PSYC1022: The Psychology of Addiction

Topic 11: Brain mechanisms of impaired behavioural regulation

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Outline:

- Frontal damage in addiction
- Orbitofrontal Cortex (OFC)
  - Expected reward
  - Expected costs
  - Reversal learning
  - Time costs
  - Delay discounting
- Dorsolateral Prefrontal Cortex (DLPFC)
  - Temporal horizon
  - Self-control
  - Contextual control

Cerebral lobes: the frontal lobe (pink), parietal lobe (green) and occipital lobe (blue)

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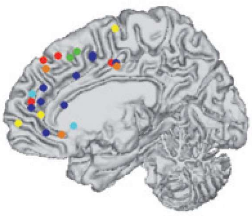
Frontal damage in addiction

Table 1 | **Processes associated with the prefrontal cortex that are disrupted in addiction**

Process	Possible disruption in addiction	Probable PFC region
Self-control and behavioural monitoring: response inhibition, behavioural coordination, conflict and error prediction, detection and resolution	Impulsivity, compulsivity, risk taking and impaired self-monitoring (habitual, automatic, stimulus-driven and inflexible behavioural patterns)	DLPFC, dACC, IFG and vlPFC
Emotion regulation: cognitive and affective suppression of emotion	Enhanced stress reactivity and inability to suppress emotional intensity (for example, anxiety and negative affect)	mOFC, vmPFC and subgenual ACC
Motivation: drive, initiative, persistence and effort towards the pursuit of goals	Enhanced motivation to procure drugs but decreased motivation for other goals, and compromised purposefulness and effort	OFC, ACC, vmPFC and DLPFC
Awareness and interoception: feeling one's own bodily and subjective state, insight	Reduced satiety, 'denial' of illness or need for treatment, and externally oriented thinking	rACC and dACC, mPFC, OFC and vlPFC
Attention and flexibility: set formation and maintenance versus set-shifting, and task switching	Attention bias towards drug-related stimuli and away from other stimuli and reinforcers, and inflexibility in goals to procure the drug	DLPFC, ACC, IFG and vlPFC
Working memory: short-term memory enabling the construction of representations and guidance of action	Formation of memory that is biased towards drug-related stimuli and away from alternatives	DLPFC
Learning and memory: stimulus–response associative learning, reversal learning, extinction, reward devaluation, latent inhibition (suppression of information) and long-term memory	Drug conditioning and disrupted ability to update the reward value of non-drug reinforcers	DLPFC, OFC and ACC
Decision making: valuation (coding reinforcers) versus choice, expected outcome, probability estimation, planning and goal formation	Drug-related anticipation, choice of immediate reward over delayed gratification, discounting of future consequences, and inaccurate predictions or action planning	lOFC, mOFC, vmPFC and DLPFC
Salience attribution: affective value appraisal, incentive salience and subjective utility (alternative outcomes)	Drugs and drug cues have a sensitized value, non-drug reinforcers are devalued and gradients are not perceived, and negative prediction error (actual experience worse than expected)	mOFC and vmPFC



Goldstein & Volkow (2011)

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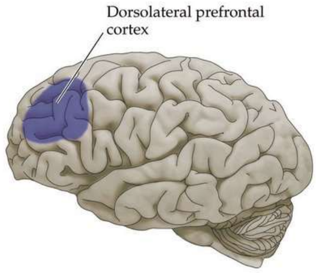
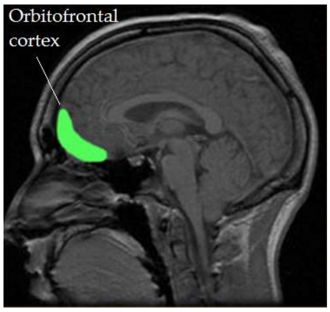
OFC vs. DLPFC





Two key frontal regions:

OFC: encoding the expected value of rewards (the drug), encoding the costs associated with rewards (expected harms), switching reward seeking when the payoff is reduced & foresight into the future consequences of reward-seeking behaviour.

DLPFC: foresight into future consequences of behaviour, exerting contextual modulation of expected reward calculations made by the OFC, enhancing expected drug value in some circumstances & decreasing it in others (self-control).

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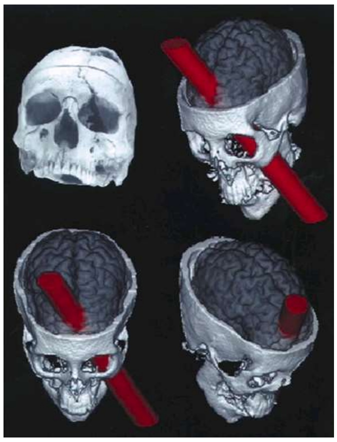
Phineas Gage

Gage had a steel rod punch through his skull severely damaging the left frontal lobe.

- following recovery he was a changed man (unreliable, callous disregard for loved ones, drinking heavily, swearing excessively, hypersexual, poor social interaction, poor empathising & failed to learn from mistakes).
- preserved intellectual function, including memory & planning.
- Lived for another 12 years, later maintaining employment & normalising his behaviour.



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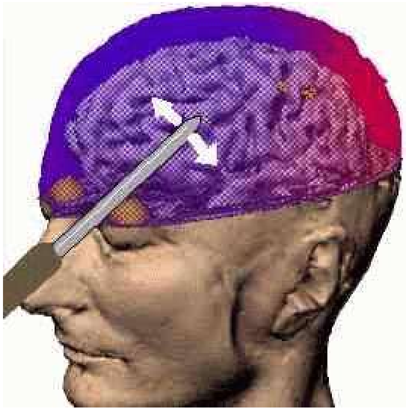
Frontal lobotomy

Moniz (1935): heard of the effects of ablation of PFC in chimps. One of the animals was apparently "cured" of an "experimental neurosis".
- Lobotomies were used in 1930s to 1950s to treat a wide range of severe mental illness

Freeman: believed the frontal lobe was involved in the ability to project an image of the individual into the future coupled with a recognition of this image as the self. A second contribution of the frontal lobes was in providing an "affective facet, the emotional charge connected with that image."
- "prefrontal lobotomy bleaches the affective component connected with the consciousness of the self." (Dolan, 2007).



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OFC & expected reward

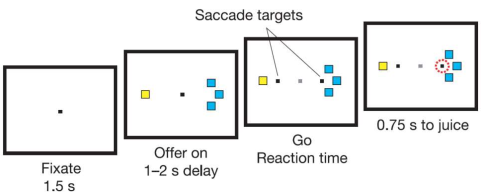
Padoa-Schioppa et al. (2006): firing rate of single OFC neurons was recorded using single cell electrophysiology in vivo.

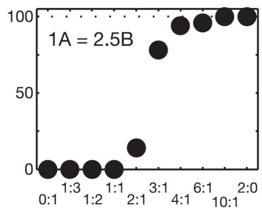
Task: monkeys presented with a fixation cross, followed by a choice between two possible rewards signalled by coloured squares. The monkey received the reward he/she gazed at (saccades).

- Example below: One shot of grape juice (Juice A, yellow square) or three shots of peppermint tea (Juice B, blue squares).

The magnitude of juice A & B offered was varied across trials. Offers included: 1B:3A, 1B:2A, 1B:1A, 2B:1A, 3B:1A, 4B:1A, 6B:1A, 10B:1A & 'forced choices' 0B:1A and 2B:0A.

- Monkeys prefer juice (A) but their preference switched to peppermint if more was offered. The monkey chose A when 1B or 2B was available, but switched to B when 3B, 4B, 6B or 10B was available. The indifference point indicated that 1A = 2.5B.





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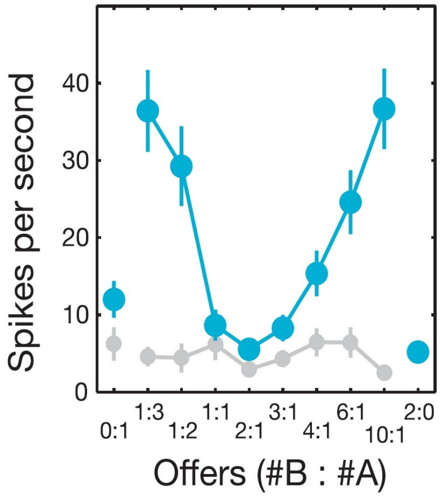
OFC & expected reward

Padoa-Schioppa et al. (2006)

Where the relative value of the chosen reward was higher than the alternative (1B:3A, 1B:2A, 6B:1A, 10B:1A), the OFC cell fired, whereas when the two rewards offered were more closely matched in value (nearer the indifference point, i.e. 1B:1A, 2B:1A, 3B:1A, 4B:1A), the OFC cell did not fire.

- OFC cells appear to encode the expected relative value of a to-be-chosen reward (US= juice A or B), signalled by a predictive (Pavlovian) stimulus (CS= yellow or blue squares).

Presumably, an addict, when faced with the possibility of taking their drug or going to the gym, will have a greater OFC cell firing rate encoding the greater expected relative value of taking the drug over going to the gym.



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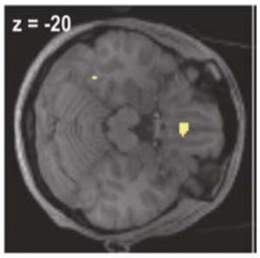
OFC & expected reward

Tanaka et al. (2008): used FMRI to measure brain activity whilst human subjects pressed a button to earn money. The probability of the response producing money (contingency) was varied across blocks of trials.

- Participants' beliefs about the causal effectiveness of the response in producing money traced the objective strength of the response-money contingency (i.e. how effectively the response actually produced money).
- Level of activation within the OFC corresponded with the objective strength of the response-money contingency, suggesting this region is important for encoding the expected probability of reward when performing a reward-seeking response.



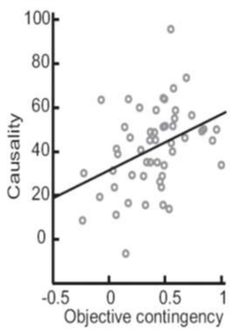


Figure 2. Plot of causality value against global objective correlation.

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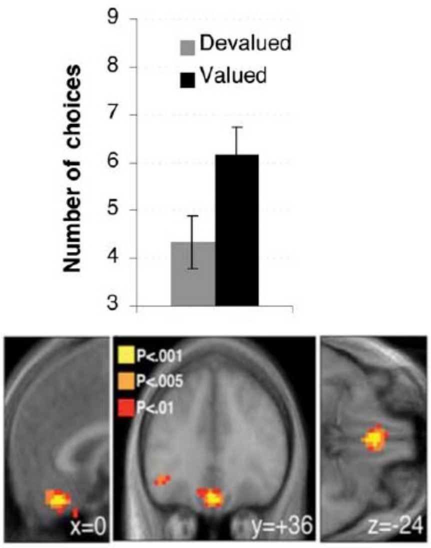
OFC & expected reward

Valentin et al. (2007): human participants learned that one response produced chocolate milk & a different response produced tomato juice.
Devaluation: the value of one of these drinks was reduced by feeding the participants to satiety with that drink.
Test: participants were given the opportunity to again make the two responses. Participants reduced their choice of the devalued drink, indicating that it has reduced relative value compared to the valued drink.

- OFC was more active during responding for the valued drink than the devalued drink.

Indicates the OFC encoded the expected value of the reward during choice of the reward.



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OFC & expected reward

Ostlund & Balleine (2007): used PIT procedure with rats.

Pavlovian training: stimulus 1 (S1) predicts one type of food (US1) & stimulus 2 (S2) predicts a second type of food (US2)

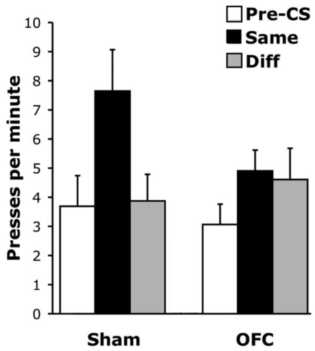
Instrumental training: learned that two responses (R1, R2) earned these same two foods (US1, US2)

Test "Sham": found that each stimulus selectively increased the response that was paired with the **same** food compared to the response that produce the different (**diff**) food (i.e. S1 increased R1 over R2, and S2 increased R2 over R1).

- each stimulus must have elicited an expectation of the food with which it was paired, which in turn elicited the response which had produced that food.

Test OFC: lesions abolished this PIT effect

- OFC lesion had knocked out rats' ability to generate a reward expectancy in response to Pavlovian (predictive) stimuli & then use this expectancy to drive response choice.



Pavlovian training	Instrumental training	Test
S1 – US1 S2 – US2	R1 – US1 R2 – US2	S1:R1/R2 S2:R1/R2

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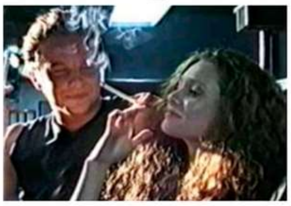
OFC & expected drug reward

Hayashi et al. (2013): examined the role of the OFC in encoding expected drug reward value in response to drug predicting stimuli. Showed smokers a smoking video & afterwards asked participants to rate their agreement with the statement: "I'm craving a cigarette right now".

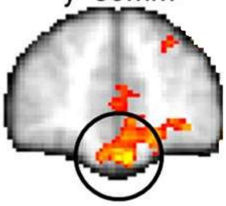
- the brain region whose activity was most strongly associated with higher craving was the OFC.
- Suggests that expectations of drug reward evoked by drug cues is encoded in the OFC.

Smoking video



Question: "I'm craving a cigarette right now"

y=50mm



Orbitofrontal cortex

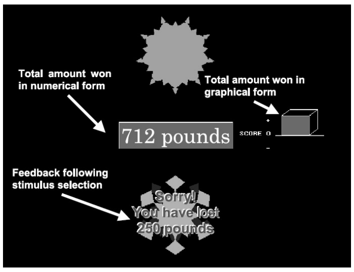
OFC & expected costs

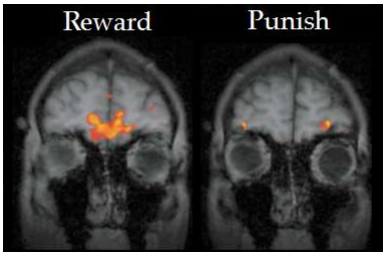
Balancing expected rewards & costs is crucial to determining how valuable the commodity is & whether one should pursue it.

O'Doherty et. al., (2001): Participants completed a task where two patterns appeared together. Touching some stimuli (S+) yielded money wins on some trials & money losses on other trials, but net gain overall. Touching other stimuli (S-) yielded some gains but mainly losses (net losses overall).

- The medial part of the OFC responded to money wins (rewards), where the lateral part responded to money losses (punishment).

- indicates that the OFC is important for encoding signals for both reward & punishment.

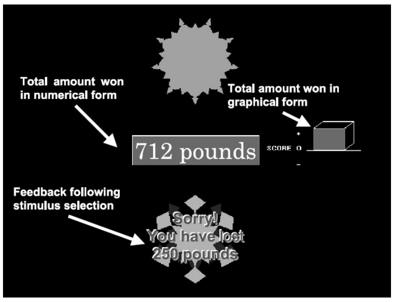


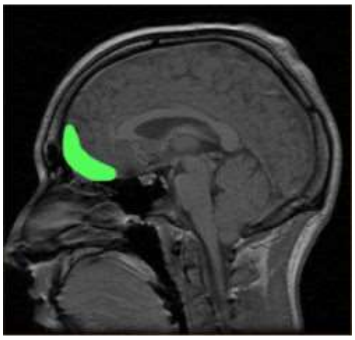


OFC & reversal learning

If the OFC encodes the costs that follow reward-seeking, then damage to this area should impair the ability to stop engaging in reward seeking following the introduction of costs.

Hornak et al (2004): ran patients with damage to the OFC on the same task
- participants simply had to learn to choose S+ rather than S- stimuli.





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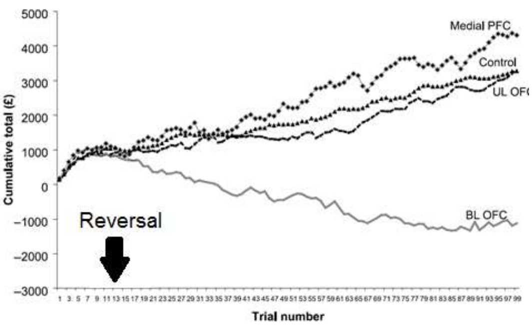
OFC & reversal learning

Hornak et. al. (2004)

All groups learned to choose the S+ over S- stimuli across the first 13 trials. The stimuli were then reversed in their relationship to money (S+ became S-, S- became S+).
- Patients with bilateral (BL) damage of the OFC continued to choose the old S+ stimuli & thus accrued net losses. Whereas patients with damage to another frontal region (medial PFC) or unilateral (UL) damage to the OFC, or no brain damage (control) showed a short dip in earnings after trial 13 while they learned the new stimulus-reward relationships, but thereafter accrued nets gains once they switched to choosing the new S+.
- OFC damage does not impair reward learning per se, but impairs the ability to modify old reward learning in the face of a reduction in the payoff.



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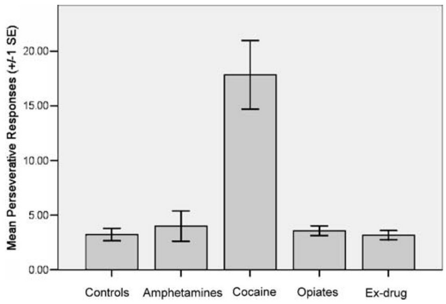
OFC & reversal learning

Reversal learning deficits have been reported in alcoholics (Fortier et al., 2008) smokers & gamblers (De Ruiter et al.,2009). But, recall Ersch et al (2008) who found a reversal learning deficit in cocaine addicts but not amphetamine or opiate addicts, or ex-addicts.

- Thus, impaired OFC function leading to a failure of reversal learning cannot readily be considered a universal impairment in drug addiction.



Ersch et al. (2008)

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OFC & reversal learning

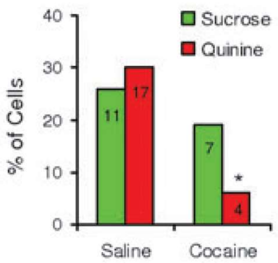
Stalnaker et al. (2006): trained rats to use odours to anticipate whether a drinking fountain would deliver a liked sweet sucrose solution or a disliked bitter quinine solution.
Control rats: ~30% of OFC cells tested responded to odours signalling sucrose or quinine

- demonstrates role of the OFC in encoding expected reward & punishment.

Cocaine rats: showed a selective reduction in % of OFC cells that responded to odours signalling quinine, but little change in the % of cells responding to odours signalling sucrose.

- Chronic cocaine altered the encoding of expected punishment in the OFC.

This impairment in cocaine addicts may be responsible for their failure to show reversal learning when reward-seeking incurs a lower payoff.



Appropriate Cue-Selectivity in Sucrose/Quinine-Expectant Neurons

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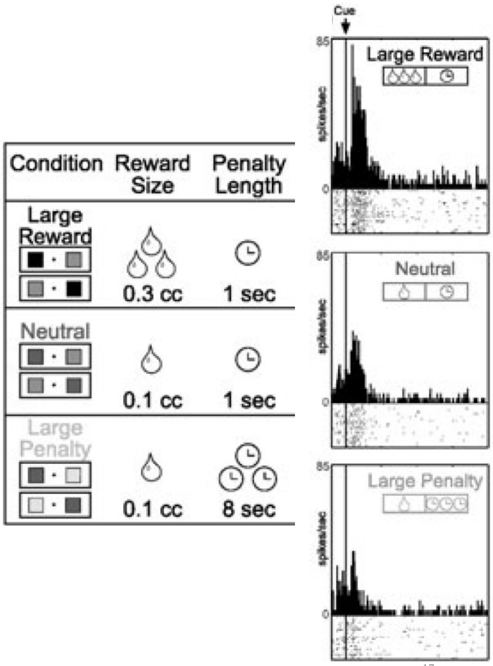
OFC & time costs

Roesch & Olson (2007): offered monkeys juice rewards with different time costs (a time-out period following the reward which incurred lost opportunity to obtain further reward). The offers were signalled by squares (cue) & comprised either 1 or 3 drops of juice combined with a 1 or 8 second time-out period.

- firing rate of OFC neurons in response to the cue encoded the expectancy of the large compared to the small (neutral) reward with the same delay.
- the OFC firing rate to the small reward was also reduced by the combination of large delay (large penalty).

Thus, OFC cells appeared to encode the *composite* value of the expected outcome (i.e. the reward minus the costs).



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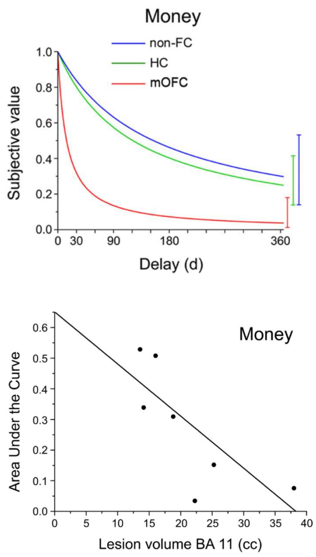
OFC & delay discounting

Sellitto et al. (2010): ran patients with lesions in the medial OFC (mOFC), control patients with lesions outside the frontal lobe (non-FC) & healthy control patients (HC).

- Damage to mOFC increased preference for small-immediate over larger-delayed rewards, resulting in steeper discount functions for future rewards in mOFC patients compared with the control groups.
- larger mOFC damage (lesion volume) was correlated with steeper discount functions within the mOFC group.

Consistent with a role for the OFC in encoding expectations about superior future payoffs in guiding behaviour towards those goals.

- Implication for addiction: damage to OFC may be responsible for individuals being less able to control drug intake by knowledge of long-term future harms.



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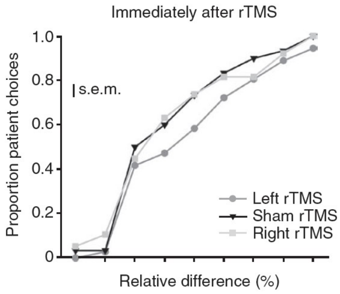
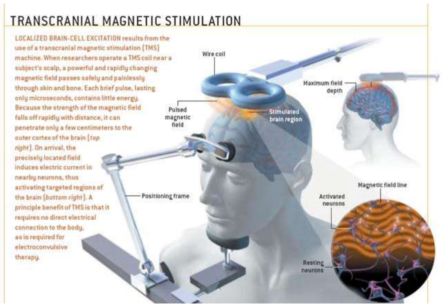
DLPFC & temporal horizon

Figner et al. (2010): used repetitive transcranial magnetic stimulation (rTMS) where a magnetic field interferes with electrical conductance within neurons of the region of the cortex underlying the magnetic coil to disrupt function of the DLPFC just prior to completion of a delay discounting task.

- The proportion of choices of the larger-later option increased as the magnitude (relative difference) of the larger-later reward increased compared to the smaller-sooner reward.
- at intermediate relative difference rTMS of the left DLPFC decreased the proportion “patient” choices causing a preference for immediate reward
- suggests that the left DLPFC plays a role in encoding information about the value of future rewards





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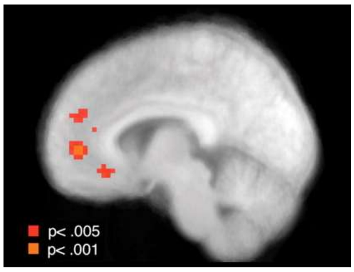
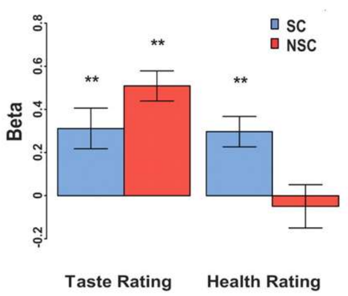
DLPFC & self-control

Hare et al (2009): studied the interaction between OFC & DLPFC in self-control. Dieting & non-dieting participants rated the taste & healthiness of food items. They were then shown pairs of pictures of these foods & asked to choose one to be eaten at the end of the experiment (SC vs. NSC).

OFC activity correlated with only taste ratings in the non-self-control subjects, whereas OFC activity correlated with both taste & healthiness ratings in the self-controllers.

- Indicates the OFC encodes the value placed on rewards
- *left* DLPFC was more active during self-control trials, in which the less tasty healthy item was chosen compared to failed self-control trials in which the more tasty unhealthy item was chosen
    - this difference was greater for the self-control group who more often made a self-controlled choice of the less tasty healthy item.





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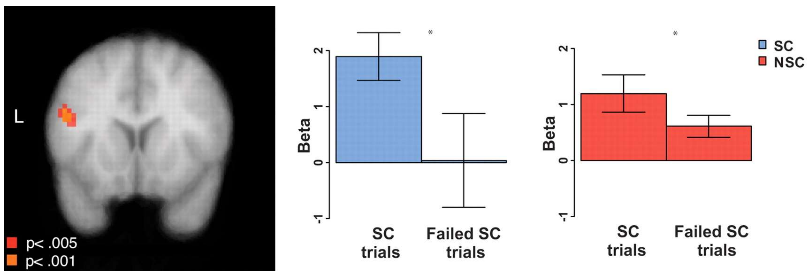
DLPFC & self-control

Hare (2009) concluded that that self-control problems arise in situations where various factors must be integrated. OFC computes goal values & the left DLPFC is required for higher-order factors, such as health, to be incorporated into the OFC value signal.

- speculated that OFC originally evolved to forecast the short-term value of stimuli & that humans developed the ability to incorporate long-term considerations into values by giving structures such as the left DLPFC the ability to modulate the basic value signal (OFC).

Figner et al. (2010): found that rTMS of the *left* DLPFC reduced choice of the larger later option in a delay discounting task.

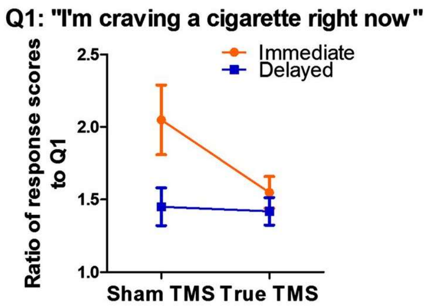
  - evidence for the left DLPFC in the regulation of behaviour towards long terms goals.



DLPFC & contextual control

Hayashi et al. (2013): smokers presented with smoking cues or neutral videos in a session in which they believed they could smoke immediately afterwards, or not smoke for 4 hours afterwards. In addition, they were given rTMS to the left DLPFC or sham rTMS

- ratio of craving produced by the smoking video over the neutral video was increased by beliefs that smoking was immediately available in the sham rTMS group, but this effect of availability on craving was abolished by rTMS to the left DLPFC.
- indicates that left DLPFC plays a role in increasing craving in response to the immediate availability of this reward
  - consistent with DLPFC role in self-control over reward valuation.

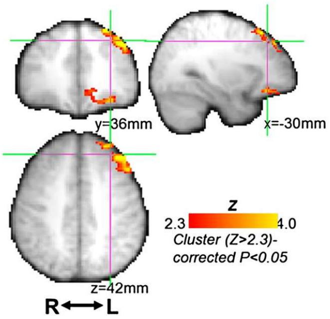


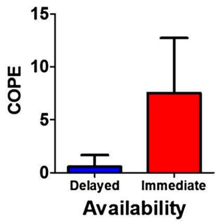
DLPFC & contextual control

Hayashi et al. (2013): *left* DLPFC activity was modified by the smoking availability manipulation

- Greater activity when subjects believed they could smoke immediately compared to when they believed they would not be able to smoke for some time.

Supports role of left DLPFC in providing modulatory information about the timing, or the delay to the reward, giving a greater signal when the reward is immediate.





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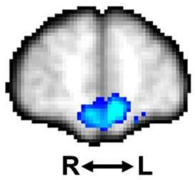
DLPFC & contextual control

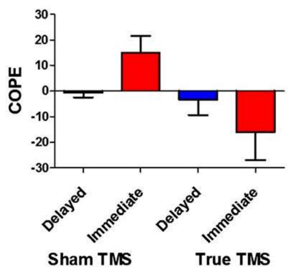
Hayashi et al. (2013): OFC activity increased when belief was that smoking was immediately available versus delayed, but only in the sham rTMS condition.

- rTMS to left DLPFC: no increase in OFC activation in response to immediate smoking availability
  - indicates that the OFC value signal concerning the prospect of smoking receives input from the DLPFC regarding the temporal availability of smoking, increasing OFC value signal if smoking is imminent.

Hayashi speculated that conscious self-control over smoking derived from knowledge of long term health consequences (exerted by the left DLPFC) may reduce the expected value of smoking (encoded within the OFC), thus reducing the propensity to initiate smoking behaviour.

- Accordingly, damage to the left DLPFC would render addicts unable to exert such self-control resulting in a perseveration of addictive behaviour despite knowledge of long term health consequences.





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Summary

Knowledge & understanding of:

- the implication of frontal neuropathology in addiction & the medical history of the frontal lobe.
- research findings & methodologies which have provided evidence for the OFC's role in expected reward, expected costs, reversal learning, time costs & delay discounting.
    - come to understand OFC importance in behavioural regulation.
- research findings & methodologies which have provided evidence for the DLPFC's role in temporal horizons, self-control & contextual control.
    - come to understand DLPFC importance in behavioural regulation.

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