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Uni-directional relationship between impulsive decision making and heroin seeking

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Introduction

The underlying neural and psychological mechanisms of vulnerability to drug addiction are still poorly understood. Accumulating evidence shows a strong relationship between drug addiction and impulsivity. Drug dependent subjects show elevated levels of impulsive behaviour. Studies in rodents showed a clear relation between pre-existing impulsivity traits and vulnerability to increased nicotine[1] and cocaine[2,3] intake and resistance to extinction of drug seeking behaviour. Since psychostimulants and opiates are pharmacologically different drugs, the question rises whether the neurobiological mechanisms underlying drug addiction are identical for stimulants and opiates, like heroin.

Goal

We aimed to study the interrelationship between impulsive choice and vulnerability for heroin seeking and taking in rats.

Methods

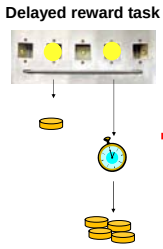


Fig. 1 Delayed reward task (DRT), to assess impulsive choice. Rats choose between a small, immediate reward or a large, delayed reward.

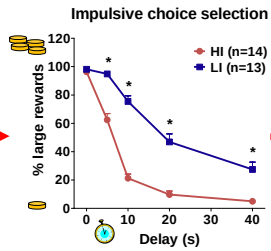


Fig. 2 Selection of high (HI) and low impulsive (LI) rats based on their indifference point (delay at which preference for large reward is 50%). *HI vs LI $p<0.001$

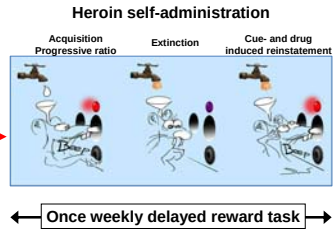
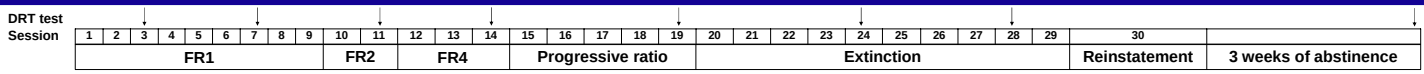


Fig. 3 HI and LI rats were tested in a heroin self-administration paradigm, including acquisition, progressive ratio, extinction, cue- and drug induced reinstatement. Once weekly impulsive choice was re-tested.

Results



Heroin self-administration of HI and LI rats

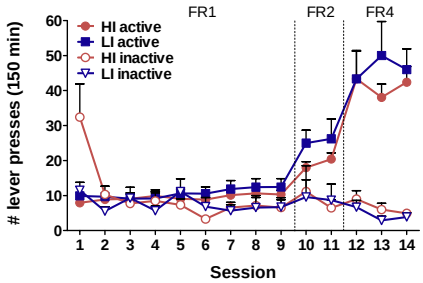


Fig. 4 Acquisition of heroin self-administration (100 mg/kg/infusion, 2.5hr sessions) did not differ between HI and LI rats (FR = Fixed Ratio).

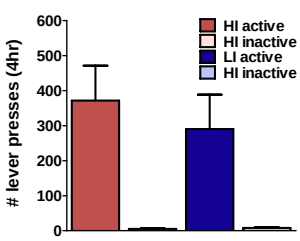


Fig. 5 Similar motivation to self-administer heroin in HI and LI rats (4hr sessions).

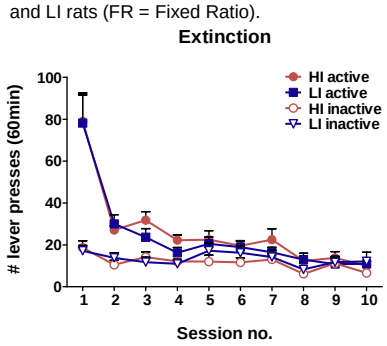


Fig. 6 Extinction of heroin seeking did not differ between HI and LI rats (1hr sessions).

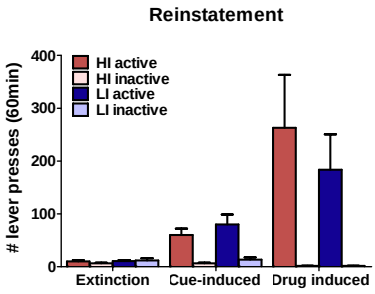


Fig. 7 Cue-induced and drug-induced (0.25 mg/kg heroin s.c.) reinstatement of heroin seeking did not differ between HI and LI rats.

Impulsive choice during heroin self-administration

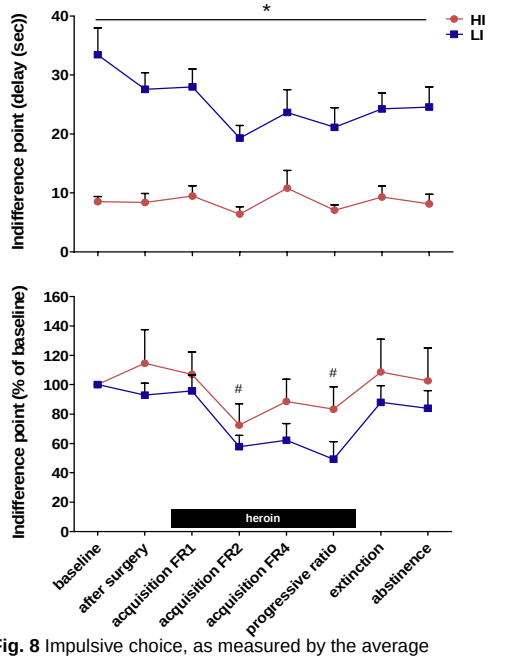


Fig. 8 Impulsive choice, as measured by the average indifference point of distinct experimental stages, increased during heroin self-administration and decreased after 5 weeks of abstinence (session $p<0.05$). *HI vs LI $p<0.001$, #FR2, PR vs baseline, after surgery, extinction, abstinence $p<0.05$

Conclusion

- Impulsive choice does not predict enhanced vulnerability to heroin seeking, as opposed to stimulants. This suggests different underlying neural mechanisms for the vulnerability to opiate and psychostimulant dependence.
- Heroin self-administration resulted in a transient increase in impulsive decision making, resembling elevated impulsivity found in heroin dependent subjects. This suggests that elevated impulsivity in heroin dependence results from heroin intake rather than premorbid impulsivity.
- Clinically, targeting impulsivity might be more effective in stimulant rather than opiate dependence.

1. Diergaarde, L et al., Biological Psychiatry 63, 301–308, 2008
2. Dalley, J.W et al., Science 315, 1267-1270, 2007
3. Belin, D et al., Science 320, 1352-1355, 2008

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ZonMw

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