KING'S College LONDON

INSTITUTE OF PSYCHIATRY, PSYCHOLOGY & NEUROSCIENCE

Module:
Biological foundations of mental health

Week 5:
Reward, emotion and action

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Topic 3
The reward system of the brain

Reward

- Humans, as well as other organisms engage in behaviours that are rewarding
- The pleasurable feelings provide positive reinforcement so that the behaviour is repeated.
- There are natural rewards as well as artificial rewards, such as drugs of abuse

Natural Rewards

Food, Water, Sex, Nurturing

↓

Pleasure feelings

↓

Reinforcement of the behaviour

↓

Repetition of the behaviour

The reward system of the brain

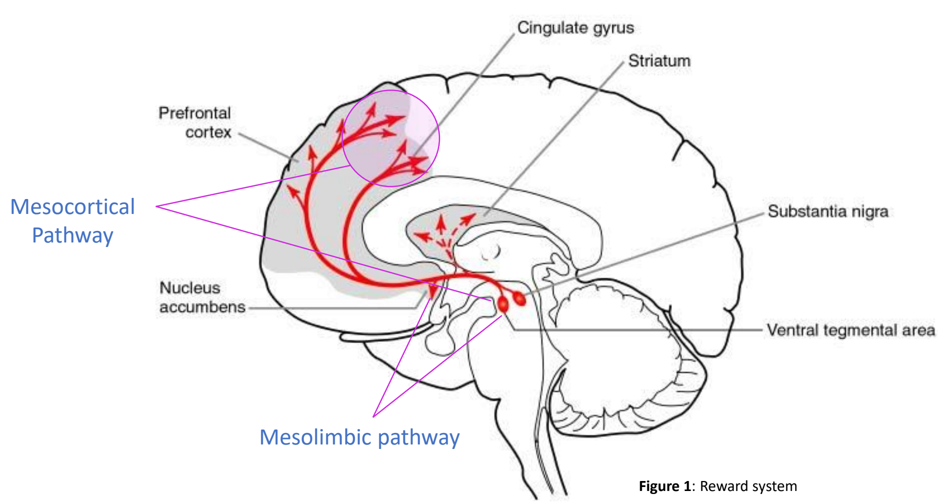


Figure 1: Reward system

Discovery of the reward pathway

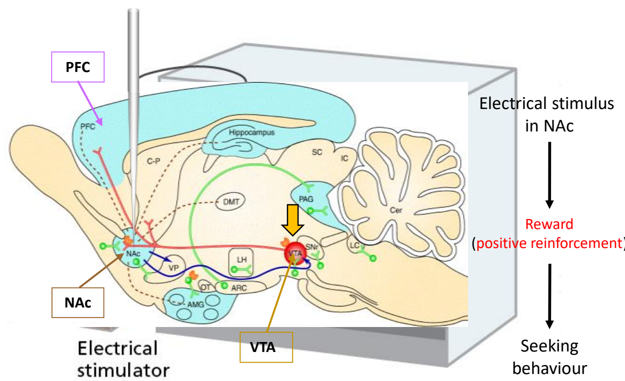


Figure 3: Self-stimulation experiments pioneered by Olds and Milner (1954)

Figure 2: Reward pathways along the medial forebrain bundle

Reinforcing drugs stimulate the release of dopamine in the NAc

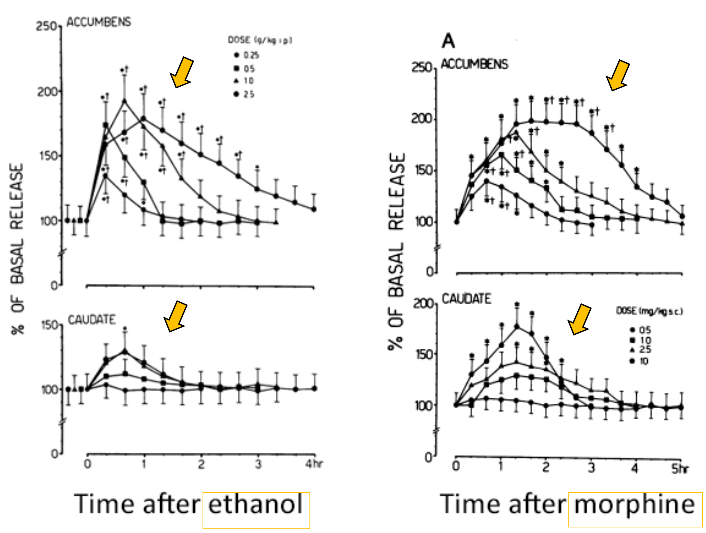


Figure 4: Drugs stimulate the release of dopamine

Striatal Dopamine neurotransmission abnormalities in obesity and addiction

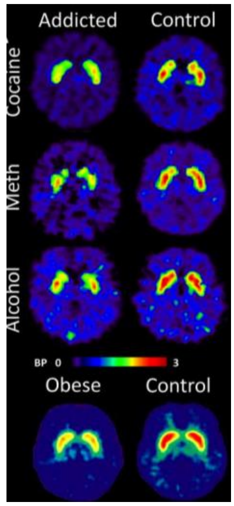


Figure 5: PET scans for quantification of dopamine D2/D3 receptor levels in the human brain

Consequences for dopamine function in drug abusers

- Dopamine's impact on the reward circuit in the brain of drug abusers becomes abnormally low, and the ability to experience any pleasure is reduced.
    - This is why the abuser eventually feels flat, lifeless, and depressed, and is unable to enjoy things that previously brought them pleasure.
- They need to take drugs just to try and bring their dopamine function back up to normal.
- They develop tolerance, requiring larger amounts of the drug to create the dopamine high.

Reinforcing drugs use different mechanisms to increase dopamine release in the NAc

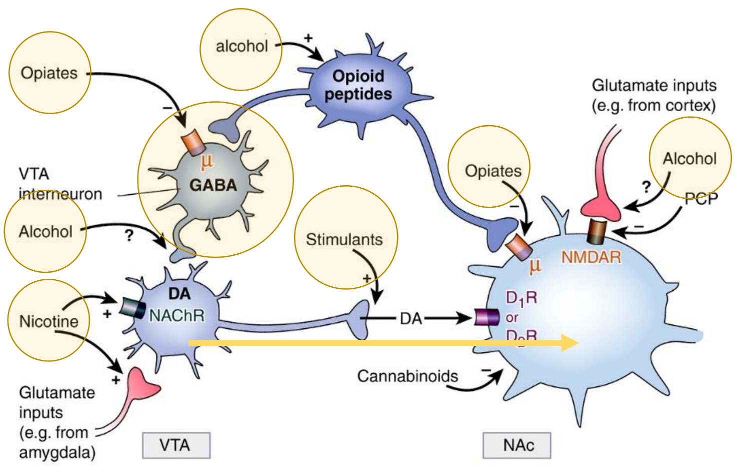


Figure 6: Mechanisms to increase dopamine release

Opiates (heroin) and alcohol:
↓ GABA transmission in the VTA => disinhibition of dopamine neurons => dopamine release

Nicotine:
Excites dopamine cells directly

Psychomotor stimulants (cocaine, amphetamines):
interact with the DA transporter (DAT) => ↑ extracellular dopamine levels.

Opiates and alcohol can also act directly on the NAc, in a dopamine-independent manner

Rewarding mechanisms: More than dopamine

- Perspective on dopamine's role in reward has changed slightly
- Dopamine now thought to be involved in aspects of reward other than direct experience of pleasure
- Mesolimbic dopamine system plays important role in reward, but perhaps the role many not be as hedonic as previously thought
- The readings below refer to experimental examples that suggest that dopamine is not a pleasure signal, but a signal for motivated behaviour
- Current view: dopamine increases motivation components of reward
- Another alternative hypothesis holds that dopamine causes 'learning'

Suggested reading material (see reading list for this topic)
Hnasko TS, Sotak BN, Palmiter RD (2005). *Nature*, 438:854–857.
Robinson et al, *Behav Neurosci*. 2005 Feb;119(1):5-15
Berridge & Kringelbach, *Neuron* Volume 86, Issue 3, 6 May 2015, Pages 646–664

The reward system: more than the mesolimbic VTA/NAc pathway

KEY
Red arrow = input from the vmPFC
dark orange arrow = input from the OFC
light orange arrow = input from the dACC
yellow arrow = input form the dPFC
brown arrows = connections of the reward circuit
Amy = amygdala
dACC = dorsal anterior cingulate cortex
dPFC = dorsal prefrontal cortex
Hipp = hippocampus
LHb = lateral habenula
hypo = hypothalamus
OFC = orbital frontal cortex
PPT = pedunculopontine nucleus
S = shell
SNc = substantia nigra pars compacta
STN = subthalamic nucleus
Thal = thalamus
VP = ventral pallidum
VTA = ventral tegmental area
vmPFC = ventral medial prefrontal cortex

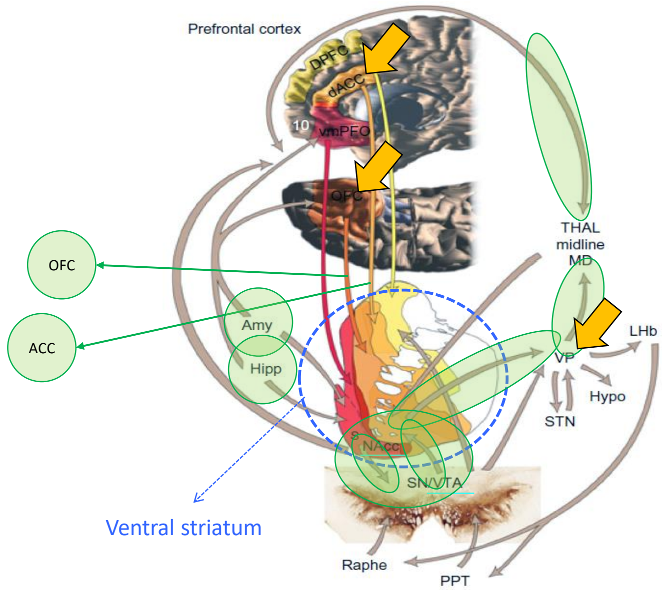


Figure 7: Key structures and pathways of the reward circuit

The Monetary Incentive Delay (MID) Task

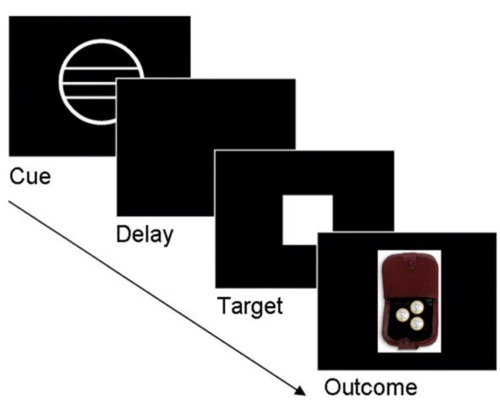
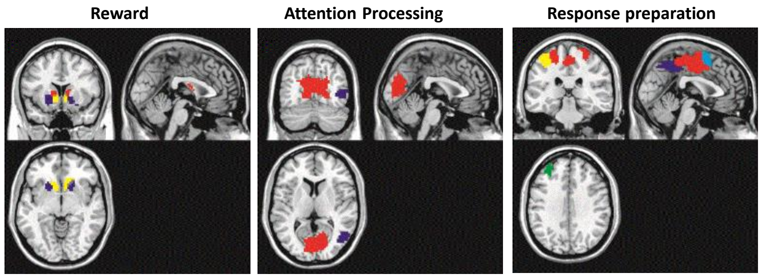


Figure 8: Structure of the MID Task

Studying the neural basis of reward anticipation and its relation to psychopathology



Associations of Functional clusters and externalizing behaviours			
	Reward cluster	Attention processing cluster	Response preparation Cluster
ADHD (in boys)	Low activation	Non-significant	Non-significant
Addiction (alcohol)	Non-significant	Neg association	Neg association

Figure 9: Functional brain clusters activated during reward anticipation in the MID task

Summary

- The reward system refers to a group of structures that seem to be frequently involved in mediating rewarding experiences
- While the mesolimbic VTA-NAc pathway is implicated in pleasurable and potentially addictive behaviors, the substrates of pleasure are not confined to these structures
- Dopamine is not the only neurotransmitter involved
- The actual network dedicated to creating the feelings we associate with these experiences is likely more complex
- Current research using neuroimaging approaches aims at better understand the distinct contribution of components of the reward system in psychiatric disorders such as drug addiction, ADHD and depression

Figure references

1. **Figure 1 & 6**: Hyman SE, Malenka RC, Nestler EJ (2006). Neural Mechanisms of Addiction. The Role of reward-related learning and memory. *Annu. Rev. Neurosci*. 29:565-98, doi: 10.1146/annurev.neuro.29.051605.113009
2. **Figure 2**: Mouse figure from: 'Resetting the Addictive Brain | DiscoverMagazine.com'. *Discover Magazine*. Accessed 31 March 2016. http://discovermagazine.com/2015/may/17-resetting-the-addictive-brain.
3. **Figure 4**: Di Chiara G and Imperato A (1988). Drugs abused by humans preferentially increase synaptic dopamine concentrations in the mesolimbic system of freely moving rats, *PNAS* 85, 5274 – 5278.
4. **Figure 5**: Tomasi D, Volkow ND (2012). Striatocortical pathway dysfunction in addiction and obesity: differences and similarities. *Crit Rev Biochem Mol Biol* 48: 1-19, DOI: 10.3109/10409238.2012.735642
5. **Figure 7**: Haber SN, Knutson B (2010). The Reward Circuit: Linking Primate Anatomy and Human Imaging. *Neuropsychopharmacology*. 35(1): 4–26.
6. **Figure 8**: Knutson B1, Westdorp A, Kaiser E, Hommer D. FMRI visualization of brain activity during a monetary incentive delay task. *Neuroimage*. 2000 Jul;12(1):20-7.
7. **Figure 9**: Jia T, Macare C, Desrivières S, Gonzalez DA, Tao C, Ji X, Ruggeri B, Nees F, Banaschewski T, Barker GJ, Bokde AL, Bromberg U, Büchel C, Conrod PJ, Dove R, Frouin V, Gallinat J, Garavan H, Gowland PA, Heinz A, Ittermann B, Lathrop M, Lemaitre H, Martinot JL, Paus T, Pausova Z, Poline JB, Rietschel M, Robbins T, Smolka MN, Müller CP, Feng J, Rothenfluh A, Flor H, Schumann G; IMAGEN Consortium (2016). Neural basis of reward anticipation and its genetic determinants. *Proc Natl Acad Sci* U S A. pii: 201503252.