

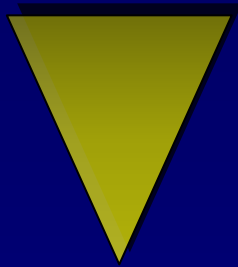


*Department of Experimental Psychology,
University of Cambridge, UK*

**Psychological and neurobiological mechanisms
of relapse and vulnerability to relapse:
implications for treatment**

Daina Economidou

Recreational drug use



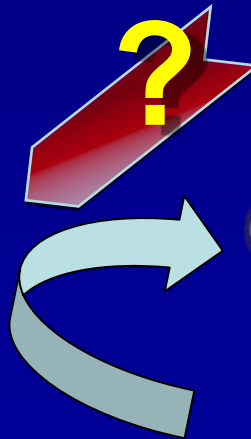
Escalated drug taking



**Compulsive
drug seeking and taking**

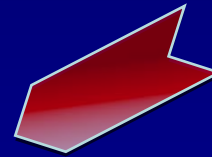


**Cease Drug Taking
Drug Abstinence**



**Maintenance of
drug abstinence**

Impulsivity



5-Choice Serial Reaction Time Task (5-CSRTT)



Low impulsive (LI) rats

High impulsive (HI) rats

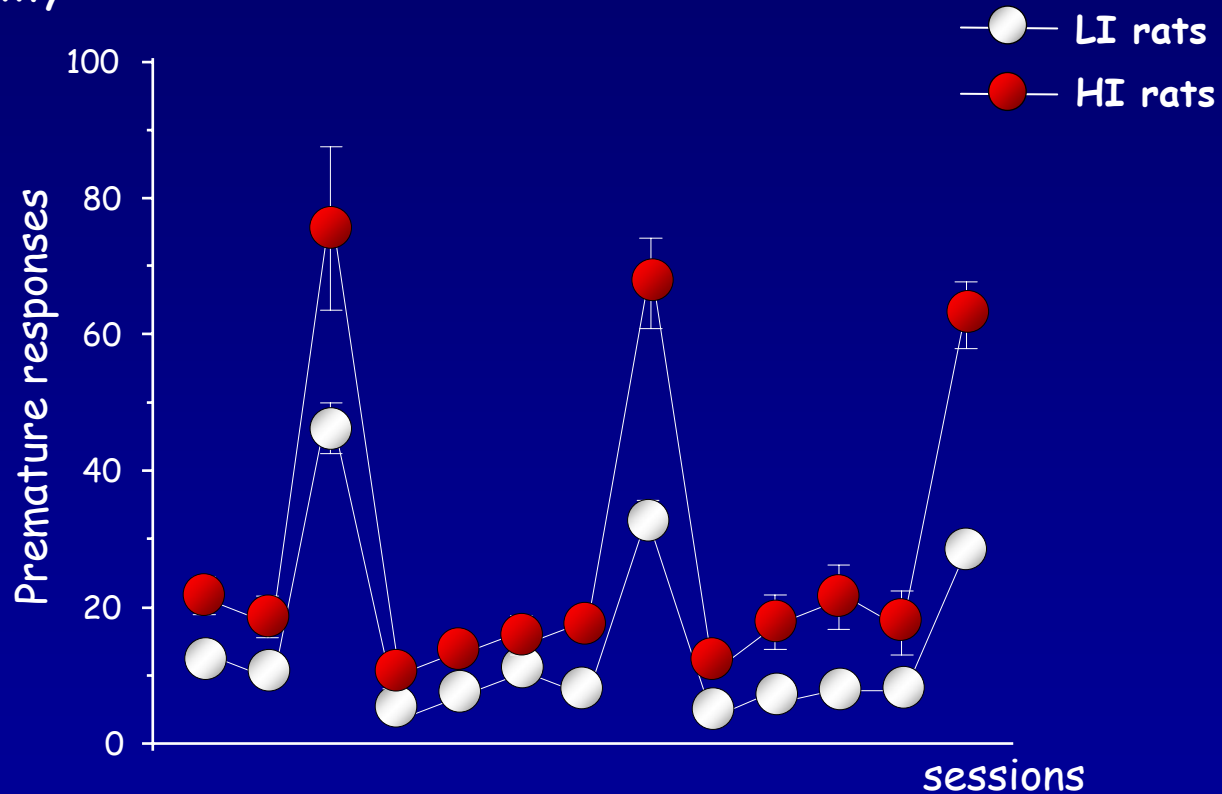


Relapse
to cocaine seeking
following punishment-induced abstinence

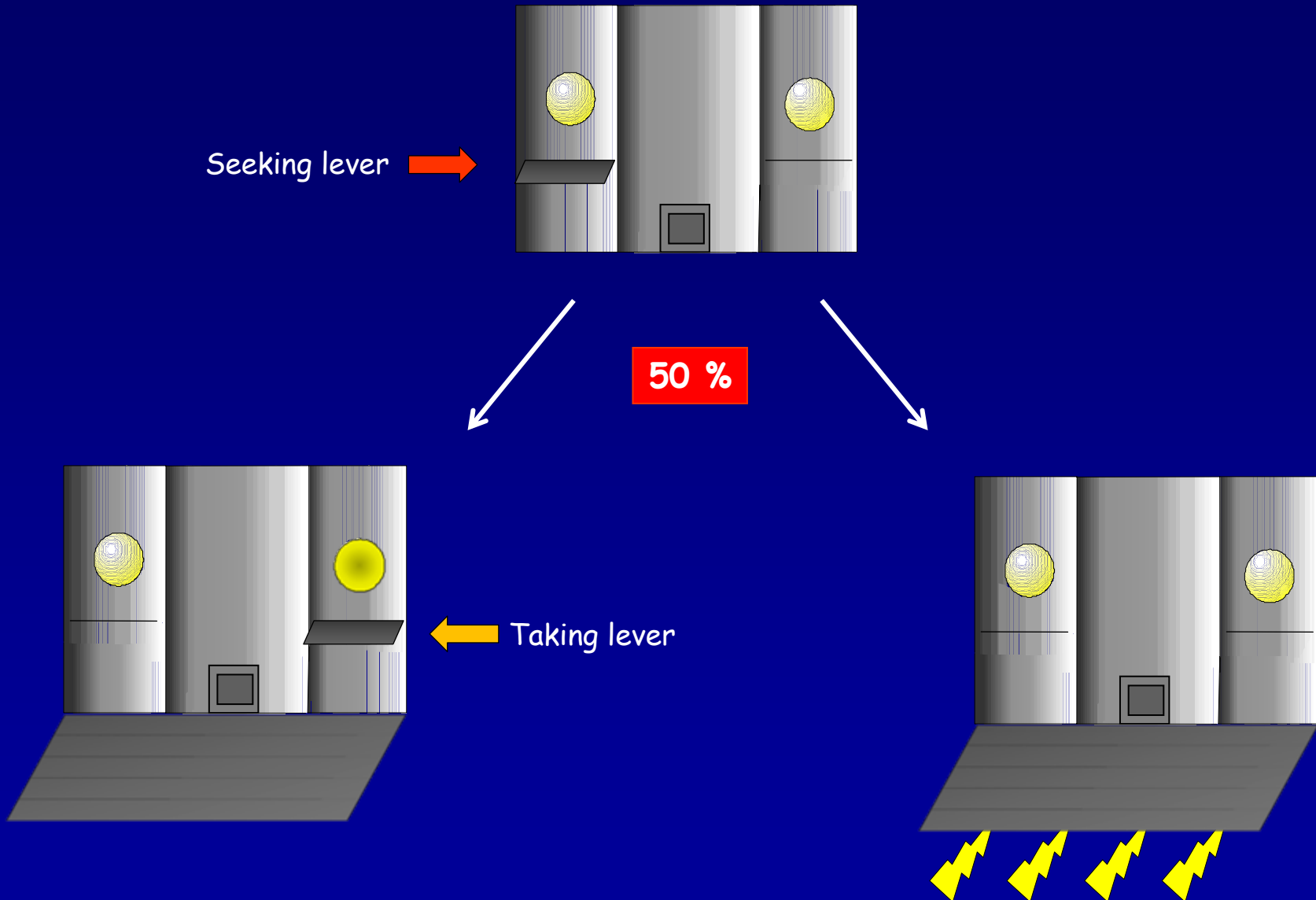


High (HI) and Low Impulsive (LI) rats in the 5-CSRTT

* "Waiting impulsivity"



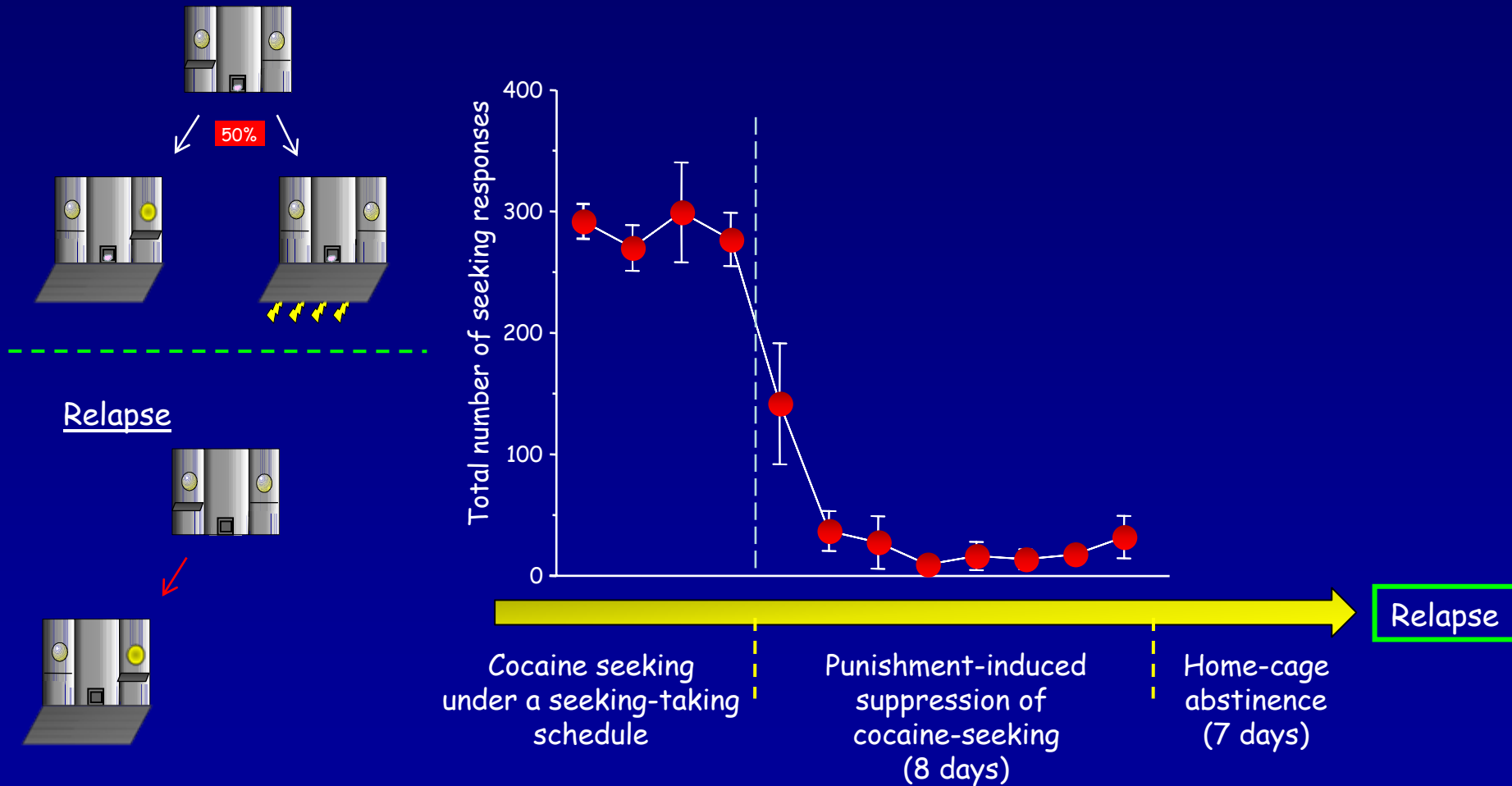
Punishment-induced suppression of cocaine seeking



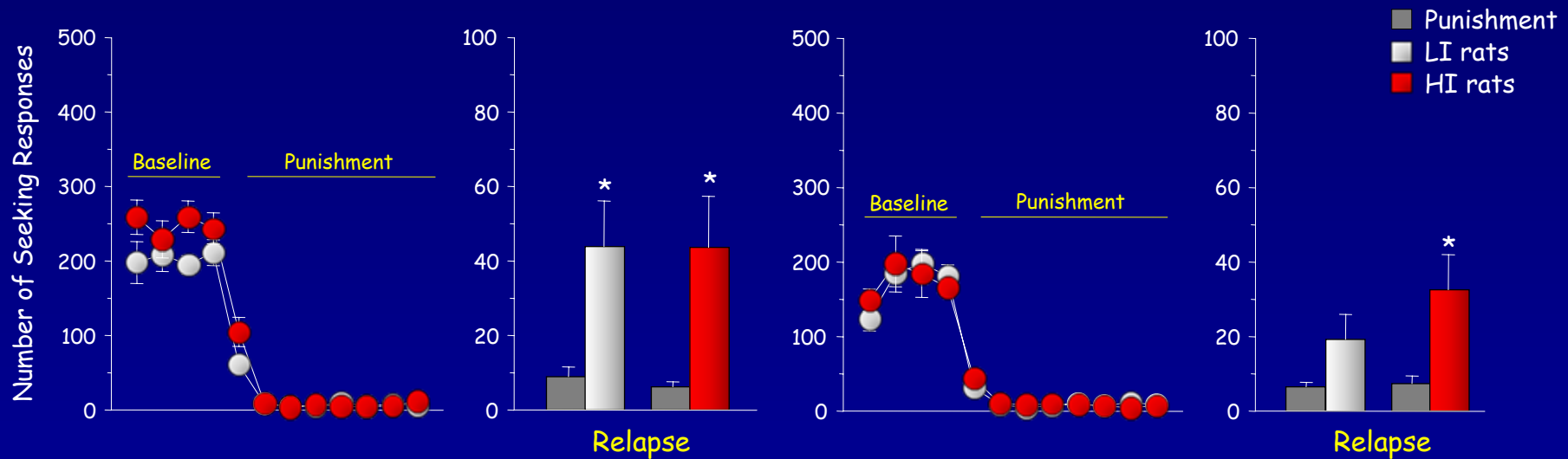


Compulsive drug seeking by rats under punishment: effects of drug taking history

Pelloux Y et al., *Psychopharmacology* 2007

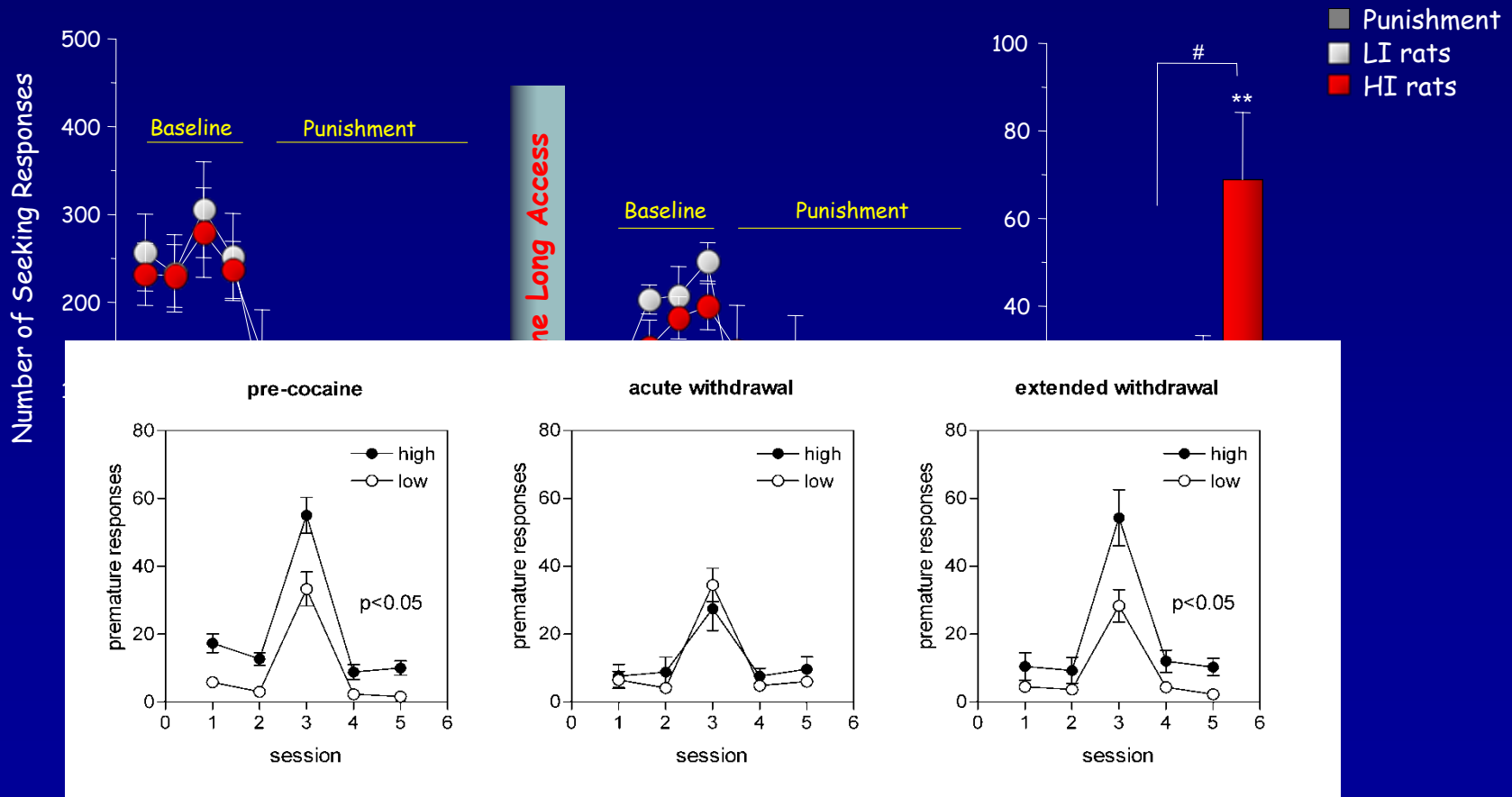


Relapse to cocaine-seeking in HI and LI rats following short cocaine taking history



* $P < 0.05$ versus punishment

Relapse to cocaine-seeking in HI and LI rats following cocaine long access (12 days, 6h/day)

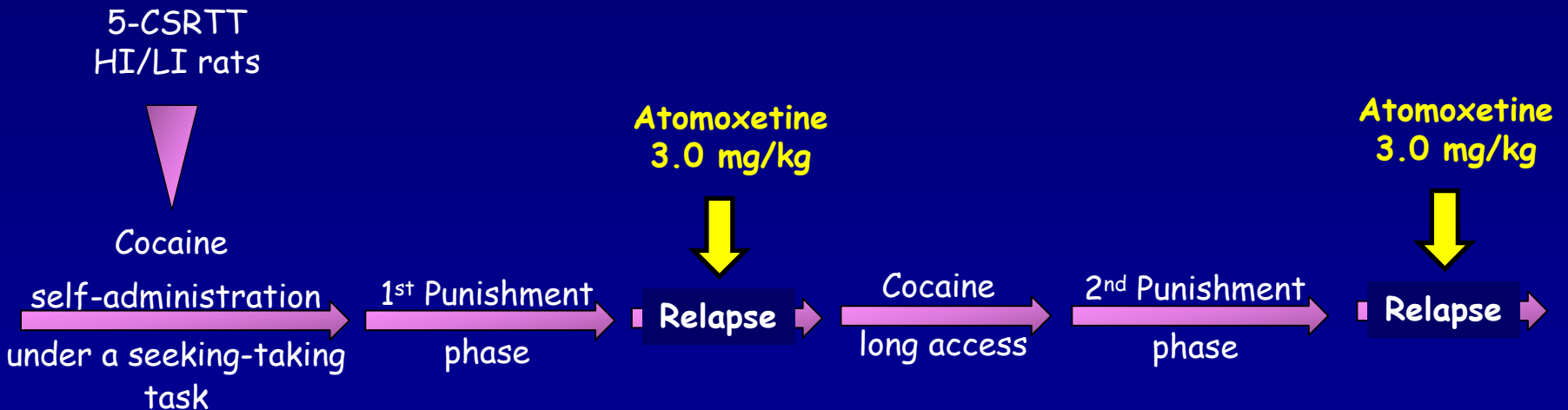


$**$ $P < 0.01$ versus punishment

$\#$ $P < 0.05$ HI versus LI rats

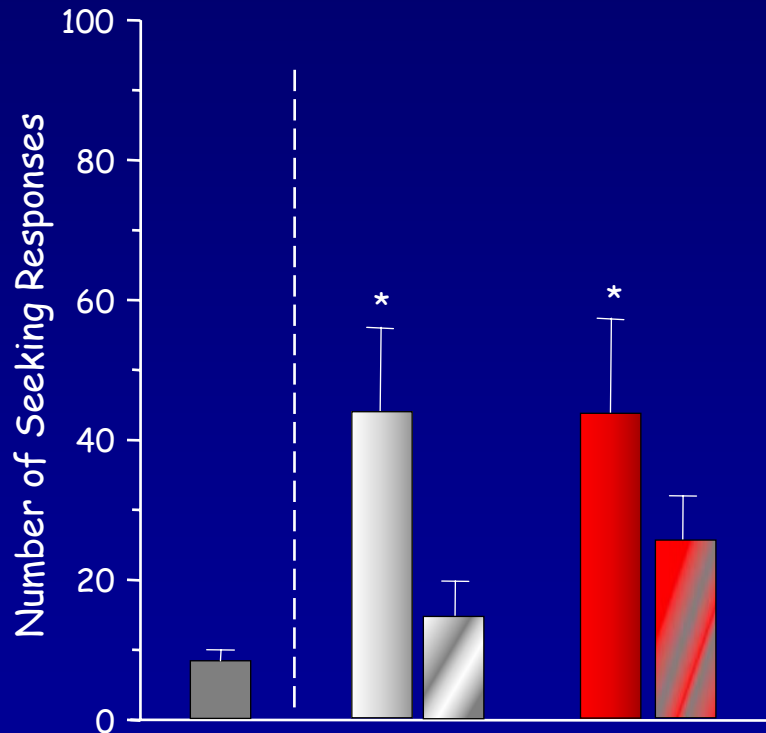
Atomoxetine

- ➡ Selective noradrenaline reuptake inhibitor
- ➡ Clinical efficacy in the treatment of ADHD
- ➡ Shown to reduce impulsive behaviour in both human and animal studies

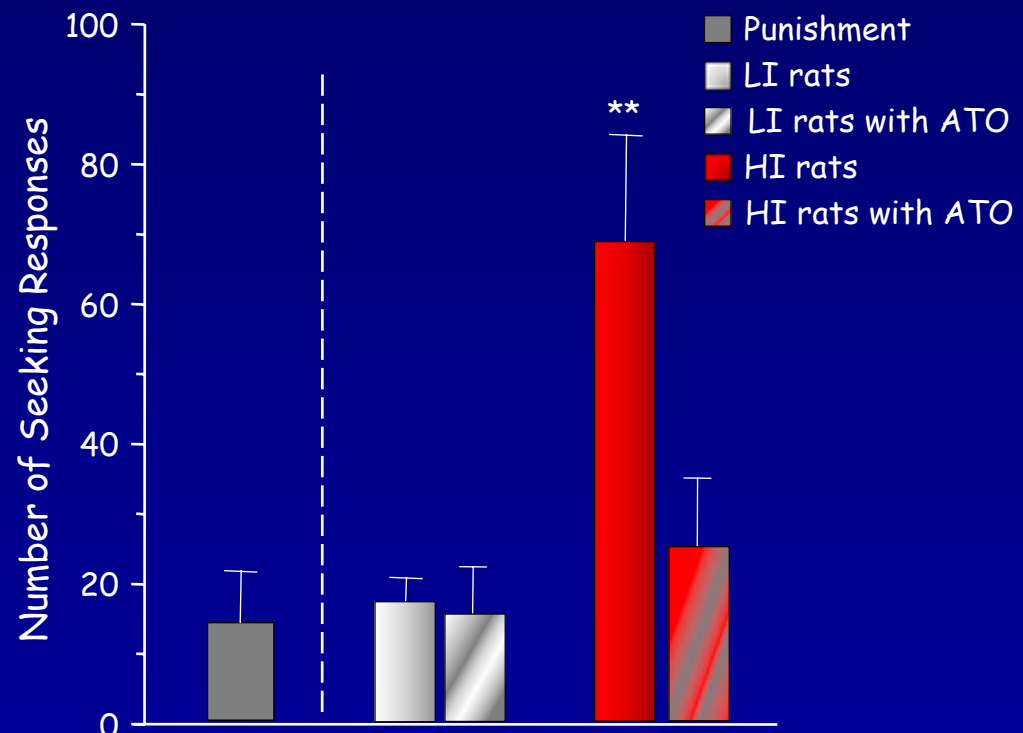


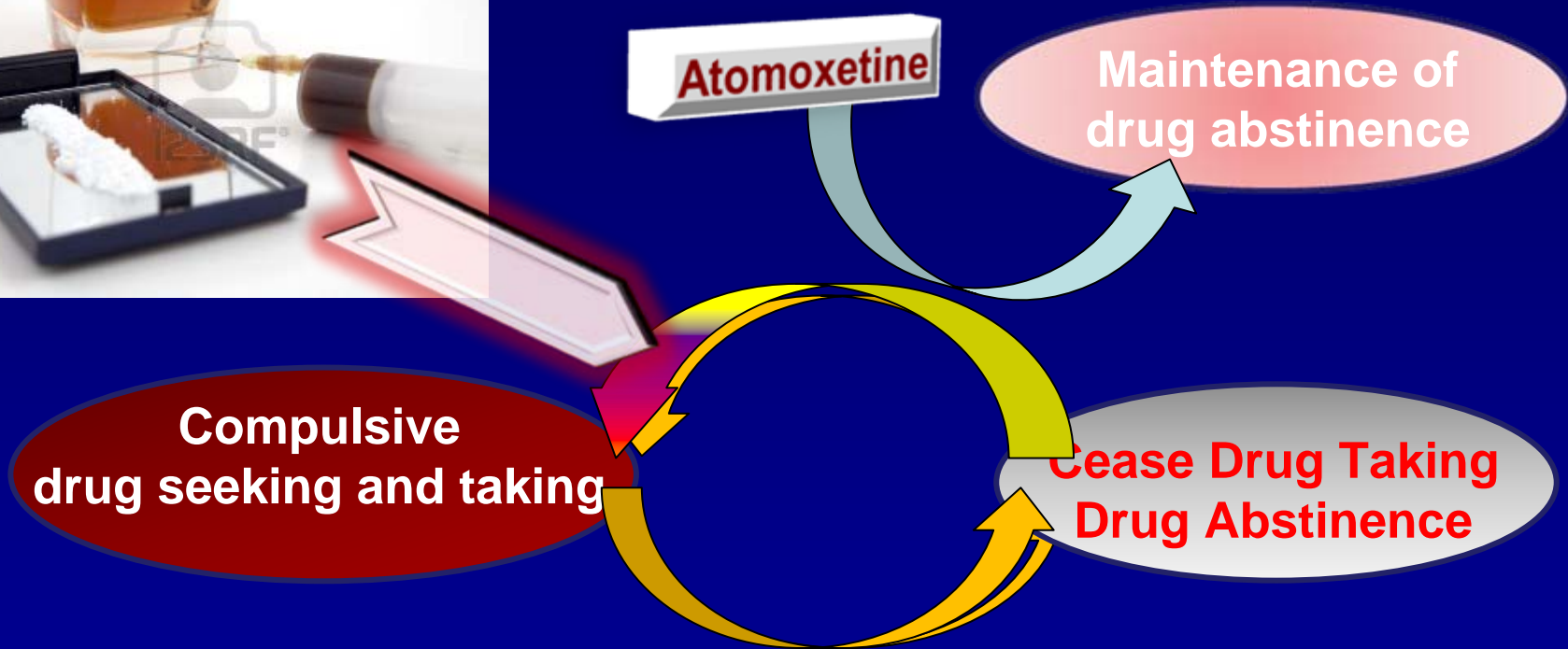
Effect of atomoxetine (3.0 mg/kg, IP) treatment on relapse to cocaine-seeking following punishment-induced abstinence in HI vs LI rats

Following cocaine short access



Following cocaine long access





- Second-order schedule of reinforcement → Cocaine seeking
→ Heroin seeking
- Cue-induced relapse to cocaine seeking following abstinence

*Non-selected animals

Animal models to study CS-controlled drug-seeking and relapse



- Second-order schedule of reinforcement
- Cue-induced relapse following abstinence



Atomoxetine (ATO) Vs Methylphenidate (MPH)

(NET < SERT < DAT)

(DAT < NET < SERT)

- ➔ Clinical efficacy in the treatment of ADHD
- ➔ Reduce impulsive behaviour in both human and animal studies
- ➔ **Distinct pharmacological properties**

	ATO	MPH
NET	5	339
DAT	1451	34
SERT	77	>10000
Ki, nM		

Bymaster et al., Neuropsych. 2002

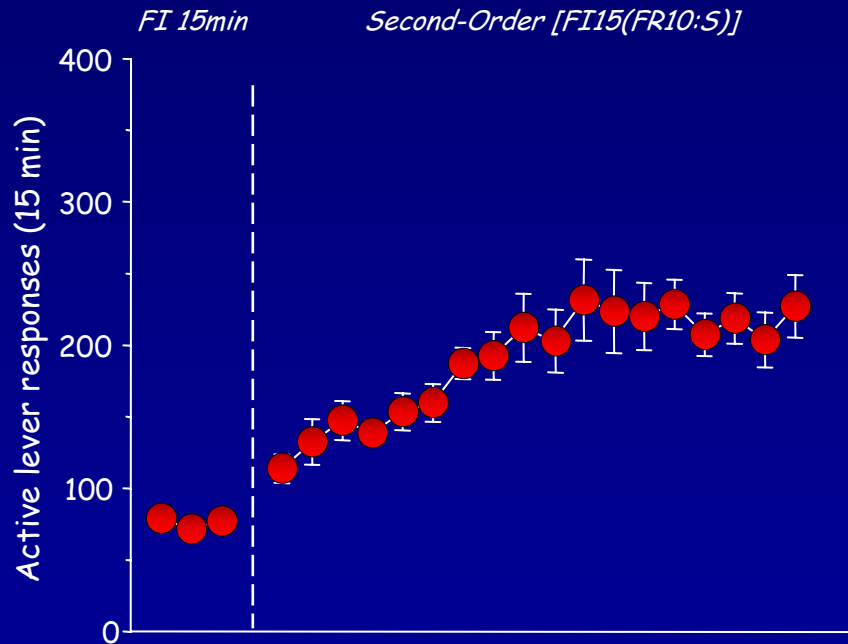
Cocaine seeking under the second-order schedule of reinforcement



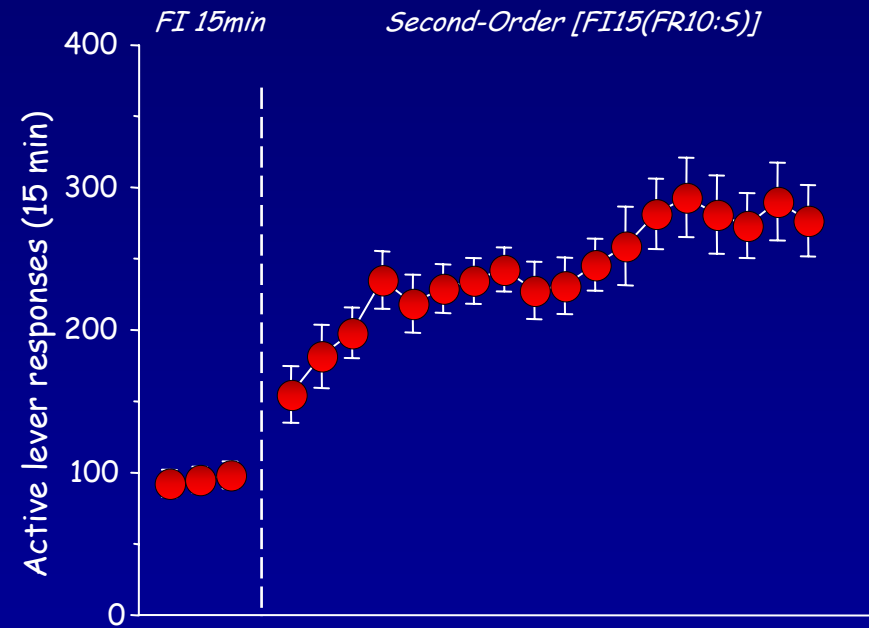
Typical pattern of responding under the second-order schedule of reinforcement

1st drug-free seeking interval

Cocaine

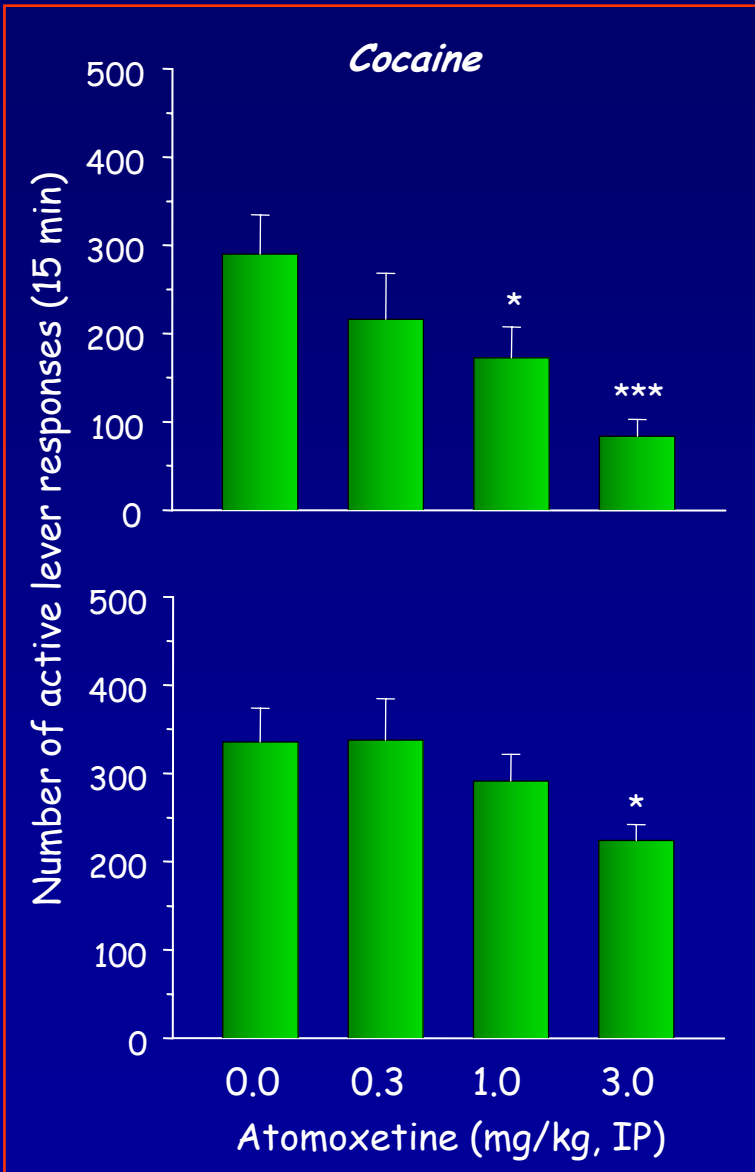


Heroin

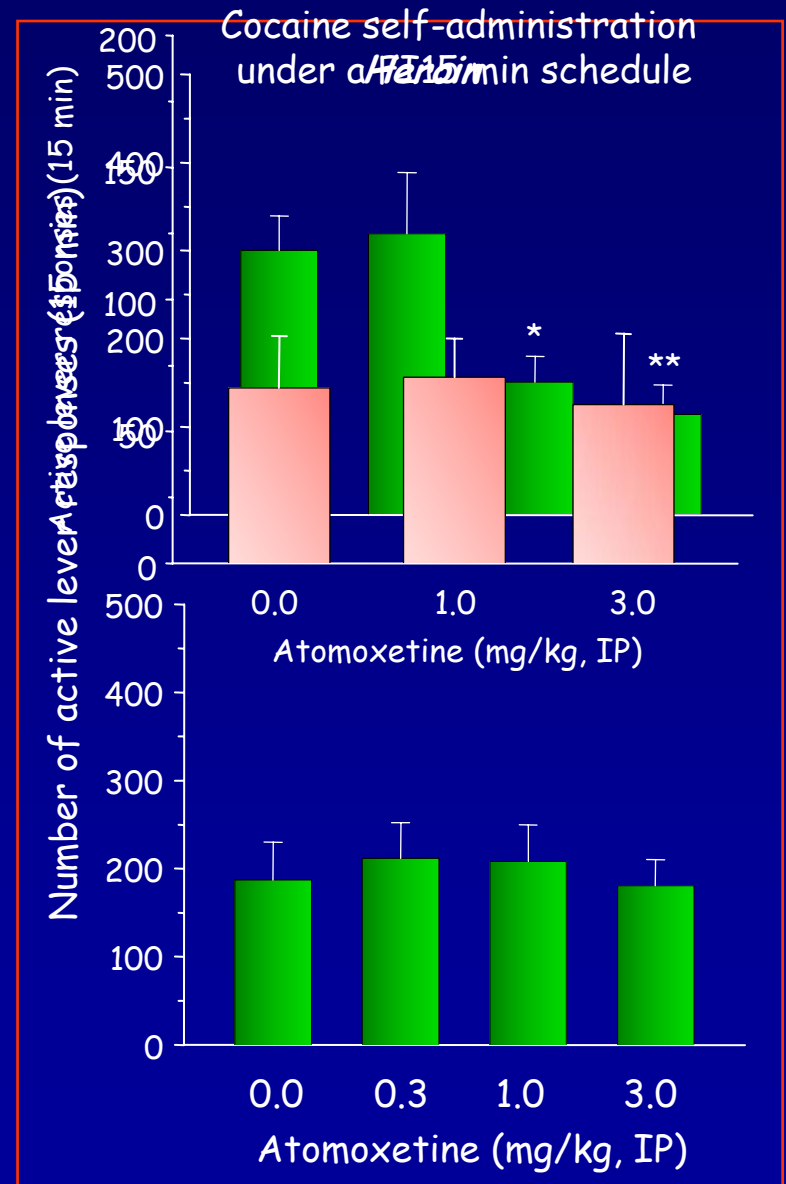


Effect of atomoxetine treatment on cocaine and heroin seeking under the second-order schedule of reinforcement

1st Interval

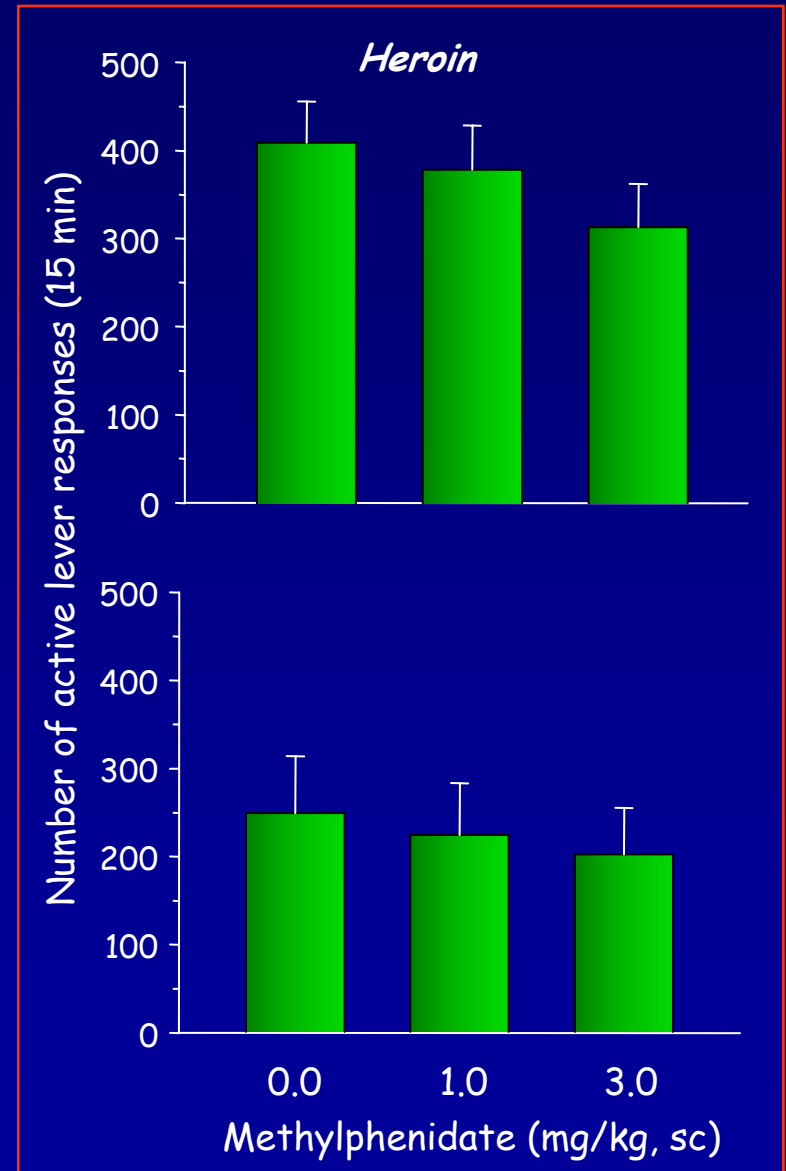
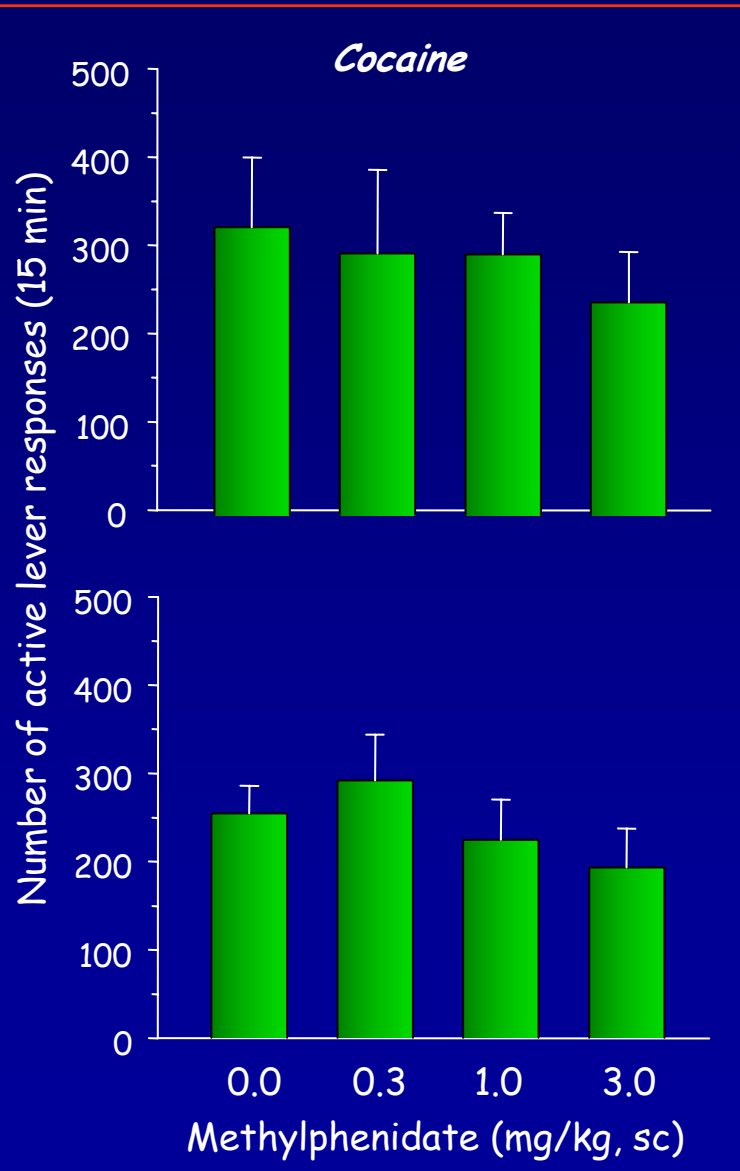


2nd Interval

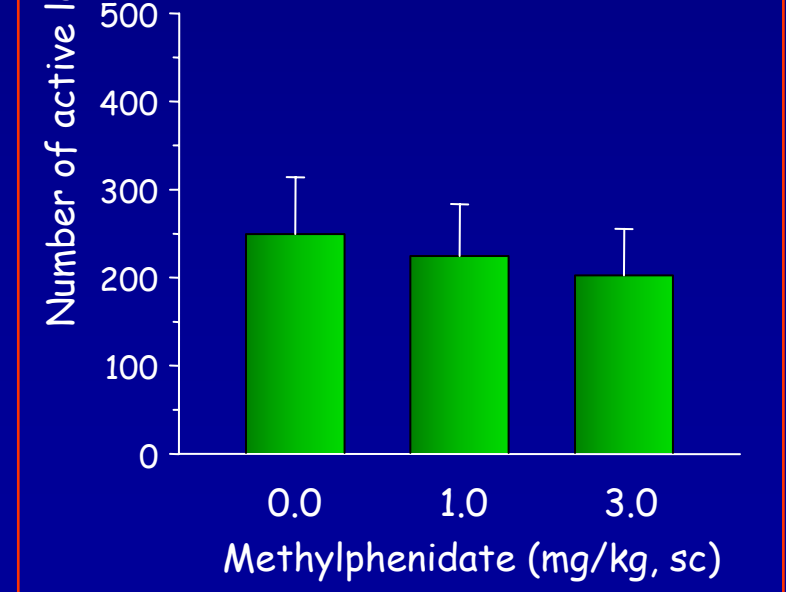
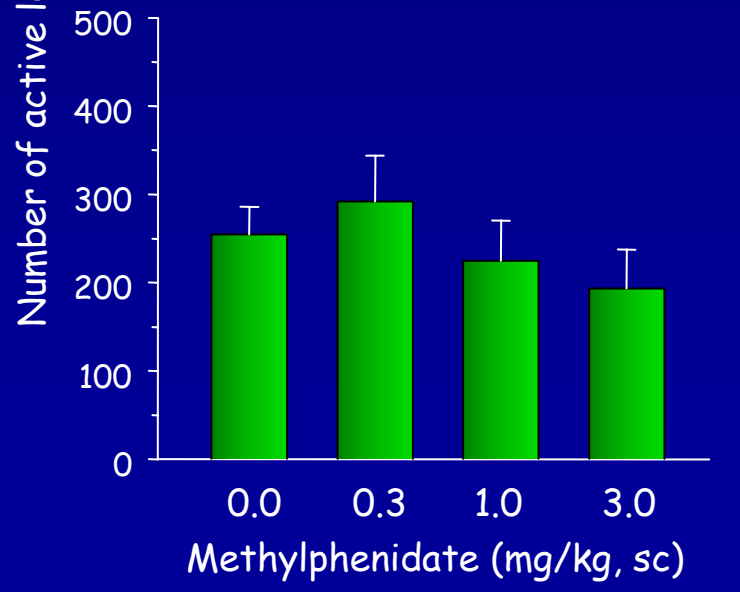


Effect of methylphenidate treatment on cocaine and heroin seeking under the second-order schedule of reinforcement

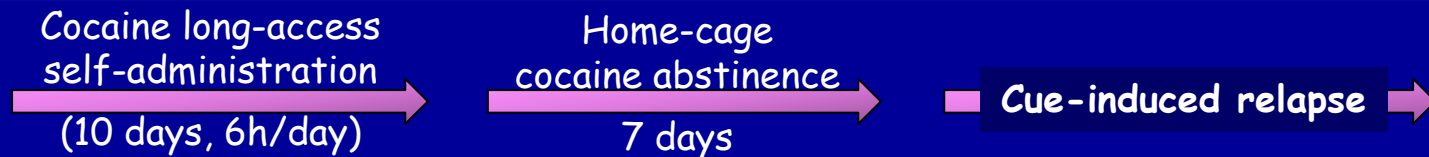
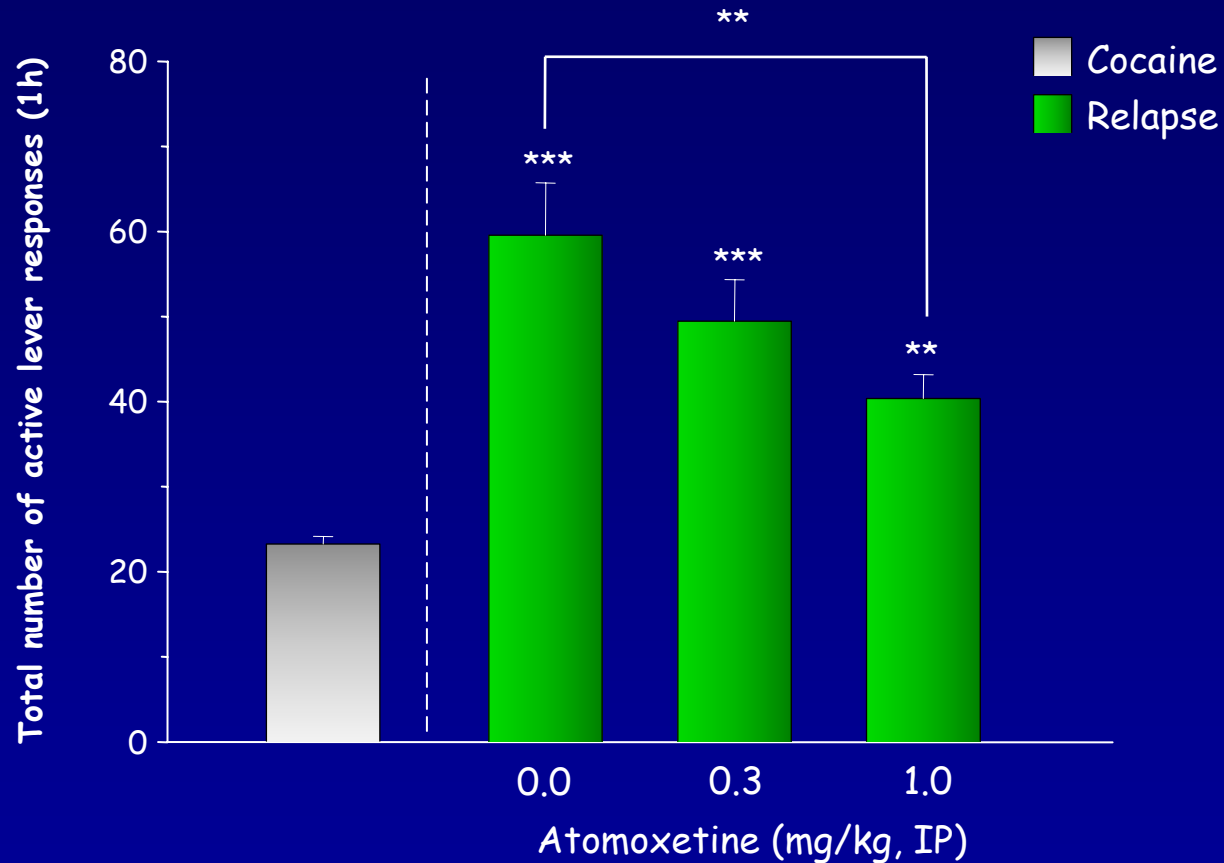
1st Interval



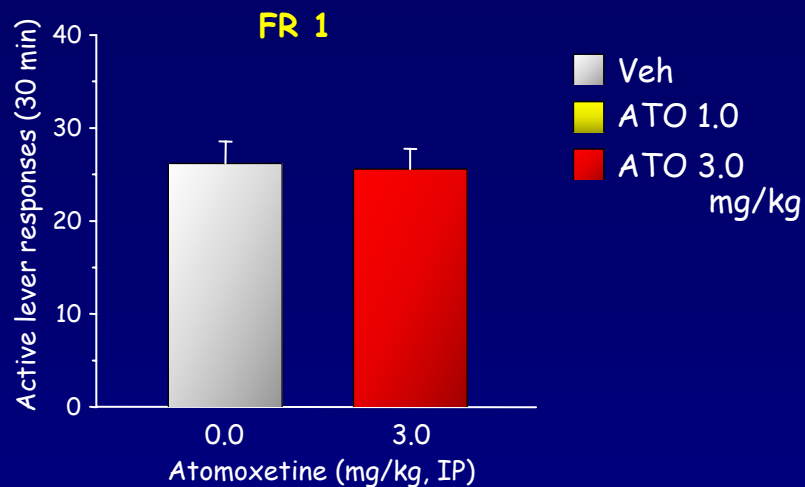
2nd Interval



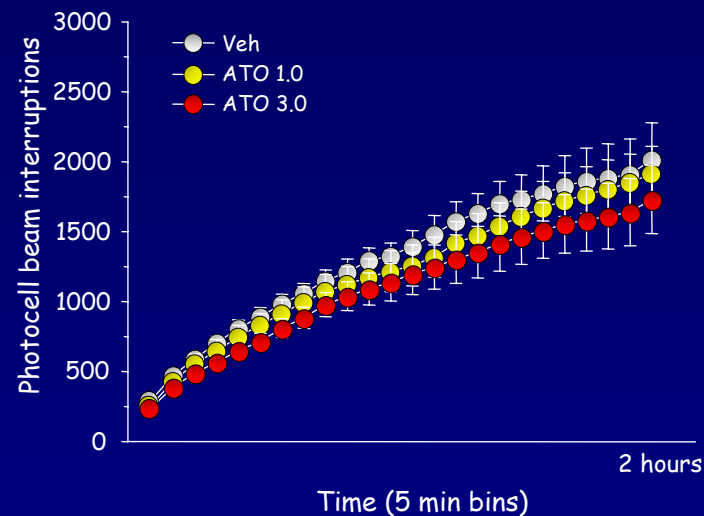
Effect of atomoxetine treatment on cue-induced relapse to cocaine seeking following abstinence



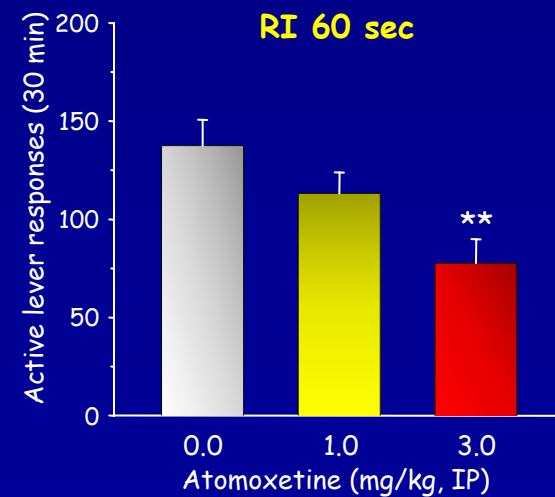
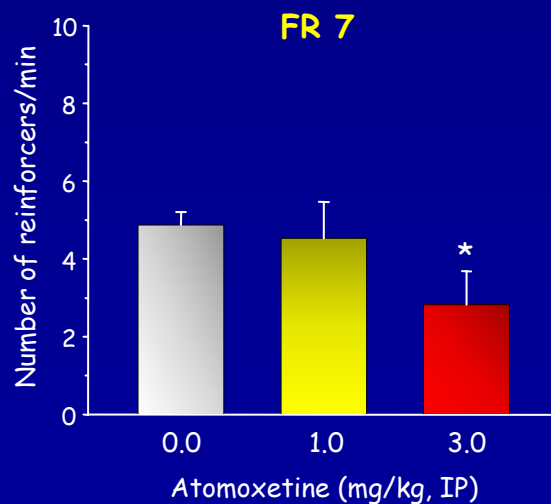
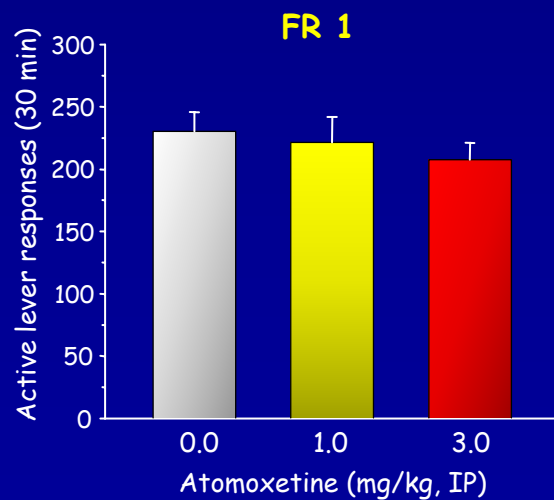
Cocaine self-administration



Spontaneous locomotor activity



Sucrose self-administration



CONCLUSIONS

- ★ Atomoxetine treatment selectively decreased both CS-maintained cocaine- and heroin-seeking.
 - ★ Atomoxetine treatment significantly attenuated the reinstatement of cocaine-seeking following punishment-induced abstinence and conditioned cue re-exposure.
 - ★ These effects were highly selective for cue-controlled drug-seeking and relapse.
-
- ★ Selective NET inhibition by atomoxetine may provide a novel potential therapy for relapse prevention to both stimulant and opiate drug-seeking.
 - ★ An important consideration for the use of atomoxetine in drug addiction treatment is its well known increased tolerability and patient compliance.

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Experimental psychology 2nd floor



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Lilly

Answers That Matter.

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