Addiction: from impulse to compulsion

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What is an impulse and how can we understand impulse control disorders?

The nature of the impulse

The strength of executive control
What is an impulse and how can we understand impulse control disorders?
The Insula
The Insula

Posterior insula

Primary interoceptive representation

Homeostatic motor function (hypothalamus and amygdala)

Environmental conditions (entorhinal and temporal poles)

Hedonic conditions (nucleus accumbens, and orbitofrontal cortex)

Motivational, social and cognitive conditions (ACC, VMPFC and DLPFC)

Anterior insula

Craig, Nat. Neurosci. 2009
The AI: from insight to behavioural control

Craig, Nat. Neurosci. 2009
The AI: from insight to behavioural control

Insula
neurobiological substrate of obsessions:

OCD

Craving in addiction
Interest of preclinical models: prospective longitudinal studies
Maximisation of decision-making requires the AI

Forced
Free
2-pellet + free

Choice training

Good decision makers
(n = 16)

Lesioned good decision-makers
(n = 9)

Lesioned poor decision-makers
(n = 9)

Sham good decision-makers
(n = 7)

Sham poor decision-makers
(n = 7)

RGT

RGT pre

RGT post

1 pellet TO: 6s
2 pellets TO: 444s
1 pellet TO: 12s
2 pellets TO: 222s
2 pellets TO: 122s
2 pellets TO: 222s
2 pellets TO: 444s

Time

n = 48

d9 d10 d24 d28 d29 d48

Instruemental response

FR1 FR3 FR5 PR FR5 rFR5
Maximisation of decision-making requires the AI in rats

Good decision-makers

Lesioned \((n=9)\)  
Sham \((n=7)\)

Poor decision-makers

Lesioned \((n=9)\)  
Sham \((n=7)\)

Decision-making score

Exploration  Exploitation

Lesioned  Sham

Pre  Post  Pre  Post

\(0 \quad 10 \quad 20 \quad 30 \quad 40 \quad 50\)
Maximisation of decision-making requires the AI in rats

Good decision-makers

![Graph showing lever presses over sessions for good decision-makers with lesioned and sham conditions.]

Poor decision-makers

![Graph showing lever presses over sessions for poor decision-makers with lesioned and sham conditions.]

Mean presses of initial active lever

Sessions

Previous New

Sum of active lever presses

Good decision-makers:

![Breakpoint bar graph with lesioned and sham conditions.]

Poor decision-makers:

![Breakpoint bar graph with lesioned and sham conditions.]

Daniel et al., In Prep
The insula and impulses

Does the insula contribute to impulse control?

Does interception/the insula contribute to the nature of the impulse?
Inter-individual differences in impulse control: example of waiting impulsivity

How do we measure impulsivity?
5-choice serial reaction time task
Inter-individual differences in impulse control: example of waiting impulsivity

How do we measure impulsivity?
5-choice serial reaction time task

Belin et al., Science 2008
High impulsivity trait is an endophenotype of vulnerability to compulsivity

Example of drug OCD-like behaviour

schedule-induced polydipsia

Ansquer et al., Biol. Psy 2014
High impulsivity trait is an endophenotype of vulnerability to compulsivity

Example of drug OCD-like behaviour schedule-induced polydipsia

**OCD Psychopathology**

- Repetitive behaviours
- Aimed at reducing distress or preventing some dreaded situation
- Excessive or unreasonable
- Interfering with activities
- Responsive to SSRI

**SIP Animal model**

- Repetitive adjunctive drinking behaviour
- Anxiolytic behaviour
- Excessive behaviour, unrelated to thirst
- Rigid and maladaptive
- Sensitive to SSRI
High impulsivity trait is an endophenotype of vulnerability to compulsivity

**Graph A**
- **Impulsivity (% premature responses)**
- **Time (sessions)**
- **Groups**: HI (n=6), LI (n=6)

**Graph B**
- **SIP (Water Intake ml/hour)**
- **Time (sessions)**
- **Groups**: HI (n=6), LI (n=6)
High impulsivity and compulsivity: NAergic mechanisms

**Highly impulsive rats**

**Low impulsive rats**

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SIP (Water consumption mL/hour)

Sessions

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SIP (Water consumption mL/hour)

Sessions

Ansquer et al., Biol. Psy 2014
High impulsivity and compulsivity: NAergic mechanisms

Belin-Rauscent et al. unpublished
Impulsivity and the anterior insular cortex

Belin-Rauscent et al., Mol. Psy. 2015
Impulsivity and the anterior insular cortex

Belin-Rauscent et al., Mol. Psy. 2015
Impulsivity and the anterior insular cortex

Belin-Rauscent et al., Mol. Psy. 2015
Compulsivity and the anterior insular cortex

Belin-Rauscent et al., Mol. Psy. 2015
Impulsivity → quantitative nature of interoceptive cues

Compulsivity → qualitative nature of interoceptive cues
Towards an evidence? AI and escalation of cocaine intake

Dalley et al., Science 2007
Towards an evidence? AI and escalation of cocaine intake
Towards an evidence? AI and escalation of cocaine intake

A

B

C

Rotgé et al., In Prep
Baseline

Reward system

Insula

Aversive system

Chronic aversiveness

Impulsivity

Baseline

Reward system

Insula

Aversive system

Chronic aversiveness

Compulsivity
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Intrastriatal shifts in the course of drug exposure

2DG metabolic activity decreases

D2 binding site decreases

Porrino L. 2004
Intrastriatal shifts in the course of drug exposure

Belin et al., 2013
Intrastriatal shifts in the course of drug exposure
Intrastriatal shifts in the course of drug exposure

Murray J., Belin-Rauscent A. et al. 2015
Intrastriatal shifts in the course of drug exposure

Murray J., Belin-Rauscent A. et al. 2015
Intrastriatal shifts in the course of drug exposure

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DLS
BLA
Veh a15
B/M-ipsi
Veh a15

Veh B/M

Veh a10 a15
a15-ipsi

BLA CeN
Lever presses (Log)

CeN
Lever presses (Log)

Amygdalo-striatal manipulations

Amygdalo-striatal manipulations

Murray J., Belin-Rauscent A. et al. 2015
Intrastriatal shifts in the course of drug exposure

Murray J., Belin-Rauscent A. et al. 2015

**A**
- M1 Stimulation
- DLS pMSNs AP recording
- BLA Stimulation

**B**
- Spike probability
- Neurons

**C**
- BLA - M1 1ms
- BLA - M1 5ms
- BLA - M1 50ms
- BLA - M1 100ms
- BLA - M1 200ms
- BLA - M1 300ms
- BLA - M1 500ms
- BLA - M1 1000ms

**D**
- Spike probability
- Up regulated (n=19)
- Down regulated (n=16)
- Non regulated (n=13)

**E**
- M1 Stimulation
- DLS pMSNs AP recording
- APS-CNQX infusion
- BLA Stimulation

**F**
- Spike probability
- Stimulation conditions

Murray J., Belin-Rauscent A. et al. 2015