

## PSYC1022: The Psychology of Addiction

### Topic 10: Cognitive impairments & psychiatric comorbidity

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#### Outline:

- Types of impairments
  - Attention
  - Memory
  - Reversal learning
  - Habits/response inhibition
- Psychiatric comorbidity
  - Impulsivity
  - Psychosis
  - Depression

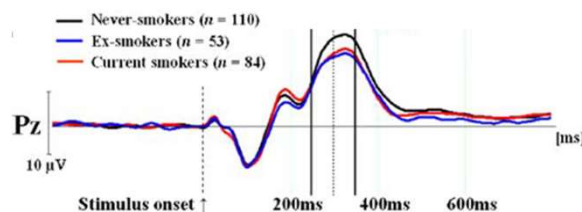


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## Impairments: Nicotine & Attention

Neuhaus et al. (2006): examined attention impairments in ex-smokers to determine if there were persistent abnormalities.

- Oddball paradigm: same stimulus presented repeatedly, randomly interspersed with a different stimulus.
- Electroencephalography (EEG): records electrical activity of the brain from the scalp using a network of electrodes
- Found the characteristic P300 waveform in response to the oddball stimulus after the oddball had been presented
  - never-smokers showed a larger P300 compared to current-smokers & ex-smokers
    - impairment increased in those who had smoked for greater years
- Implies that the impairment was caused by damage from accumulated exposure to nicotine, rather than withdrawal.



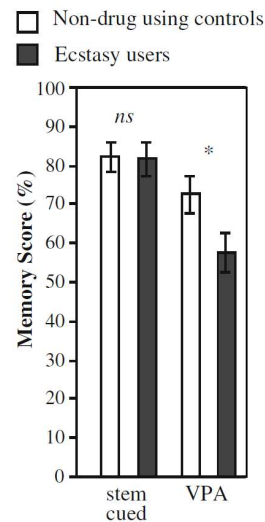
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## Impairments: MDMA & Memory

MDMA produces neurotoxic damage in both animals (Wang et al., 2004) & humans (Cowan et al.).

Brown et al (2010): investigated memory deficits in human ecstasy users

- Verbal Paired Associates (VPA) task: subjects learn a word pair such as “frog–table” by deliberately generating a sentence or visual image (mnemonic) linking the two words. At test they are given the word “frog” & asked to recall the associated word (i.e. “table”)
- Stem cued recall task: subjects are given a list of words (e.g. calorie, vehicle, football). Then at test, subjects are asked to complete a series of stems (e.g. cal\_\_\_\_, veh\_\_\_\_, foo\_\_\_\_) with words they saw on the list.
- Ecstasy users showed a selective memory impairment in the VPA but not cued stem completion.
  - impairment apparent only in complex memory tasks



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## Impairments: Reversal learning

Lucantonio et al. (2012)

Reversal learning test: probes the ability to change behaviour in the face of changed outcomes that occur as a result of that behaviour.

- Acquisition: a rat is reinforced with food for pressing a lever on their left-hand side (“correct”), whereas pressing a lever on their right-hand side (“incorrect”) is punished by a time-out period.
- Reversal stage: the “correct” & “incorrect” levers are switched
  - number of errors in choosing the “old-correct” (“left”) lever indexes the inability to learn the new “correct” response strategy (now I should press “right” lever to obtain food)

Evidence that cocaine & meth render animals less able to learn to switch strategies

- bears similarity to addicts who must stop taking drugs in the face of adverse consequences

Drug	Species	Experimental procedure	Training dose; treatment schedule	Withdrawal period	Behavioral impairment	Refs.
Cocaine	Monkey	EA	2 or 4 mg kg <sup>-1</sup> per day i.p.; 14 days, 1 injection per day	9 and 30 days	Object discrimination reversal task	71
		SA	0.1 to 0.5 mg kg <sup>-1</sup> per infusion; 9 months, 6 infusions per day	3 days	Reversal task; delayed match-to-sample task	72
	Rat	EA	30 mg kg <sup>-1</sup> per day i.p.; 14 days, 1 injection per day	3–6 weeks	Odor discrimination reversal task; reinforcer devaluation task; delay discounting task	73,97,86,87,89
		SA	0.75 mg kg <sup>-1</sup> per infusion; 14 days, 60 infusions per day	4 weeks	Odor discrimination reversal task; Pavlovian overexpectation task	74, F.L. et al. <sup>a</sup>
Methamphetamine	Mouse	EA	30 mg kg <sup>-1</sup> per day i.p.; 14 days, 1 injection per day	2 weeks	Instrumental reversal task; delayed matching-to-position task	75
	Rat	EA	2 mg kg <sup>-1</sup> s.c.; 1 day, 4 injections	3–5 days	Reversal discrimination task; attentional set shifting task	76

EA, experimenter-administered; SA, self-administered; i.p., intraperitoneal injection; s.c., subcutaneous injection.

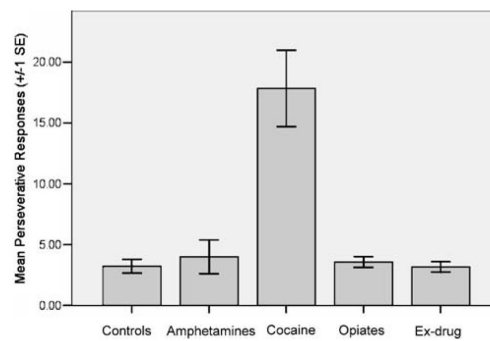
<sup>a</sup>F. Lucantonio et al. *Soc. Neurosci. Abst.* 707.707/MMM709, 2010.

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## Impairments: Reversal

Ersch et al (2008): found a reversal learning deficit in cocaine addicts, but not amphetamine or opiate addicts, or ex-addicts.

- Whether an impairment could be seen in these groups using a learning procedure more similar to the animal model remains to be seen.
- For now, we might conclude that reversal learning abnormalities may be a contributory factor in addiction, but is not necessary for addiction.



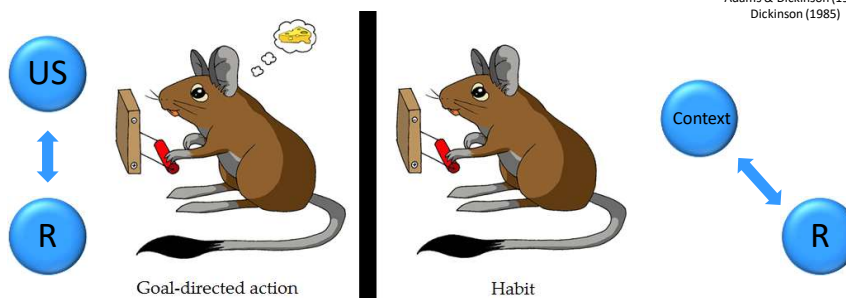
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## Impairments: Habits/Response Inhibition

Two types of instrumental behaviour that determine how an organism comes to make a reward-seeking response:

1. A “goal-directed” instrumental response is where the animal retrieves an idea of the reward (US) & how valuable it is & selects the response (R) which it believes will produce that reward.
2. “Habitual” instrumental responses are acquired after extended training. Here, the animal no longer retrieves an idea of the reward, rather, the context/cues elicit the response or automatically.

Adams & Dickinson (1981)  
Dickinson (1985)



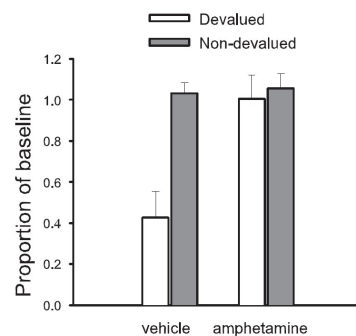
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## Impairments: Habits

It has been argued that addicts are more prone to habit learning (Hogarth et al. 2012)

Nelson & Killcross (2006): outcome-devaluation procedure in chronic amphetamine vs. vehicle control rats.

- Instrumental training: Rats learned to press a lever (R) for food (US)
- Devaluation: Food was devalued by making rats sick after they had eaten it.
- Test: rats in the “vehicle & devalued” group were given the opportunity to press the lever & they chose not to, compared to “vehicle & non-devalued” counterparts. But, rats that had been chronically pre-exposed to “amphetamine & devalued” failed to show this devaluation effect.
  - indicates that amphetamine exposed rats were less able to act intentionally & favoured habits.



Pacitti, Balleine & Killcross (2018): rats chronically exposed to meth also show habit dominated instrumental behavior.

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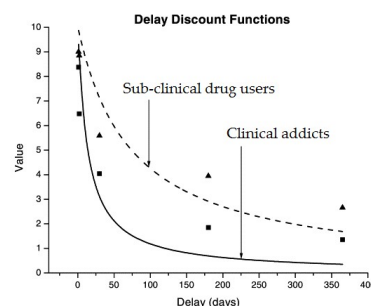
## Psychiatric: Impulsivity

Impulsivity: the tendency to do things without thinking about the consequences.

Standford et al (2009): Impulsivity found in a variety of psychiatric conditions.

MacKillop et al (2011): Delay discounting task: subjects say which they would prefer, a smaller amount of money now, or a larger amount of money later.

- From this data, one can calculate a discount function, which indicates that the perceived value of the delayed money decreases with longer delays
- addicts had much steeper discount functions compared to sub-clinical users, suggesting they are more impulsive in being attracted by immediate rewards, and/or have shorter ‘temporal horizons’ for contemplating future prospects



Conclusion from MacKillop et al. 2011;  
Figure adapted from Reynolds et al. 2004

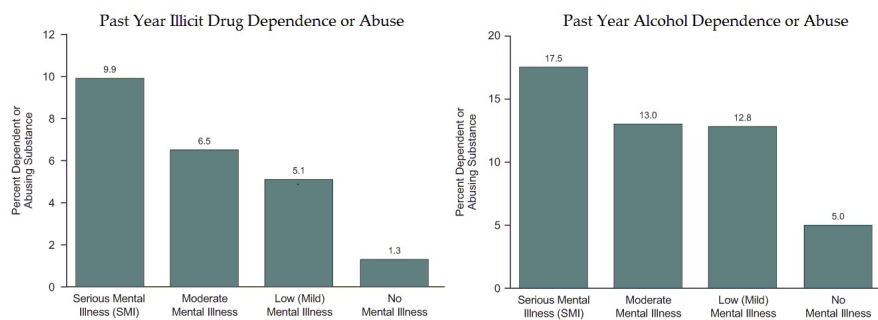
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## Psychiatric Comorbidity

Comorbidity between substance use disorders & mental illness is well documented.

2014 SAMHSA (US national survey): 43.6m mental illness, 20.2m substance use disorder & of these 7.9m had “dual diagnosis”

2011 SAMHSA: probability of substance use disorder diagnosis increased linearly with the level of mental illness severity (figure below).

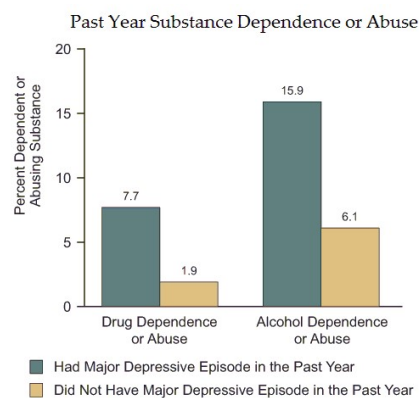


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## Psychiatric: Depression

The relationship is especially strong for depression & substance use disorders.

- SAMHSA (2011): a depressive episode in the previous year was associated with nearly a threefold increase in the likelihood of drug or alcohol dependence.
- Causality: Does drug use cause mental illness, or mental illness cause drug use, or are both caused by a third variable?



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## Psychiatric: Psychosis

Moore et al (2007): meta-analysis of longitudinal studies which assessed the psychiatric status of youth prior to cannabis use & again in adulthood after some had used cannabis.

- These studies can shed light on whether cannabis use lead to psychiatric illness, by looking at whether psychiatric status changes following cannabis exposure.
- Key measure was the odds ratio for the risk of psychosis diagnosis at follow-up. The odds ratios reflect the increased risk of diagnosis of psychotic symptoms in individuals who had engaged in heavy cannabis use compared to those who had not.
- Overall odds ratio was 2.09, indicating a doubling of the risk of psychotic symptoms given heavy cannabis use.

Methamphetamine has also been linked to psychosis (McKetin et al., 2006)

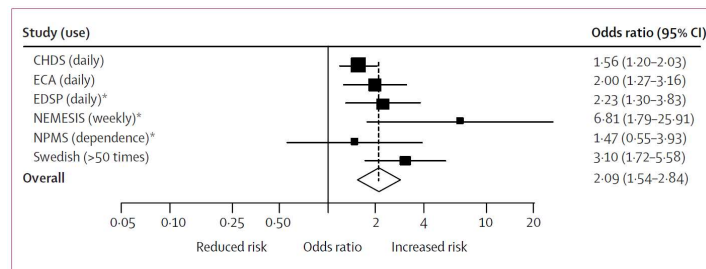


Figure 2: Forest plot showing adjusted odds ratios and 95% CI for any psychosis outcome according to most frequent use of cannabis in individual studies

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## Psychiatric: Depression

Moore (2007): average odds ratio across studies for diagnosis of depression given heavy cannabis use was 1.49. A 50% increase in the risk of becoming depressed if one used cannabis heavily in adolescence compared to the non-heavy cannabis using population.

- However, there was more inconsistency between studies in this finding
  - some reported a lower odds ratio, closer to 1 meaning equal risk
  - one study found an odds ratio <1, suggesting a lower risk of depression

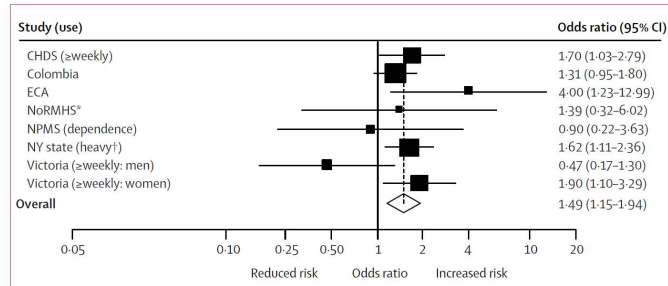


Figure 4: Forest plot showing adjusted odds ratios and 95% CI for depression outcomes according to most frequent use of cannabis in individual studies

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## One impairment or many?

Hart et al. (2012): such impairments in addicts often fall within the normal range of the population as a whole, albeit within the lower range.

- If these impairments/disorders cause addiction, why isn't the entire population addicted? The answer is that addiction is determined by a multitude of factors
  - You need to both try & enjoy the drug to establish drug use in the first place, whereas it is the growth of a combination of the impairments described in this lecture which multiply ones risk of falling into the severe or clinical category as one's drug use career progresses.

Cognitive	Learning	Psychiatric
Attention	Reversal	Impulsivity
Memory	Habit	Depression
		Psychosis

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## Summary

Knowledge of and understanding:

- that chronic nicotine use is associated with impaired attention as measured by EEG during the oddball task.
- that MDMA users perform more poorly on complex memory tasks compared to non-users.
- of reversal learning paradigms & that animals exposed to cocaine & meth are less able to switch strategies in the face of changed outcomes.
- of goal-directed actions & habits & that animals chronically exposed to amphetamine & methamphetamine show a bias for habits.
- impulsivity & the finding that individuals with substance use disorders appear to be more attracted to immediate rewards compared to larger future rewards.
- substance use disorders are often comorbid with mental health disorders, particularly psychosis & depression, but that does not mean that one causes the other.

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