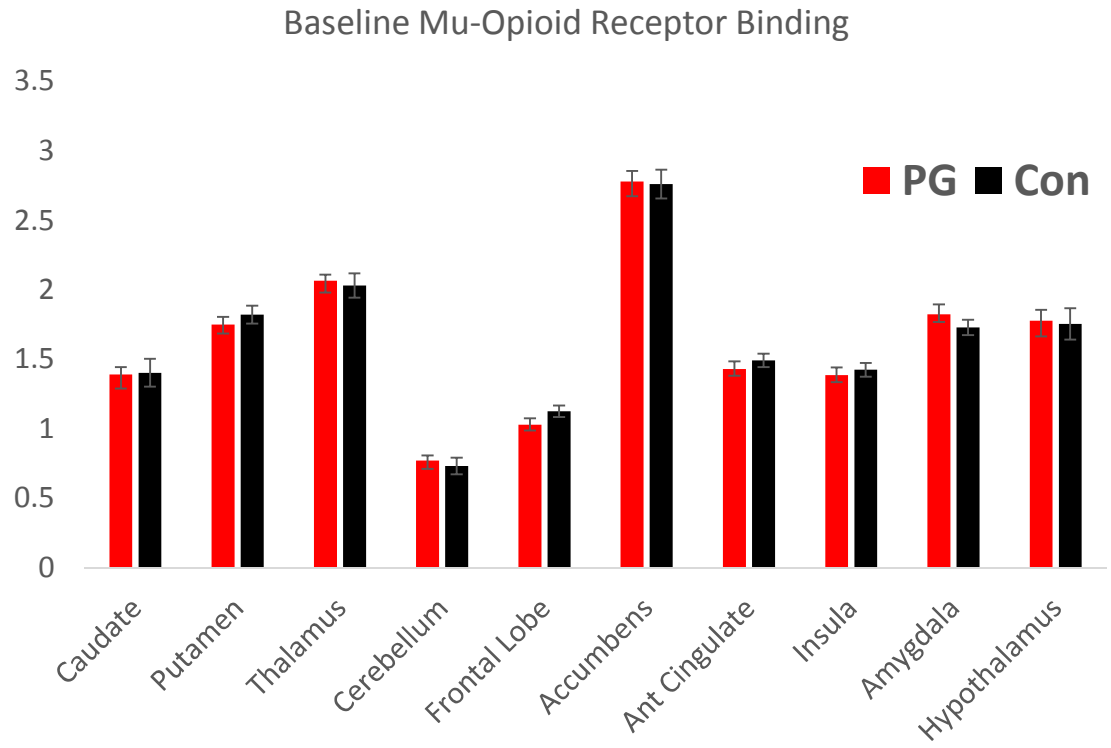
BASELINE POST-AMPH

Amphetamine (0.5 mg/kg) releases endogenous opioids, displaces ligand from receptors → *lower* binding (Colasanti et al 2012, Mick et al 2014)

14 male PG attending UK National Problem Gambling Clinic compared against 15 male HV; scanned on two occasions

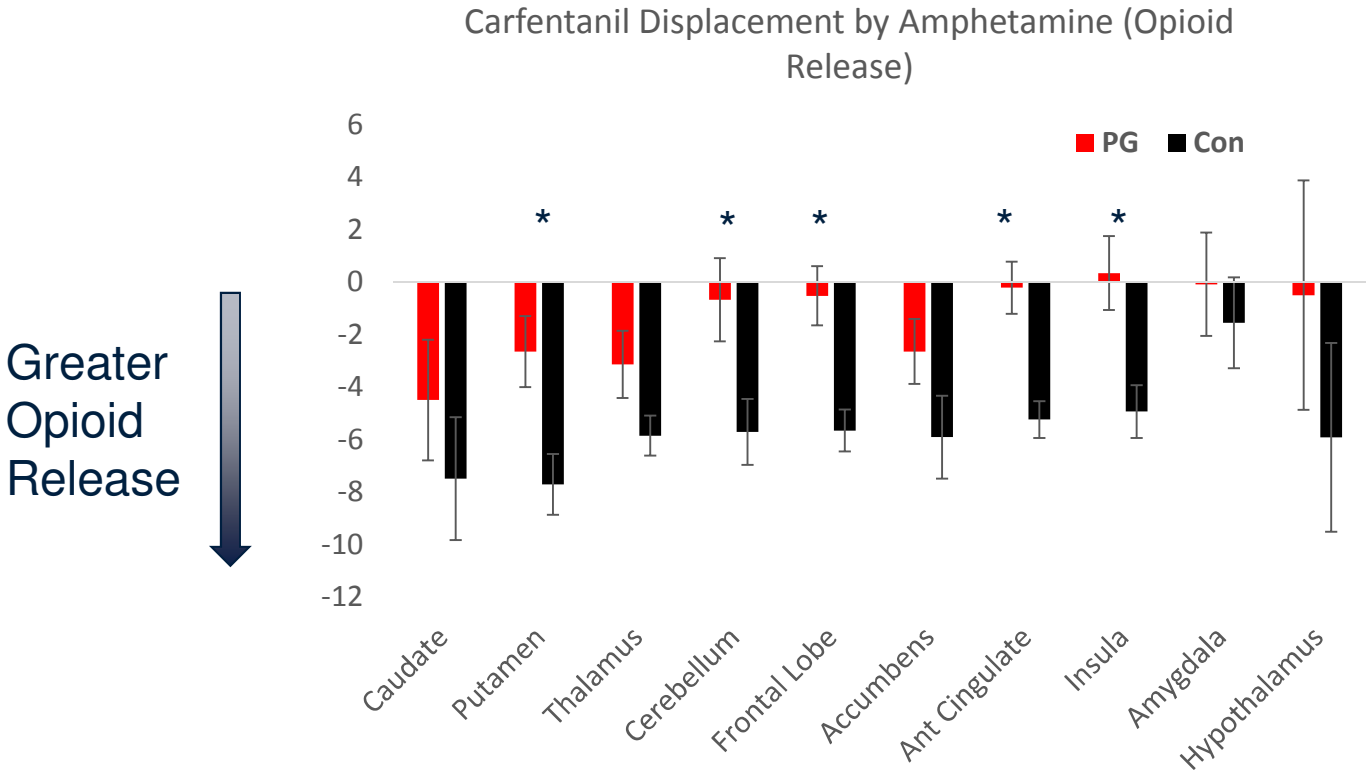
	PG	HV
Age	34.3 (7.7)	34.4 (8.7)
PGSI*	18.0 (5.2)	0.2 (0.6)
AUDIT*	6.9 (3.9)	3.6 (2.5)
BDI*	8.7 (7.9)	0.6 (1.8)
Smokers	n=3	n=2

Hypothesis 1: Baseline Opioid Receptors



H1: not supported

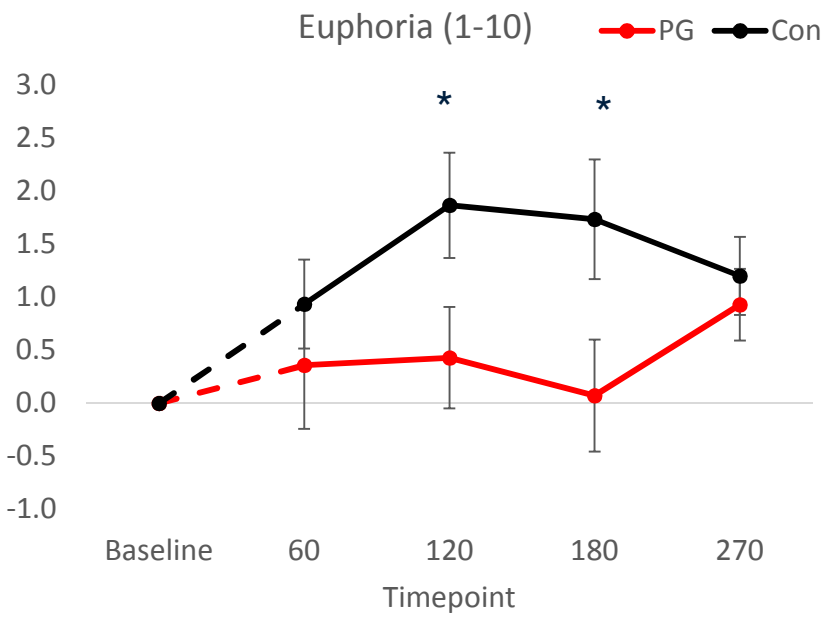
Hypothesis 2: Opioid Release in PG

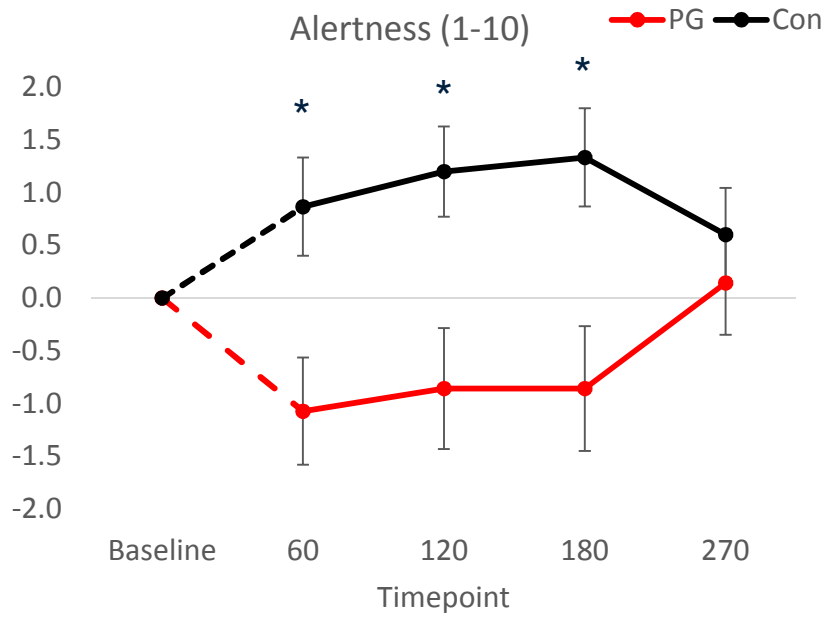


Marked opioid release in healthy group (8/10 ROIs)

Blunted opioid release by Amph in PGs

Hypothesis 3: Subjective Responses to Amphetamine





Blunted euphoria and alertness following Amph in PGs (no effect on anxiety & restlessness)

Opioid study: conclusions

- No difference in baseline MOR in pathological gamblers
- In healthy volunteers, amphetamine reduced MOR binding across 8 of 10 ROIs → quantitative measure of opioid release
- Evidence of blunted opioid release to a standard amphetamine challenge in pathological gamblers, across multiple brain regions
- Pathological gamblers also show attenuated euphoria to amphetamine (c.f. Boileau et al 2014)
- If pathological gamblers have *reduced* opioid release, why would NTX - an opioid *blocker* - be an effective treatment?
- Does the opioid challenge need to be behaviourally relevant? (i.e. gambling induced opioid release)

Cognitive approach to gambling

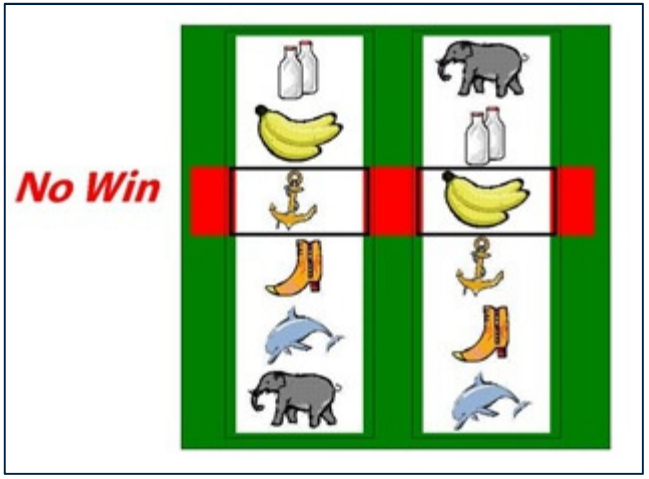
Gamblers' excessive play is driven by cognition distortions that creates an inappropriate expectancy of winning

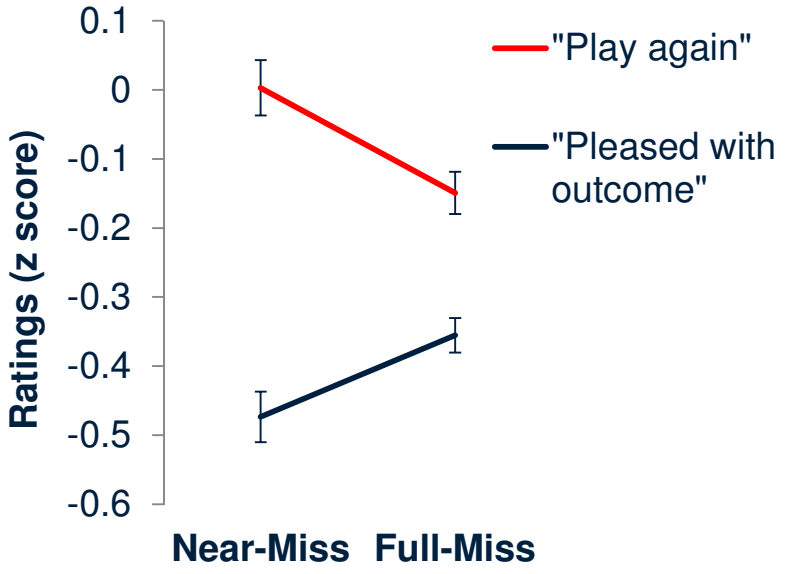
Two important types

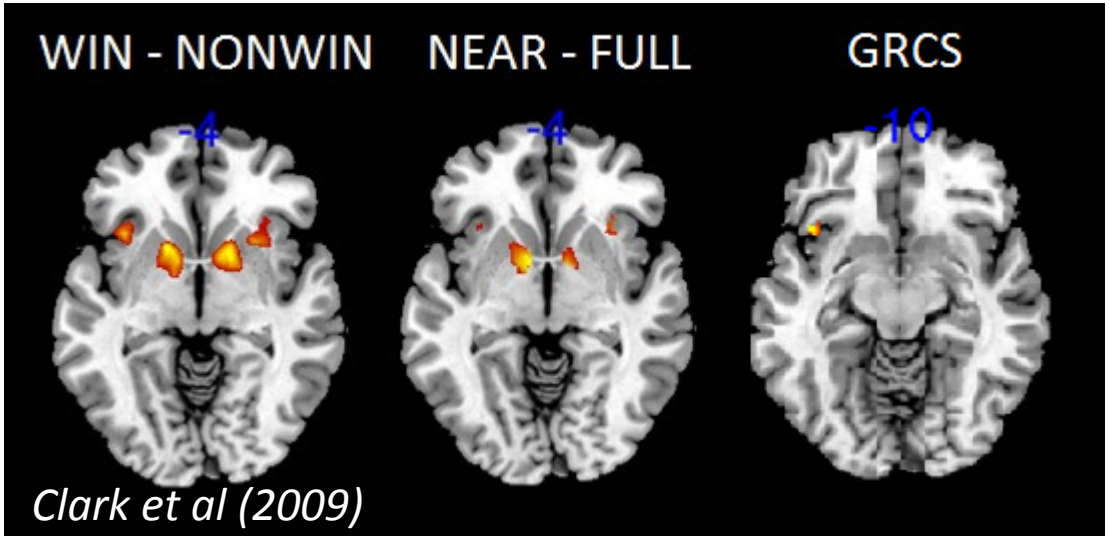
- The gambler's fallacy (random sequences)
- The illusion of control (confusion of skill and chance)

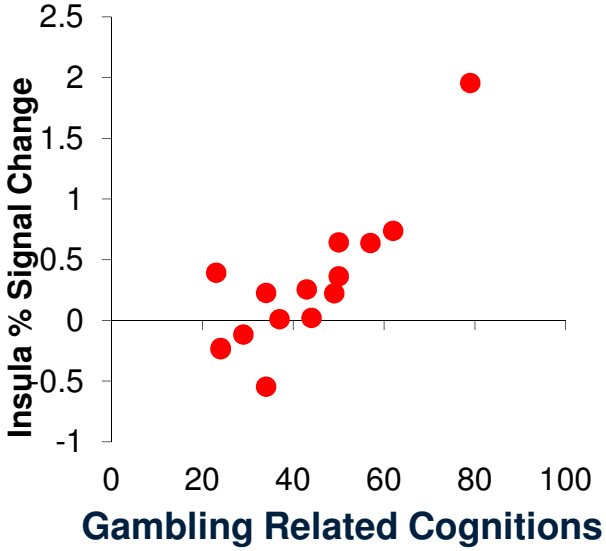
Problem gamblers may be more susceptible to these cognitive distortions than the general population

Near-Miss Outcomes









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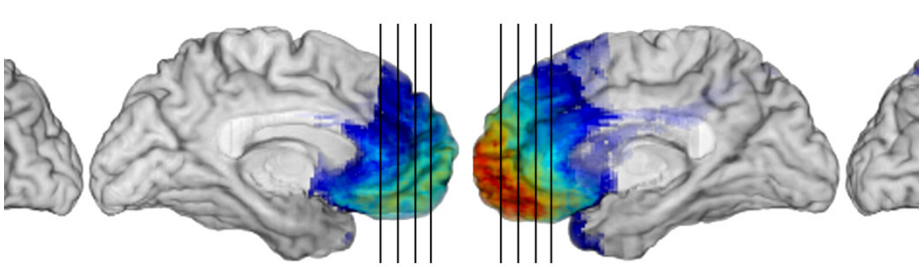
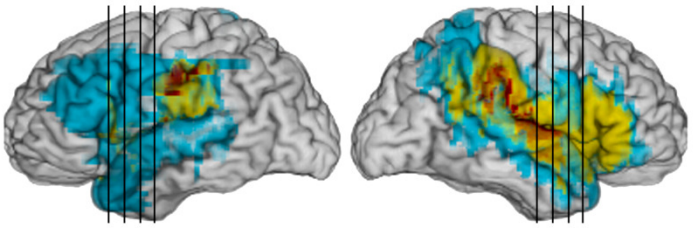
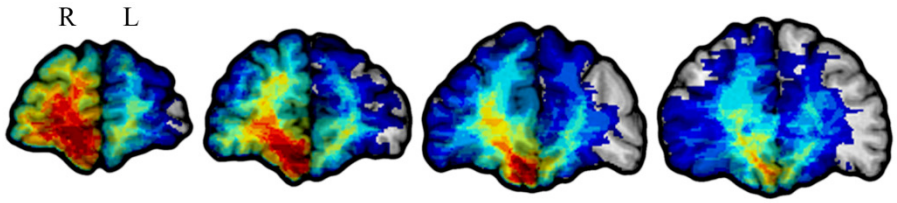
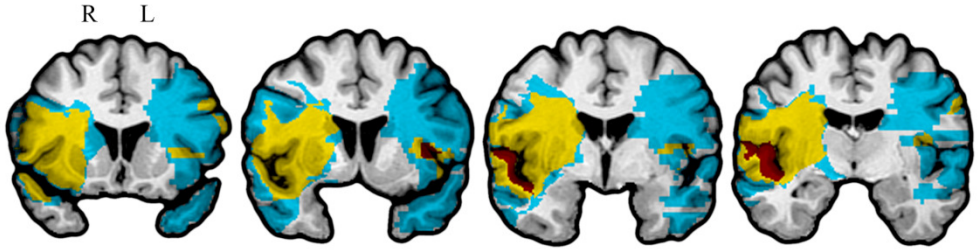








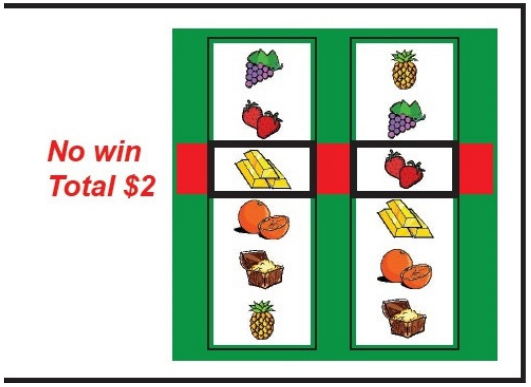
VMPFC **INSULA**

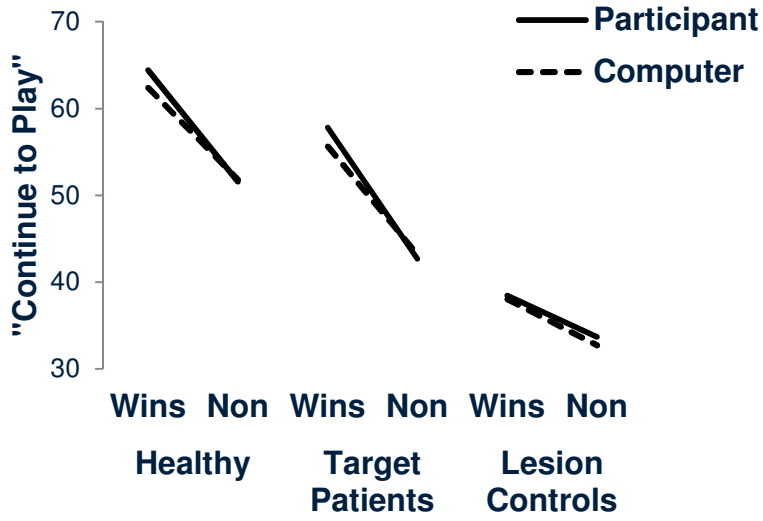
"Target Group"

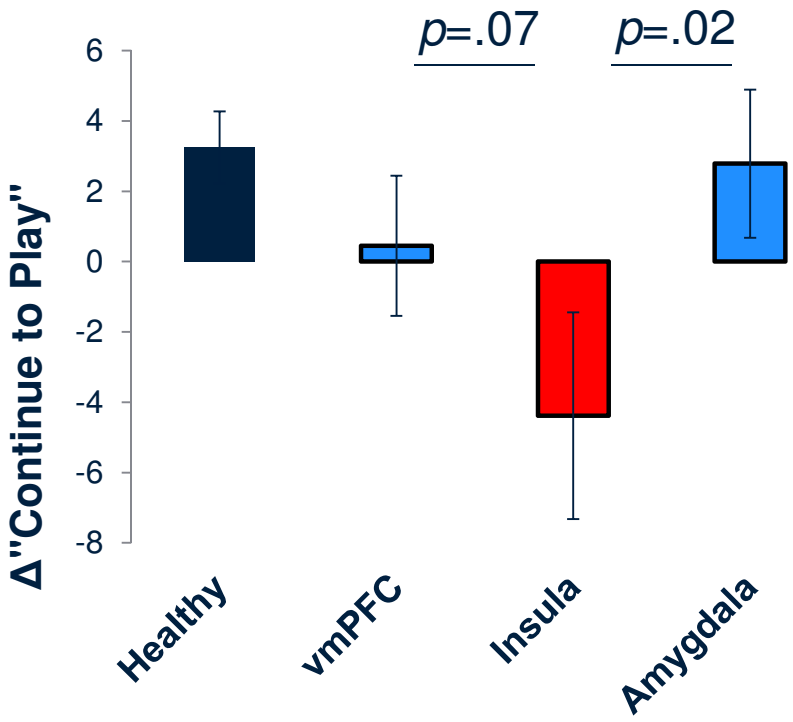
	vmPFC	Insula	Amygdala	HC	Lesion Con
N	17	8	6	16	13
Age	52.1 (16.8)	53.3 (16.8)	49.7 (9.9)	60.1 (9.8)	51.9 (19.5)
Education	14.2 (2.5)	13.8 (4.7)	14.2 (3.1)	14.7 (2.3)	14.4 (2.7)
Side (B:L:R)	13:2:3	0:4:4	1:5:0	--	2:7:4
Real gambling	8:5:1	6:2:0	5:1:0	6:10:0	4:3:1
SOGS	0.8 (1.6)	0.0 (0.0)	0.2 (0.4)	0.8 (1.4)	0.4 (0.7)
GRCS	48.4 (31.1)	36.6 (14.2)	33.0 (9.6)	44.8 (16.1)	34.6 (15.6)

Clark, Studer, Bruss, Tranel, Bechara 2014 PNAS

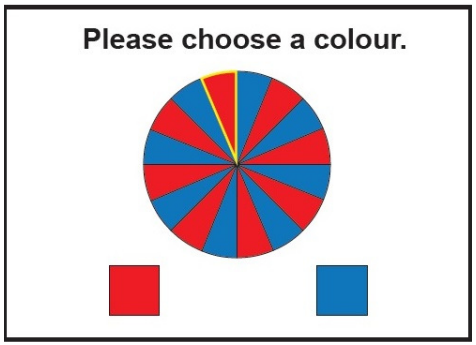
Effects of Near Misses



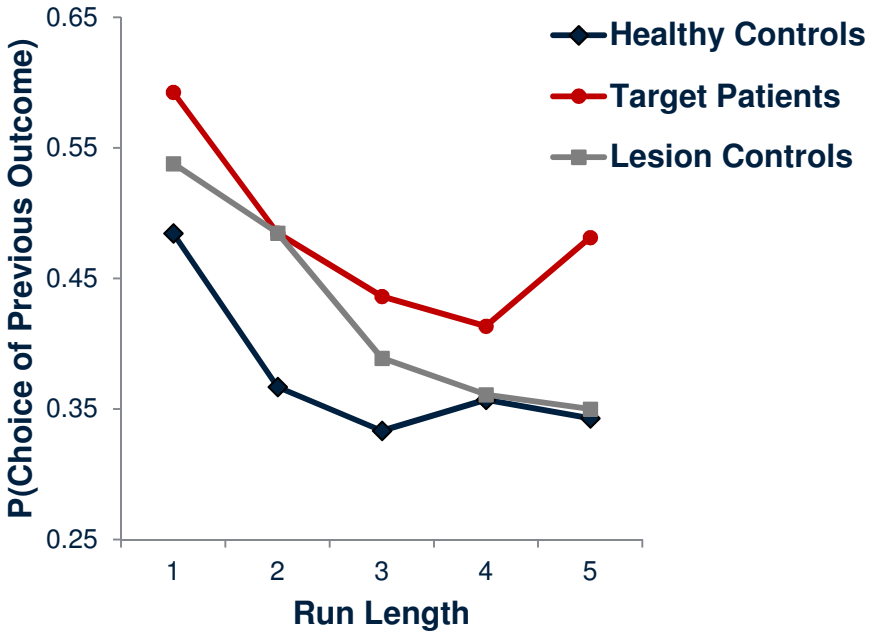


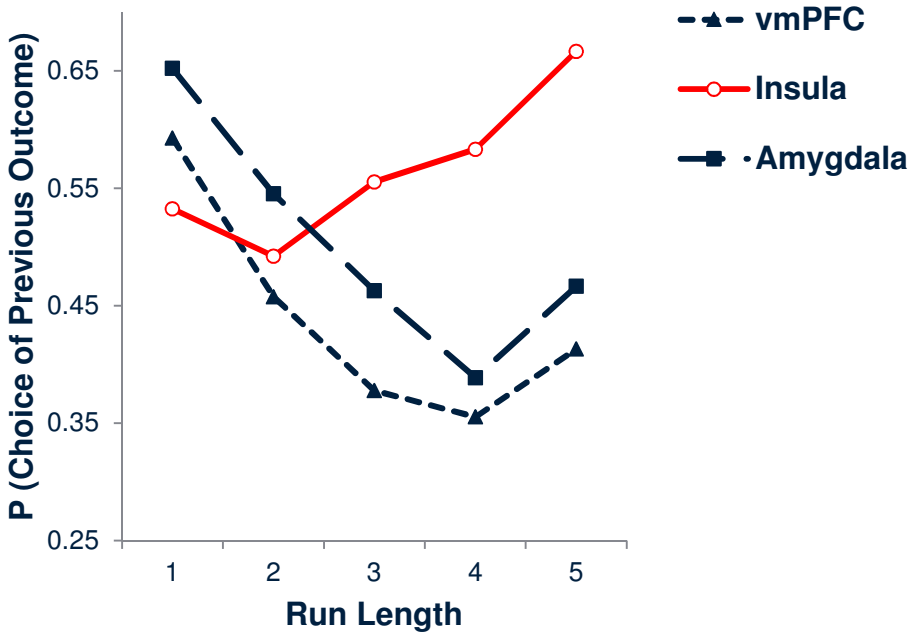


- Motivational response to *near-misses* (minus full-misses) abolished in insula group



The Gambler's Fallacy

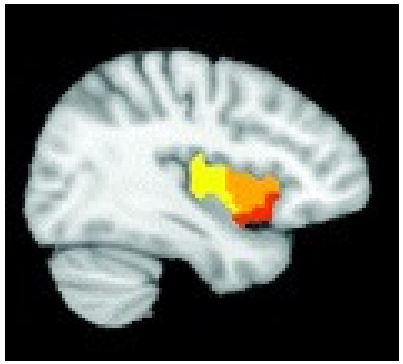




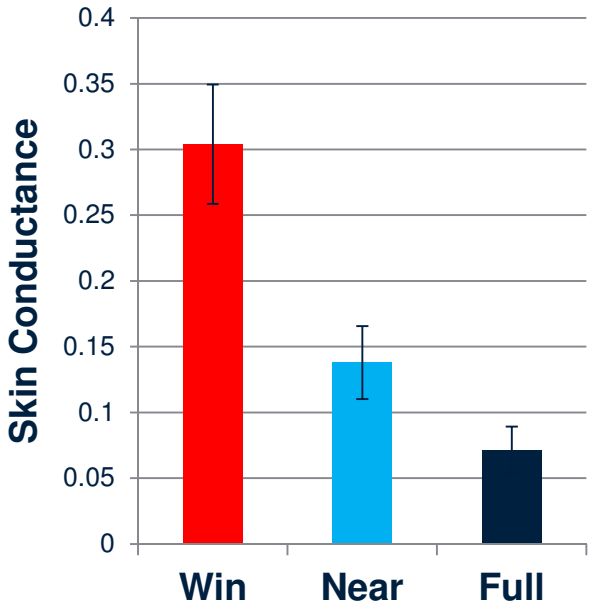
- GF: less likely to choose RED after a run of REDs
- Effect abolished in group with insula damage

Clark et al (2014 PNAS), task design see Studer et al (2015 J Behav Dec Making)

Why the Insula?



- Key reception zone for bodily input and arousal - ***interoception***
- Gambling associated with increased physiological arousal (HR, cortisol)
- Skin conductance responses to wins and near-misses
- Insula overactivity in pathological gambling? Target for bodily treatments (e.g. mindfulness / biofeedback)



Conclusions

- Neuroscience studies inform our understanding of treatments for problem gambling: *both* pharmacological *and* psychological.
- Data from PET imaging are highlighting increasing disparity between neurochemistry in problem gamblers vs drug addictions: are the effects in drug addiction drug-induced, or is the addictions model of PG an over-simplification?
- Decision-making and outcome processing involve a brain *network*; neglected role for the insula in gambling distortions.

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