For slides, electronic handouts, and related material, see **www.pobox.com/~rudolf/psychology**.

Part 1: Emotion

Overview

We will begin by considering the functional relevance of emotions and their possible evolutionary origins. We will look at how emotions can be measured. We will review three major theories of emotions (the James–Lange, Cannon–Bard, and Schachter theories). We will look briefly at the neurobiology of emotion.

Emotion: definitions and functions

Everybody knows what emotions are… yet they can be difficult to define in a manner that allows experimental study. As a central theme we shall consider under the umbrella of 'emotion' all processes in humans and other animals that involve the assessment of *value.*

Obvious functions

Simple emotions such as fear are driven by motivationally-significant stimuli and events; 'emotional' behaviour can be highly adaptive for an animal. Fear of heights makes you less likely to be near (and therefore fall off) cliffs; fear of snakes and spiders makes you less likely to be bitten and poisoned by them (however unlikely that is in today's urban environment). Other emotions, especially those in the social domain, are more complex to understand.

Emotions: rationally irrational?

Schelling (*1*), Frank (*2*) and others view emotions as important because they are *involuntary* and *difficult to fake*; they advertise our inner states. In some situations, they are like a Doomsday machine (*3*). The idea is that if your behaviour is controlled by rational mechanisms, you might change your mind, and people can bargain with you. If your behaviour isn't rational, you may do better. Imagine it's 1962, and you're President of the USA. The Soviet Union has just dropped an atomic bomb on New York, but the premier responsible has just been assassinated, so you know they will not attack again. Your nation's policy is to retaliate with a nuclear strike. But at this moment, you have nothing to gain by killing the citizens of Moscow, so you might pause. The problem is that by the time you're at this point, your freedom of choice may cause you not to retaliate (because it isn't particularly to your advantage at this time), but your opponent's knowledge that you might think and behave this way is what prompted the attack in the first place. What you needed is a deterrent that everyone would *believe* — for example, automatic retaliation that you could not prevent. This is taken to its extreme in Stanley Kubrick's famous film *Dr Strangelove (Or, How I Learned to Stop Worrying and Love the Bomb).*

A similar argument may be applied to emotions. They may be threats: if a man is known to fly into uncontrollable rages (and, critically, is known *not to be faking it*), people will think twice before upsetting him — even if the rage is not helpful at the moment it comes. They may be promises: in choosing a sexual partner, you may be more secure if they display *emotional* responses to you (with signals that are hard to fake, like dilated pupils and flushed skin) because that means that their commitment is not under rational control — they can't help it — so they're less likely to leave if a (rationally) better proposition than you comes along. (It's no coincidence that polygraphs — lie detectors — are based on measuring hard-to-fake emotional responses such as skin conductance.)

Evolution of emotions

Examples like these indicate that emotions may have benefits to the possessor, but also to other people; however, there are potential evolutionary mechanisms for both (see e.g. *3, 4, 5*).

In fact, the first person to study the evolution of emotions was Darwin (*6*). He noted that the same emotional responses (such as facial expressions) tended to accompany particular emotions, across human races and cultures. He compared human emotional behaviour with similar behaviours in other species. Darwin suggested that 'emotional expression' evolves from similar behaviours that signal what an animal is likely to do next. If such behaviours benefit the animal, they may evolve as a communication device and become to some extent independent of the original behaviour that they predicted.

For example, rising up, facing one's enemy, and exposing one's teeth and / or claws are all necessary parts of animal combat. However, once enemies start to recognize this pattern of behaviour as signalling impending aggression, there would be a distinct advantage for any aggressor that could communicate their aggressive intent effectively enough to cause the opponent to withdraw without actually fighting. As a result, elaborate threat displays might evolve (while actual combat might decline). Darwin also noted that signals conveying opposite intent should be, and are, highly distinguishable — for example, displays of submission involve opposite movements to displays of aggression (his 'principle of antithesis'; see figure).

Measuring emotion

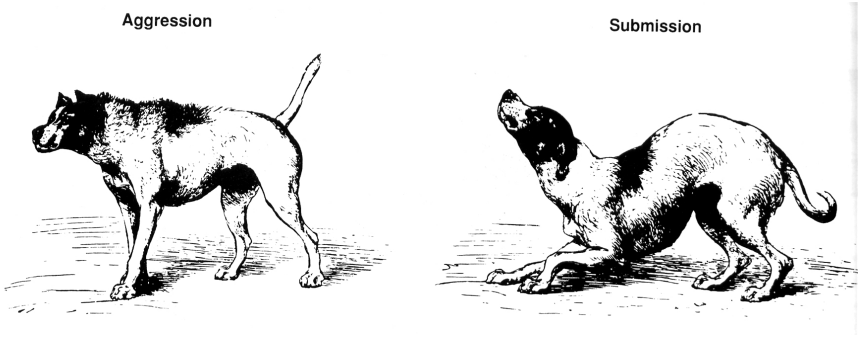
Emotional responses have at least *three* components:

- *subjective* (e.g. the feeling of fear)
- *behavioural* (e.g. facial expression, immobility, avoidance behaviour)
- *physiological* (e.g. autonomic responses including changes in heart rate, blood pressure, respiratory rate, pupil size, skin conductance, EEG patterns, and hormone secretion)

All can be measured in humans. Self-report techniques can be used to assess subjective feelings; observational and other measurement techniques can assess behavioural and physiological measures. Clearly, behavioural and physiological responses can be measured in animals. However, subjective experience generally cannot. Yet there are ways to infer central 'emotional' states in animals; we will mention one later.

Universal emotions? Facial expression of emotion

Darwin's early work on facial expression of emotions has been extended by Ekman (*7, 8*), who identified six cross-cultural **'primary emotions'** in humans — surprise, fear, anger, disgust, happiness, and sadness (see figure). Ekman views these as *universal*, and hence likely to be *innate.*



Above: *Ekman's universal facial expressions.* ***Right:*** *Woodcuts from Darwin's (6) book on emotional behaviour across species.*

The James–Lange theory of emotion

Common sense might suggest that emotional expression results from emotional experience — that if are trekking in the jungle and see a tiger with cubs, we first feel fear (emotional experience), and this causes autonomic changes and a tendency to leave rapidly (emotional expression). James (*9*) and Lange (*10*) independently suggested that the opposite might be true: that the emotional experience is a *consequence* of the bodily response, and depends on perceptual awareness (feedback) of that response. This theory, now known as the James–Lange theory, was initially based on anecdote and philosophical argument.

Note that James's theory allowed that emotions could be induced by 'visceral' (autonomic) feedback, such as an increase in heart rate, and also by feedback from skeletal muscle activity. We will return to this below when considering facial expression of emotion. Smile — do you feel happier?

The Cannon–Bard theory of emotion

Cannon (*11*) objected to the James–Lange theory on several grounds, based on the experimental evidence available at that time:

1. *total separation of the viscera from the CNS did not impair emotional behaviour observed in laboratory animals* (e.g. following sympathectomy or vagal nerve section);
2. *the same visceral changes occur in very different emotional states* (implying that they could not be the sole cause of different emotions);
3. *the viscera are relatively insensitive structures* (e.g. surgical trauma to the viscera often produces surprisingly little discomfort);
4. *visceral changes are too slow to be a source of emotional feeling;*
5. *artificial induction of the visceral changes typical of strong emotions does not actually produce emotional experience*. Marañon (*12*) injected 210 subjects with adrenaline; the majority (71%) reported only physical symptoms; most of the rest reported having feelings 'as if' they were emotions; a very few reported actual emotions, and they recalled memories of an emotional event during the experiment.

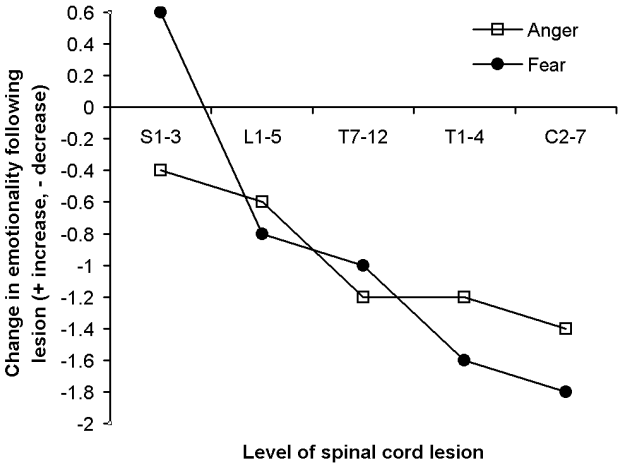
This theory was later extended by Bard (*13*). The Cannon–Bard theory essentially states that emotionally significant events *independently* cause emotional experience and physiological responses.

Many of the points made by Cannon have subsequently been disputed. Let's look at evidence that has accumulated since then.

Subjective responses in paraplegic subjects

Hohmann (*14*) found that subjective feelings of anger and fear *were* diminished in subjects who had suffered spinal cord injury, and this effect was greater with progressively higher lesions of the cord (see figure). (These lesions would affect both autonomic function and skeletal musculature, to differing degrees depending on the site.) These subjects were perfectly capable of acting *as if* they were angry, in appropriate situations — but subjectively, this anger lacked intensity and emotional colouring. This suggests that at least some part of emotional experience does depend

upon the brain's ability to interact with the body, though other aspects of emotional expression do not.



Data from Hohmann (14) showing a decrease in 'emotionality' following spinal cord lesions; the higher the lesion, the more its effect. A description by one of the subjects is given below.

"It's a sort of cold anger. Sometimes I act angry when I see some injustice. I yell and cuss and raise hell, because if you don't do it sometimes, people will take advantage of you. But it just doesn't have the heat to it that it used to have. It's a mental kind of anger."

Visceral responses to different emotions

Although emotional states induce a number of physiological changes, some of which may not differentiate between different emotional states, some studies have found that different emotions induce different 'profiles' of physiological response.

For example, Ax (*15*) measured 14 different physiological variables while inducing fear or anger in subjects in the laboratory (by insulting them or delivering electric shocks, respectively). Of these, 7 differentiated between fear and anger (e.g. diastolic blood pressure increased more in anger than fear; muscle tension increased more during fear than anger).

Visceral responses to relived emotions and facial expression of emotion

Ekman *et al.* (*16*) found similar emotion-specific autonomic changes. They asked professional actors to either (1) reconstruct facial expressions of emotions, muscle by muscle — akin to the 'technique' or 'external' system of acting favoured by Delsarte and Laurence Olivier — or (2) to relive past emotional experiences, akin to 'method acting' as advocated by Stanislavsky and Robert de Niro. Some autonomic measures differentiated between emotions (e.g. anger and fear produced equivalent increases in heart rate, but only anger increased finger temperature). These results held for both directed facial actions and reliving emotional experience.

As an aside, it was Charles Darwin who first suggested that feedback from facial expression was an important factor in determining subjective emotional feelings:

> "The free expression by outward signs of an emotion intensifies it. On the other hand, the repression, as far as this is possible, of all outward signs softens our emotions." (*6*)

Emotional interpretation of skeletal muscle activity?

Laird (*17*) attempted to test James' view that emotions could follow from patterns of skeletal muscle activity. He falsely informed a group of subjects that they were participating in an experiment to measure activity in facial muscles; they were kitted out with fake electrodes attached to their faces. Laird then got them to make a range of facial movements, muscle by muscle; they were unaware of the nature of their expressions, but the patterns they made included smiles and frowns. While this was happening, they viewed cartoon slides; regardless of content, they rated as funnier the slides they'd seen while 'smiling'. They also described themselves as happier whilst 'smiling', angrier when 'frowning', and so on. However, note that autonomic changes can accompany simulated emotional expressions (*16, see above*), so this experiment does not distinguish the role of skeletal muscle feedback from autonomic feedback.

Schachter's cognitive labelling theory

Schachter (*18*) held that Cannon was wrong in considering emotional experience to be independent of bodily changes, that James was right to consider that physiological changes precede the experience of emotion, but that James was wrong to consider the bodily changes to be solely responsible for emotional feelings. Schachter's *cognitive labelling theory* suggested that physiological arousal is necessary for emotional experience, but that the nature of this arousal is immaterial — what matters is how we interpret that arousal. This theory is therefore also known as the *two-factor* theory of emotion. Lazarus (*19*) developed another version of what is known in general as **cognitive appraisal theory** — the idea that cognitive processing is essential for, and / or substantially influences, emotional reactions. (Whether cognitive processing is 'essential' for emotion depends on how you define cognition!)

Labelling of autonomic arousal

The classic demonstration of this theory was by Schachter & Singer (*20*). They injected subjects with a 'new vitamin' to 'test its effect on vision'. This injection was in fact adrenaline (known as epinephrine in the USA). The groups varied as follows:

1. *Epinephrine informed.* These subjects were injected with adrenaline (though they thought it was this 'new vitamin'), and informed of its side effects — tremor, palpitations, flushing, etc.
2. *Epinephrine ignorant.* These subjects were injected with adrenaline, but told that the injection was mild and had no side effects. (Therefore, the subject had no external explanation of the effects of the adrenaline.)
3. *Epinephrine misinformed.* These subjects were injected with adrenaline, but inaccurately told that it would produce numb feet, itching, and headache.
4. *Placebo.* These subjects were injected with saline, and told that it would have no side effects.

Before receiving their 'vision test', subjects waited in a room with another 'participant', who was a stooge. This stooge either acted euphorically, or angrily. The subjects' emotional experience was then assessed in two ways: (1) by self-report scales (e.g. 'How good or happy would you say you feel at present? 0 = I don't feel at all happy… 4 = I feel extremely happy'), and (2) by observers' ratings through a one-way mirror of the degree to which they joined in the stooge's behaviour (e.g. initiating activity with the stooge or agreeing with him).

Self-report results (higher scores indicate greater euphoria; lower scores indicate anger); ↑ and ↓ indicate significant differences from the other groups.

	Condition	
Group	Euphoric stooge	Angry stooge
Epi informed	0.98 –	1.91 –
Epi ignorant	1.78 ↑	1.39 ↓
Epi misinformed	1.90 ↑	*data lost*
Placebo	1.61 –	1.63 –

The results (above) indicate that subjects who experienced *unlabelled arousal* (those injected with adrenaline who were either ignorant or misinformed of its effects) were more likely to experience emotion, but the *quality* of that emotion could be influenced by the cognitive context of the subject — the *labelling* of that arousal. The observers' rating provided similar results.

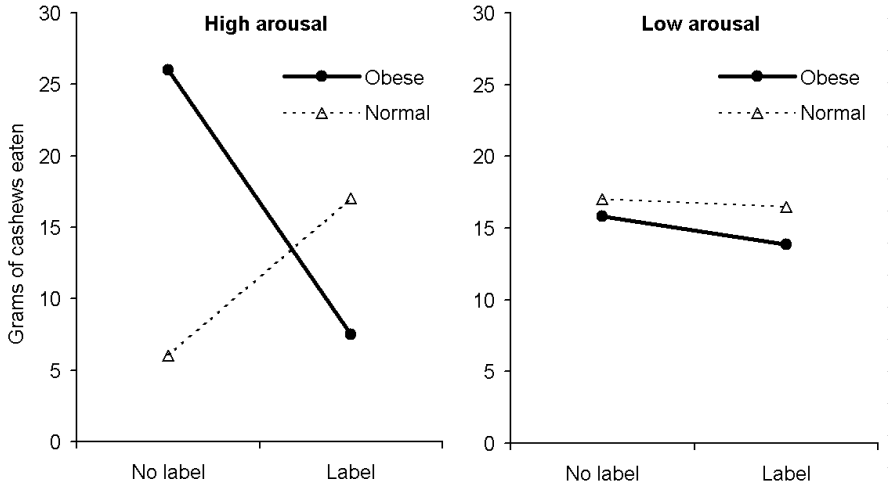
Others (e.g. *21*) have since suggested that subjects' ability to label arousal is not all that flexible; they found that the unexplained effects of adrenaline were not interpreted as positive emotions in the presence of a euphoric stooge (i.e. they failed to replicate some aspects of the results of *20*), suggesting that unexplained autonomic arousal is simply a bit unpleasant. We'll consider some more examples with positive emotions in a moment.

Another example of manipulating cognitive appraisal

Speisman *et al.* (*22*) showed participants a film of aboriginal boys undergoing ritual circumcision with jagged flint knives. The soundtrack emphasized either (1) the pain, jaggedness of the knife, etc. — 'trauma'; (2) the boys' anticipation of entering manhood — 'denial'; (3) the traditions of the aboriginal people — 'intellectualisation'; (4) there was no commentary — silent control. Arousal, as measured by galvanic skin responses and heart rate, was highest in the 'trauma' condition, next highest in the silent control condition, and lowest in the other two, demonstrating the influence of cognitive appraisal on arousal.

Unlabelled arousal and eating behaviour

Schachter (*23*) suggested some interesting applications of his theory. He suggested that some forms of obesity arise from an inability to distinguish internal states of emotions such as anxiety from internal states of hunger, perhaps as a consequence of early experience. Slochower (*24*) tested this hypothesis. She took subjects of normal weight and obese subjects; while waiting to perform some completely irrelevant experiment, they heard feedback of their own heart rate. This feedback was false (i.e. not their own), and was either at a normal rate (*low arousal*) or abnormally fast (*high arousal*). Subjects were then either informed that the feedback machinery was faulty (*labelled* condition) or not (*unlabelled*, in which case they believed that the heart rate was their own).



Data from Slochower (24).

The results (shown above) indicated that normal people's eating is suppressed by unlabelled arousal or anxiety. In contrast, this stressor increased eating in obese subjects. There are a number of explanations of this effect, not just Schachter's — perhaps the eating relieves the anxiety, for example — but the induction of binge eating by stress is a well-documented phenomenon.

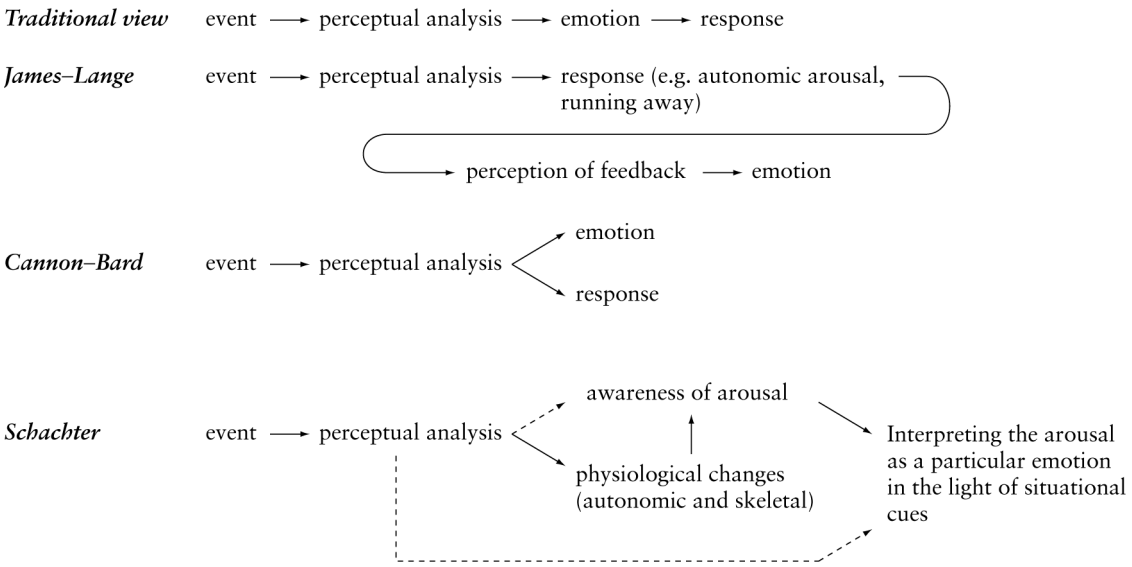
The Capilano Bridge experiment

Dutton & Aron (*25*) tested the hypothesis that nonspecific arousal is *interpreted* according to the context using a dramatic experiment on a suspension bridge over the Capilano River canyon, near Vancouver. This bridge is 1.5 m wide, 140 m long, and 70 m above a canyon. It's made of wooden planks, the handrails are fairly low, and it wobbles quite a lot. Male subjects were asked 'survey questions' by an attractive female interviewer. As part of the survey, they were asked to invent a short story about an ambiguous picture of a woman. They were also invited to call the interviewed if they wanted further information about the research. In one group, the subjects were interviewed on the suspension bridge (*high arousal*); a control group were interviewed on a solid, stable wooden bridge only 3 m above a small brook (*low arousal*), and a third group were interviewed 10 minutes after they'd been on the Capilano bridge (*low arousal* by this time). The stories invented by the men in the high arousal condition contained significantly more sexual imagery (interpreted as sexual attraction towards the interviewer) and they were four times as likely to call her as men in either of the low arousal conditions. This suggests that arousal can be *misattributed* to the wrong source.

Influence of false feedback

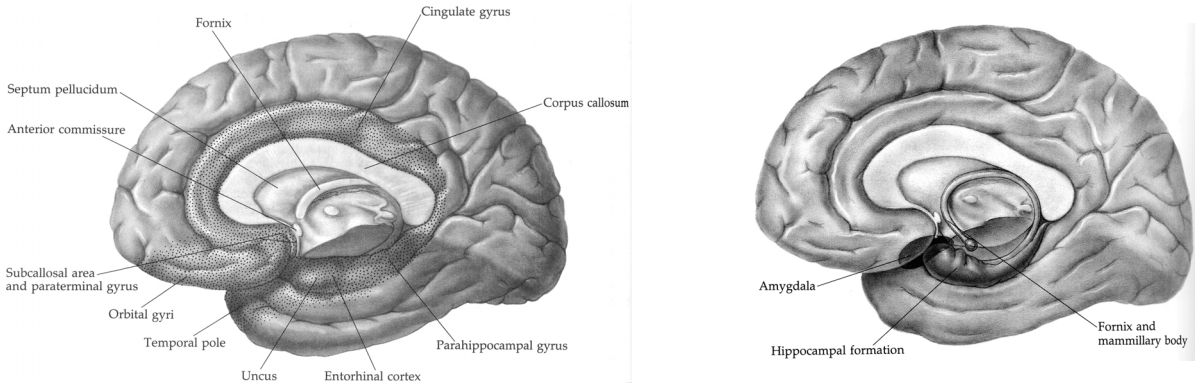
Valins (*26*) showed male subjects slides of female semi-nude *Playboy* models. At the same time, they were provided with audible feedback of their heart rate. In fact, the heart rate was not their own, but was a pre-recorded sound programmed to increase, decrease, or stay the same for a proportion of the slides. This is a *false feedback* paradigm. Subjects rated the slides as significantly more attractive when the 'heart rate' changed when they saw the slide (whether it increased or decreased), and this preference persisted for some time. They also chose these slides more often as payment for their participation! This suggests that even faked arousal can be misattributed.

Summary of theories of emotion



Neural basis of emotion: an overview of the limbic system

The term 'limbic' was coined by Broca (*28*) for the cortical structures encircling the upper brain stem (*limbus*, Latin for edge or border). These cortical regions are considered phylogenetically 'primitive' cortex, based on their microscopic appearance. The 'limbic lobe' was suggested to have a role in emotional experience and expression by Papez (*29*) (his name rhymes with 'apes'). This concept was later elaborated by MacLean (*30*), who introduced the expression 'limbic system' to refer to the limbic lobe and its connections with the brainstem, and added further structures to the system. The limbic system is not precisely defined: as the limbic lobe was considered the neural substrate for emotions, structures whose functions have to do with motivation and emotion have since been added to the anatomical definition. A modern definition of the limbic system in primates would certainly include cingulate and

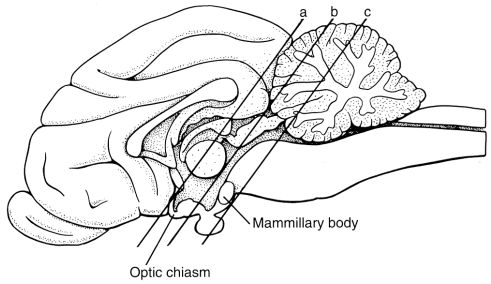


Different views of the limbic system. ***Top left:*** *Medial views of the brain, with 'limbic' cortex stippled.* ***Top right:*** *The same view but showing the location of the amygdala and hippocampus deep within the medial temporal lobe. From Martin (27)9).*

orbitofrontal cortex (both part of the frontal lobe); the amygdala, hippocampal formation, and parahippocampal gyrus (part of the medial temporal lobe); the septal nuclei (or septum, within the basal forebrain); the mammillary bodies, the rest of the hypothalamus, and the anterior and medial thalamic nuclei (in the diencephalon); and the nucleus accumbens and ventral pallidum (part of the basal ganglia).

Attribution of emotional processing to the limbic system

In the 1920s a series of experiments looked at the expression of *sham rage* in cats. *Decorticated* cats (whose neocortex has been removed, leaving the basal ganglia and diencephalon intact) exhibited tail-lashing, back-arching, clawing, biting, and autonomic responses including piloerection, sweating, urination, defaecation, and hypertension, accompanied by an endocrine stress response (adrenaline and corticosteroid secretion). Although such a cat appears enraged, these 'rage' responses can be brief and triggered by very nonspecific stimuli, and the rage is also poorly directed (they sometimes even bit themselves); hence, it was termed 'sham rage' (*31*). *Decerebrate* cats, where only the hindbrain and spinal cord are connected to the body, did not exhibit sham rage. Bard (*32*) found that the posterior hypothalamus was critical for the coordinated rage response (see figure). Hess (*33*) found that stimulation of hypothalamic subregions could produce sham rage, or indeed more directed attacks. It was later established that large portions of the cerebral cortex could be removed *without* producing sham rage, but these rage phenomena appeared when the lesions included limbic cortex, such as the cingulate cortex (*34*).



Bard's (32) transections of the cat brain. Transection of the forebrain (a) produces sham rage. Transection through the mid-hypothalamus (b) also produces sham rage. Transection that disconnects the posterior hypothalamus (c) abolishes this coordinated rage response; only isolated (not coordinated) responses could be elicited, and required much stronger stimuli to do so than when the posterior hypothalamus was intact.

It was data such as these that prompted Papez (*29*) to propose that a circuit connecting the structures of the 'limbic lobe' was critical for emotion. His circuit projected from the cingulate cortex to the hippocampal formation, then on via the fornix (a major tract of fibres — axons — emerging from the hippocampus) to the mammillary bodies (part of the posterior hypothalamus), from there via the mammillothalamic tract to the anterior thalamic nuclei, and then back to the cingulate cortex — suggested to be a 'higher centre' for the conscious perception of emotion and the interaction between emotion and cognition, in contrast to the unconscious basic mechanisms orchestrated by the hypothalamus.

Much of Papez's circuit is *not* considered to be involved in emotional behaviour today. In particular, there is not good evidence that damage to hippocampal structures affects emotional processing; however, other structures added to the 'limbic system' by MacLean certainly are.

The amygdala

In 1937, Klüver and Bucy described a syndrome that developed in rhesus monkeys following bilateral removal of the temporal lobes (*35, 36*). This syndrome included striking *tameness* (*37*), *emotional unresponsiveness*, 'psychic blindness' (an *inability to recognize familiar objects*), *hypersexuality* and *hyperorality* (they try to put all sorts of objects in their mouth and / or have sex with them), 'hypermetamorphosis' (this meant a strong tendency to react to every visual stimulus), and difficulties with memory. Klüver–Bucy syndrome was later found in humans following similar lesions (*38*); the patient had undergone temporal lobectomy to remove epileptic foci, and displayed all elements of the syndrome postoperatively except placing objects in his mouth. Complete K–B syndrome has since been described in humans (*39*). Allegedly, one patient was arrested whilst attempting to have sex with the pavement.

(Hypersexuality and hyperorality might be a consequence of a failure to identify visual objects correctly, or failure to attribute the correct significance to the stimuli.)

This raises a question: damage to which structure was responsible for the emotional changes in K–B syndrome? While the problems in visual processing and memory have since been attributed to damage to structures including inferior temporal cortex, rhinal cortex, and the hippocampus, the emotional changes ('fearlessness') have been localized to the *amygdala*. Named for its supposed resemblance to an almond, the amygdala is probably the structure most implicated in emotional processing.

Abnormalities in emotional processing following amygdala damage in humans

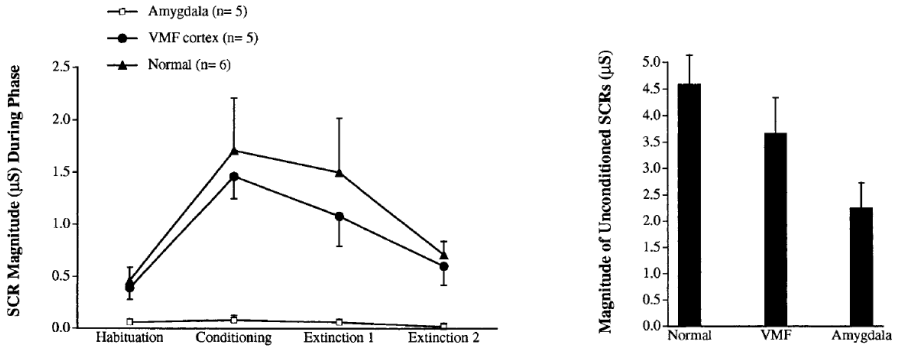
Damage to the amygdala in humans may lead to an increase in threshold of emotional perception and expression (see *40*); amygdala lesions certainly cause impairments in emotional learning (*41, 42*), deficits in the perception of emotions in facial expressions (*43*), and impaired memory for emotional events (see *44*).

Subdivisions of the amygdala

The amygdala comprises three major groups of nuclei, termed the *corticomedial, basolateral,* and *central* divisions. The basolateral amygdala (BLA) and central nucleus of the amygdala (CeA) are heavily implicated in emotional processing (see *45*); the corticomedial amygdala is important for responding to olfactory information, including *pheromones* (*46*). Pheromones are airborne chemical signals released by an individual into the environment that affect the physiology or behaviour of other members of the same species, without consciously being detected; they can certainly affect reproductive behaviour in humans (*47*).

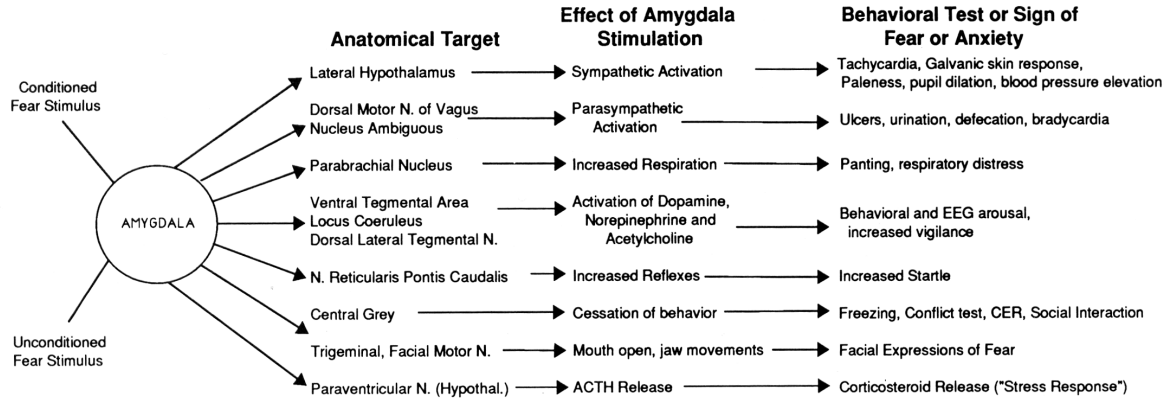
Aversive (fear) conditioning and the amygdala

Pavlovian (classical) conditioning paradigms can be used to study learned fear. If we give a human or a rat pairings of a conditioned stimulus (CS) with an aversive unconditioned stimulus (US; e.g. electric shock, or loud noises), they will develop conditioned responses to that CS. Bechara *et al.* (*41, 42*) have shown that humans with amygdala lesions (some of them with the rare Urbach–Weithe disease, in which the amygdalae calcify bilaterally) are impaired at this sort of learning (see figure).



Damage to the amygdala impairs conditioned skin conductance responses (SCRs) in humans (42). The CS was a blue slide; the US was a foghorn. (VMF: another group of patients with ventromedial prefrontal lesions, not relevant to our present discussion.)

This work builds upon a much older and more extensive literature in rats. The prototypical task involves CS→shock pairings; rats will subsequently freeze (become immobile) to the CS. This depends on the amygdala (see *48*). Information about the CS and the US (shock) arrives at the amygdala and can be associated through long-term potentiation (LTP) of glutamatergic synapses, via the usual NMDA receptor mechanism. Although the BLA and CeA can operate independently in some situations (see *45*), in this task the BLA is responsible for emotional Pavlovian learning; it receives sensory information, acts as a site of CS–US association and uses this learned information to control the activity of the CeA. In turn, the CeA acts as a 'controller of the brainstem', using its widespread projections to the hypothalamus, midbrain reticular formation and brainstem to orchestrate behavioural, autonomic, and neuroendocrine responses.



Anxiety and the amygdala

Fear is an emotional response to stimuli that predict aversive consequences. Anxiety is related; while some people say that fear is more specifically directed at a stimulus than anxiety, both have similar symptoms. Lesions of parts of the amygdala block an number of *unlearned* 'emotional' responses, such as the corticosteroid response to being forcibly restrained (see *49*).

Benzodiazepines (BZs) such as diazepam increase the effects of the inhibitory neurotransmitter GABA. Clinically, they are highly effective as anxiolytic drugs. In a commonly-used rat model of anxiety, the *elevated plus maze*, rats normally spend less time in the open (exposed, dangerous?) arms than in the closed arms; anxiolytics increase the amount of time they spend in the open arms (they're less nervous?). In tasks like this, BZs have anxiolytic effects in tasks when infused into the amygdala, and local infusion of the BZ antagonist flumazenil into the amygdala attenuates the effects of BZs given systemically. However, some anxiolytic effects of BZs survive amygdala lesions (see *49*).

Memory modulation and the amygdala

The BLA also has a prominent role in the emotional modulation of memory storage. It is part of the mechanism by which emotionally-arousing situations improve memory (see *44, 50, 51*). Humans remember emotionally-charged events better than others — in a previous generation most people would recall where they were when J.F. Kennedy was shot; today, most people would be able to report where they were on 11 September 2001. The memory-enhancing effects of emotion can be blocked by the β-adrenoceptor blocker propranolol in humans (*52*); this difference in memory for emotional versus neutral memories is not apparent in humans with amygdala lesions (*53*); intra-amygdala injections of β agonists enhance some kinds of memories even if given shortly after training, while intra-amygdala β antagonists prevent this (*54*). It appears that the BLA is the critical site for the memory-enhancing effects of systemic adrenaline and glucocorticoids, and for the amnesic effects of benzodiazepines (see *50*).

Appetitive conditioning and the amygdala

The emphasis so far has been on aversive stimuli. However, the amygdala appears to be equally involved in assessing the value of appetitive stimuli — perhaps in associating stimuli with value, whether that value is positive or negative (see *45*).

The orbitofrontal cortex

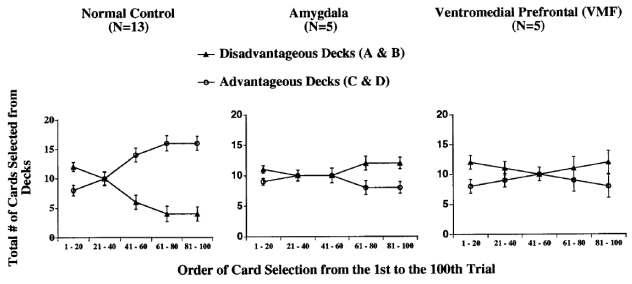
The amygdala seems to interact heavily with the *orbitofrontal cortex* (OFC), which is also strongly implicated in the way emotional stimuli control behaviour.

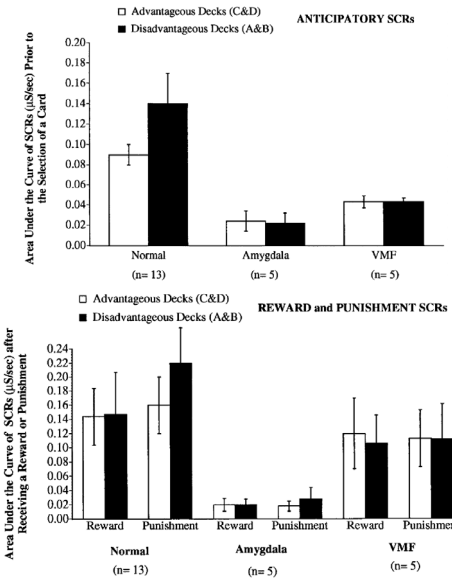
Human OFC damage

The OFC shot to fame in 1848 when Phineas Gage, a railroad construction worker in Vermont, was distracted while setting explosives in a rock and banged on the explo-

sive with a tamping iron. The powder exploded, blowing the 6kg rod into his cheek and out of the top of his head, landing about 25 metres away. He regained consciousness rapidly and survived the subsequent infection. However, his personality was completely altered (*55, 56*). He became profane, capricious, and irresponsible; his emotionality appeared altered. The tamping iron had destroyed both left and right orbitofrontal cortex (*57, 58*). Modern-day patients with OFC damage exhibit similar problems.

These patients are normal on many tests of 'intelligence', but are impaired on one task — gambling. In the Iowa Gambling Task (*59*), patients choose cards from four decks. Decks A and B have constant moderate gains but occasional substantial losses; the losses outweigh the gains, so these are 'risky' decks. Decks C and D give constant small gains, but their losses are also smaller; they give a net gain and are 'safe' decks. Normal humans exhibit a number of interesting phenomena on this task. These are (1) they learn to choose decks C and D, and avoid the risky decks; (2) they generate skin conductance responses (SCRs) when they are rewarded and punished; (3) they generate *anticipatory* SCRs before they choose a card; (4) they generate a larger anticipatory SCR before they pick a risky deck than before they pick a safe deck; (5) as they're learning, the SCR difference between the risky and safe decks develops, and subjects start to choose the safe decks, *before* they can tell you that (or how) the decks differ. In contrast, patients with OFC damage choose poorly and do not develop anticipatory SCRs that discriminate between the decks (see figure).





Top left: *normal humans learn to avoid decks A and B and to choose decks C & D. Patients with amygdala lesions or ventromedial prefrontal cortex (VMF) (= OFC) damage don't.* ***Top right:*** *amygdala and VMF patients don't show anticipatory SCRs that distinguish between their picking a risky and a safe deck.* ***Bottom right:*** *SCR responses to actual reward and punishment are normal in VMF patients, but not in those with amygdala damage (42).*

The somatic marker hypothesis

Damasio has proposed what he terms a *somatic marker hypothesis* of OFC function (*58*). He suggests that there is an underlying defect in emotional processing in OFC-lesioned patients. We may choose a number of actions; each may have effects that have a certain value to us (good or bad). Damasio has argued that 'somatic markers' ('gut feelings') provide a way of speeding up decision making. Somatic markers are signals relating to body states that we learn to associate with potential actions, probably unconsciously, as we experience the outcomes to which they lead. When we next have to make a decision involving this action, these markers influence our choice (consciously or unconsciously), so we can avoid actions that lead to particularly bad outcomes. OFC-lesioned patients are suggested not to be able to do this.

In the gambling example, the somatic marker is suggested to be the SCR generated by the sympathetic nervous system. (Is the marker the internal state that also generates the SCR, or is the SCR itself the marker? This is reminiscent of the James–Lange versus Cannon–Bard debate.) Subjects associate decks A and B with 'bad' and consequently develop an anticipatory SCR when they're considering picking it; this helps them to avoid these decks. OFC-lesioned patients don't.

Amygdala–OFC interactions

Humans with amygdala lesions perform badly on the gambling task, like OFC-lesioned patients (see figure) — the only difference being that while OFC-lesioned patients still show SCRs to actual reward and punishment, amygdala-lesioned patients don't. This tends to suggest that the more basic assessment of reward and punishment is performed by the amygdala, and the OFC response is secondary (but necessary to influence decision-making).

The anterior cingulate cortex (ACC) and emotional processing

The primate ACC seems to have many functions, including a range of motivationally-oriented unlearned behaviours. In humans, ACC lesions have produced a wide variety of symptoms, including apathy, inattention, autonomic dysregulation, emotional instability, and akinetic mutism (*60*).

Emotional significance of stimuli

Imaging studies have shown that the human ACC responds to emotionally significant stimuli such as sexual imagery. In cocaine addicts, it also responds to cocaine-associated cues and this activation is correlated with cocaine craving (e.g. *61*, *62-64*).

Depression and the anterior cingulate cortex

The anterior, ventral ('affective') ACC is now strongly implicated in the pathology of depression in humans (*65*), as well as in the control of normal mood. Depressives show increased blood flow per unit volume in the ACC (*66*, *67*). The ACC is innervated by noradrenaline- and serotonin-producing neurons (as are many areas of cortex) and drugs that increase the function of these transmitters are the mainstay of treatment for depression (e.g. selective serotonin / noradrenaline reuptake inhibitors; SSRIs / SNRIs). Metabolic activity in anterior ACC is unique in differentiating those depressed patients who eventually respond to antidepressant drug therapy from those that do not (*68*, *69*). If normal subjects think sad thoughts, metabolic activity increases here (*70*). Mayberg has suggested that hyperactivity of the ACC is a primary factor in sadness and depression. This may explain the efficacy of surgical destruction of part the ACC as a therapy for refractory depression.

Part 2: Motivation

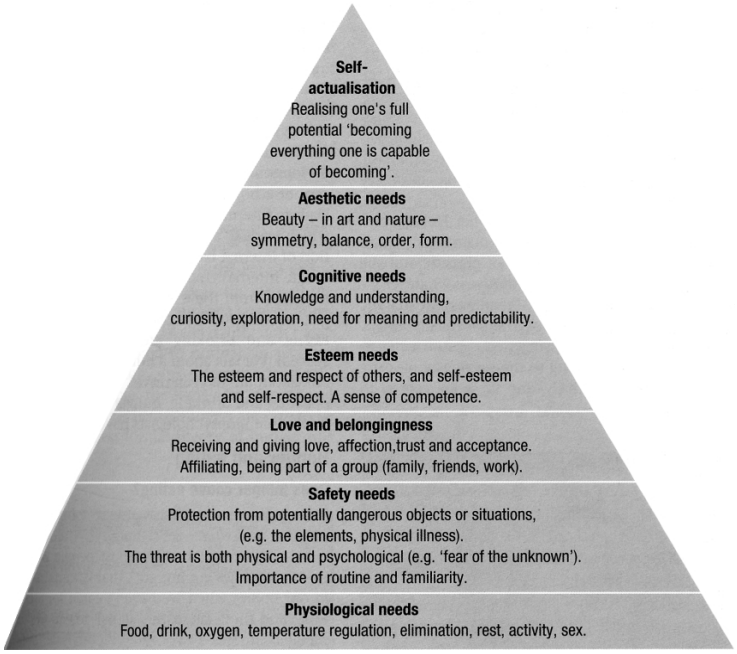
Overview

We will examine theories of motivation, from Maslow's hierarchy of needs to radical behaviourism; we'll look at the ideas of motivational states and drives, consider some hypothalamic contributions, consider the complex multi-process nature of motivated behaviour and mention behavioural economics as another analytical perspective.

Theories of motivation

Extremes of view

To ask questions about motivation is to ask *why* animals do what they do. There have been many theories of motivation over the years! At one end of the spectrum was **Maslow** (*71*), who argued that humans have a **hierarchy of needs** (physiological → safety → social → esteem → 'self-actualization', e.g. painting and composing), and must fulfil lower-level needs before addressing higher ones. It's pretty useless experimentally; it doesn't make very many testable predictions, except that nobody should starve to death for their art. Middleton Manigault, 1887–1922, did just this attempting to 'see colours not perceptible to the physical eye'.



Maslow's hierarchy of needs.

At the other end of the spectrum was Skinner (*72*), an exponent of *radical behaviourism* (see *73*). It was well known that when some events follow animals' responses (actions), they change the likelihood that the response will be repeated. Thorndike (*74*) had named this the Law of Effect, saying that events that were 'satisfying' increased the probability of preceding responses, while events that caused 'discomfort' decreased this probability. How do we know that something's 'satisfying'? Because it increases the probability of preceding responses… a circular argument?

We can illustrate this potential circularity in other ways, too. If a theory suggests that behaviour is motivated by a 'drive', but suggests that the drive exists on the basis of observed behaviour, we may have a circular argument. Suppose we arrange matters so that response R produces an outcome O. Our subject performs response R frequently. We might suggest that the subject lacks O and has an O-seeking-drive, which motivates its behaviour. But in this simple situation we have added nothing

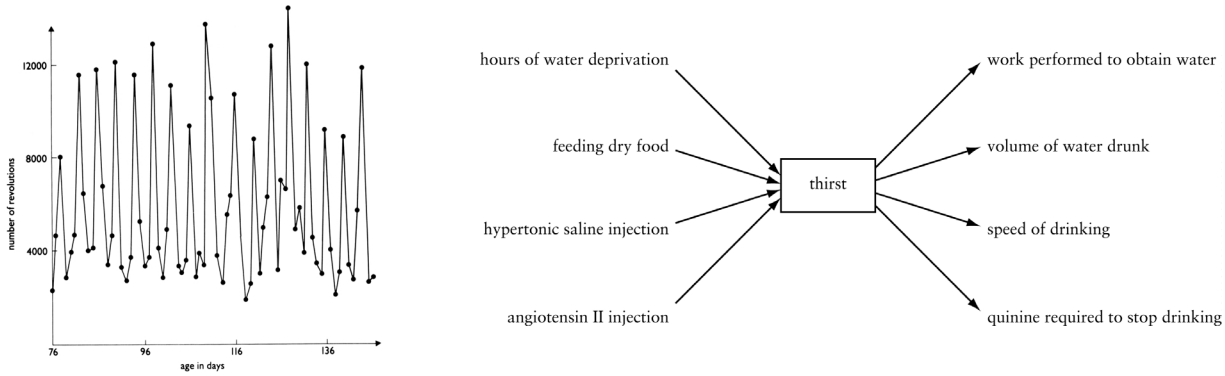
by postulating the existence of this O drive, since the argument is circular (R is motivated by O-drive; we know O-drive exists because the subject performs response R). Even worse, if R has no obvious consequence but the animal performs R, we might suggest that the animal performs R because it likes performing R — a theory that has zero predictive value. Any behaviour, however peculiar, can be explained by assuming that the behaviour itself is the subject's objective.

Skinner wanted to move away from this: he called events that strengthened preceding responses *positive reinforcers*, and events whose *removal* strengthened the preceding response he called *negative reinforcers.* Reinforcers are defined by their effect on behaviour, and therefore, to avoid a circular argument, behaviour cannot be said to have altered as a *consequence* of reinforcement (*75*). Skinner treated organisms as 'black boxes', without reference to any internal processes such as motivation. However, many would argue one must take account of 'hidden' variables (like hunger) to *explain* behaviour, rather than just to describe it. And not all attempts to suggest such hidden variables are circular arguments.

Semantic note: The term *negative reinforcement* means the strengthening of a response that removes a negative reinforcer such as electric shock — either by *escape* from the shock, or by *avoidance* of the shock. *Punishment* is the presentation of a negative reinforcer, or the removal of a positive reinforcer; it reduces the probability of the preceding response, and is therefore different from negative reinforcement.

Inferring internal states: why use concepts of drive or motivation?

Animals do not always do the same thing in the same circumstances. Yet their behaviour is often clearly not random — therefore, we seek *intervening variables* that contribute to (cause) behaviour. Ideas of drive and motivation emerge this way. For example, the activity of a female rat running in a wheel can vary considerably, but does so with a four-day cycle (*76, 77*); we might observe that this cycle corresponds to the oestrus cycle, postulating some internal variable that connects the two. Some forms of behaviour are reliably elicited by environmental stimuli — if a hand or paw makes contact with a very hot surface, it will withdraw rapidly and reflexively. But some behaviours are not so reliably connected to the environment. Male stags don't always attack when confronted with other males, but they do so in the breeding season. Rats confronted with food don't always eat it. We might postulate the internal state or variable of *hunger* to account for this variability: the rat eats more when it is hungrier.



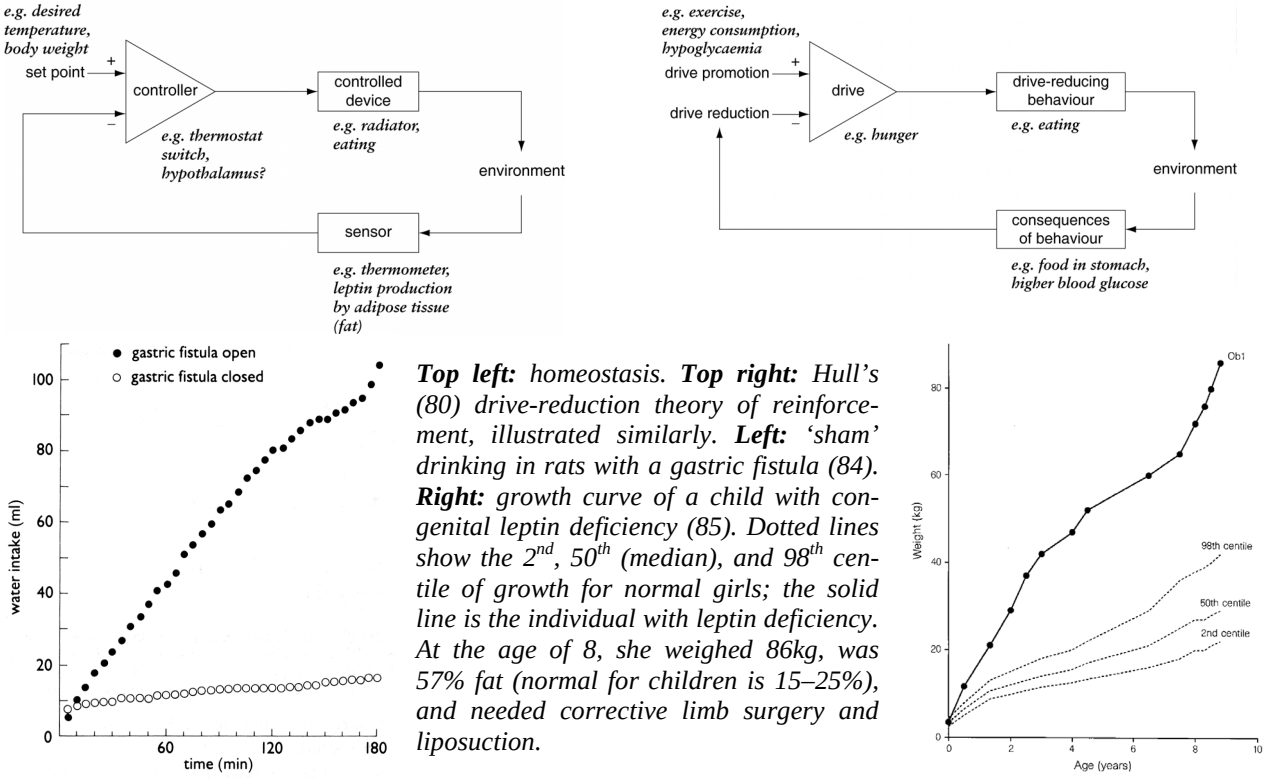
***Left:** Activity of a female rat running in a wheel (76, 77). The four-day cycle in spontaneous activity corresponds to the rat's oestrus cycle; the peaks of activity correspond to the times when the female is sexually responsive. **Right:** Thirst as an intervening variable (76).*

Furthermore, we might think the concept of hunger is useful because it predicts many things. Food-deprived people don't just eat more (and faster) when given access to food, but they perform better on arbitrary tasks such as word recognition (*78, 79*). If we allow rats to discover that an arbitrary response (such as pressing a lever) produces access to food, then we would expect a starved rat to perform more of this completely arbitrary behaviour ('work harder') than a sated rat, and this can readily be observed. A simple manipulation such as food deprivation affects a whole range of behaviours — and a motivational state (hunger) is a parsimonious way to account

for this. If someone is hungry, we might predict that they will eat lots / fast, be relatively undiscriminating amongst foods, exert effort or spend money to obtain food, and eat in preference to other potential activities. Furthermore, we can manipulate this large range of behaviours in many different ways: food deprivation makes rats eat more food / work harder for food / etc., but so does insulin injection; water deprivation makes them drink more / work harder for water / tolerate water that's more adulterated / etc., but so does eating dry food, injections of hypertonic salt solution, and angiotensin II injection. Central motivational states parsimoniously account for these kinds of findings, although there are often complexities in the details (*76*).

Motivational states and homeostasis

Hull (*80*) used motivational states as part of his theory of reinforcement. He suggested that events that *reduce drive* are positively reinforcing (so food's reinforcing when you're hungry because it reduces the hunger drive). This resembles *homeostatic* theories of motivation, such as those of Cannon (*81*). These theories suggest, for example, that we eat to regulate our blood sugar, or to regulate total body fat. There is considerable interest these days in the way the hormone *leptin*, produced by fat stores, acts to suppress eating via the hypothalamus (*82, 83*).



Top left: *homeostasis.* ***Top right:*** *Hull's (80) drive-reduction theory of reinforcement, illustrated similarly.* ***Left:*** *'sham' drinking in rats with a gastric fistula (84).* ***Right:*** *growth curve of a child with congenital leptin deficiency (85). Dotted lines show the 2nd, 50th (median), and 98th centile of growth for normal girls; the solid line is the individual with leptin deficiency. At the age of 8, she weighed 86kg, was 57% fat (normal for children is 15–25%), and needed corrective limb surgery and liposuction.*

Hypothalamic 'centres' and motivation

The hypothalamus has long been thought to play an important role in motivation. It is a set of diencephalic nuclei with access to blood-borne and CSF-borne substances and major visceral afferents; it certainly orchestrates many simple types of behavioural and endocrine responses (many of the latter via the pituitary). Early work revolved around the ideas of hypothalamic 'centres'. The lateral hypothalamus was thought to be a 'feeding centre' — for example, electrolytic lesions produced aphagia (*86*); the ventromedial hypothalamus was thought to be a 'satiety centre', as lesions produced hyperphagia (*87, 88*); the subfornical region and preoptic region are involved in the control of drinking (*89*); the medial preoptic area, which is sexually dimorphic, is required for normal copulatory behaviour (*90, 91*); defensive and offensive aggression can be altered by electrolytic lesions of the medial or lateral hypothalamus (*92*); thermoregulation is impaired by lesions of the preoptic area and anterior hypothalamus (*93, 94*), and so on.

Criticisms can be levelled at many of the studies invoking hypothalamic 'centres'. For example, electrolytic lesions destroy (and electrical stimulation stimulates) axons passing through the hypothalamus on their way elsewhere ('fibres of passage'). These include important dopaminergic axons from the midbrain to the basal ganglia and cortex; dopamine denervation contributed to the original 'lateral hypothalamic syndrome'. More restricted, excitotoxic lesions often have lesser effects. The idea that the lateral hypothalamus is a 'hunger centre' is at odds with the observation that lateral hypothalamic lesions do not always make rats eat less (e.g. if starved before surgery) — it may be that the rats are trying to regulate their body weight around a new, lower limit (*95*). Hyperphagia is more reliably produced by lesions of the paraventricular nucleus of the hypothalamus than the ventromedial hypothalamus — in fact, many hypothalamic nuclei are involved in the control of feeding (*83*). Sometimes lesions are followed by recovery of function (due to recovery of partially damaged neurotransmitter systems or reorganization). Moreover, many aspects of behaviour survive hypothalamic damage: an excellent example would be the fact that although medial preoptic area hypothalamic lesions impair copulation, they do not prevent male rats *working* for a female (*91*) — this more complex aspect of motivated behaviour depends in part on the amygdala (*96*).

So the hypothalamus appears to contribute in major ways to important motivated behaviours — but it does not control all aspects of those behaviours, and there are not discrete 'centres' for specific functions like hunger and satiety.

Non-homeostatic motivation?

However, there are aspects of motivation that homeostatic theories don't account for well. Animals can be induced to eat or drink when they're not hungry or thirsty — their consumption doesn't just depend on their physiological needs (see *97*). In humans, social and stimulus-based control of eating and drinking is very prominent. Do animals have a latent drive to take cocaine? To stimulate parts of their own brain electrically (*98*)? Do humans? This seems to push the 'drive' concept too far — to examine these forms of motivation we need to look deeper at the processes that govern instrumental behaviour.

The many faces of motivated behaviour

There are many psychological mechanisms for action. We've mentioned *Pavlovian (classical) conditioning.* Also, we mustn't forget that many forms of behaviour are *unlearned.* These include simple spinal and brainstem reflexes, which influence skeletal musculature (respiratory movements, postural reflexes, pain withdrawal reflexes, etc.) and autonomic function (such as the regulation of heart rate and arteriolar smooth muscle tone to maintain arterial blood pressure). Swallowing is a more complicated example of unlearned behaviour (*99*).

However, when we choose to measure motivation we are often interested in behaviours that are directed at obtaining particular goals, not just behaviours that animals perform once those goals are at hand. The difference can be phrased in several ways: ***appetitive* versus *consummatory*** is one popular way. In fact, it's been clear for some time that consummatory behaviour (e.g. eating, drinking, copulating — directly related to using behavioural 'goals') — is separable from appetitive behaviour (directed to obtaining these goals in the first place). For example, lesions of the preoptic area of the hypothalamus prevent rats from shivering, eating more, building nests, or running around when it gets cold — consummatory behaviour is impaired. However, these rats can still learn to press a lever to obtain hot or cool air, and can regulate their temperature this way — appetitive behaviour is intact (*93*). In fact, the two can be doubly dissociated: lesions of the medial preoptic area of the hypothalamus prevent male rats from copulating (impaired 'consummatory' response) but do not prevent them from working to obtain a female (normal 'appetitive' response). In contrast, lesions of the basolateral amygdala have the opposite effect (*91, 96*). So how is goal-directed behaviour organized psychologically?

It turns out to be complex, even in rats (see *45*). If you arrange matters so that a lever-press leads to food delivery, hungry rats will learn to press the lever **(instru-**

mental conditioning). Instrumental responding involves at least the following processes, which can be psychologically and neurally dissociated (*45*):

- Rats press levers for food because they are aware of the **contingency** between pressing the lever and obtaining the food, and because they are simultaneously aware of the **instrumental value** of the food. They know what they want, and they know how to get it. This is a form of declarative memory.
- A separate system assesses the **'hedonic' value** of the food when the rat actually eats it. (It is occasionally possible to trick the rat so that the instrumental value is high while the hedonic value is low — in which case the rat will work for something that it won't subsequently eat.)
- They also press levers because they've often pressed the lever before and been reinforced — this process does not require them to know what the lever-pressing will lead to. This is a **stimulus–response habit,** a form of procedural memory. It develops slowly but can come to dominate behaviour in the well-trained animal.
- **Pavlovian CSs** that signal food can provide a motivational 'boost' to responding.

Habits, and the influence of Pavlovian cues on motivation, may be very important in drug addiction (*100-104*), not to mention the way that supermarkets encourage people to buy things. Pavlovian cues have more of an influence when you're in the correct motivational state (e.g. food-related cues are more effective when you're hungry), which may be one reason why people buy more food in supermarkets when they're hungry (e.g. *105, 106*).

Another perspective: behavioural economics, and addiction

Finally, **behavioural economics** is a powerful set of theories for the analysis of motivated behaviour and choice (*107, 108*). Economics assumes the existence of 'rational agents', who act in their own best interest according to sensible principles (*109, 110*). Behavioural economics acknowledges that humans violate these principles in several ways, some of them predictable (*111-113*) — for example, humans often choose impulsively, focusing on the immediate consequences rather than the long-term consequences of their actions.

One important principle of economics is that you judge people's value systems by what they do, not what they say (the **principle of revealed preference**): if a smoker tells you he's just had a heart attack, is desperate to give up and is in mortal fear for his life as a result of his smoking, and then smokes a cigarette, an economist would say that the value of smoking was higher to him than the value of not smoking, whatever he says. One very useful economic measure is **elasticity of demand:** how much does a person's demand for something (e.g. cigarettes, alcohol) vary as the price (be it financial, social, medical, etc.) changes? Demand for some things is relatively **elastic** (e.g. cinema tickets — if the price goes up, your consumption may drop substantially); demand for other things is relatively **inelastic** (e.g. food when you're hungry — if the price of food goes up, you pay more).

Drug addiction can be thought of as abnormally inelastic demand. Perhaps the more someone is 'addicted', the more inelastic their demand is — they will therefore sacrifice other commodities (work, money, social interaction) rather than sacrifice drug. For example, alcohol demand in rats can be more inelastic than demand for food (*114, 115*). While this is a useful way to think about addiction, it is not an all-or-nothing phenomenon. The Treasury is well aware of the elasticity of demand for products like alcohol: tax policy is a very effective way to change consumption at the population level (e.g. *116, 117, 118*). Increasing the effective price of drugs to an individual — by making the health costs more salient to him or her, by increasing the social cost (e.g. via a public declaration of intent to quit), by increasing the financial price, by paying him/her to quit, or by decreasing the price (or increasing the availability) of alternative valued activities — helps people to quit (*119, 120*).

Bibliography

1. T. C. Schelling, *The strategy of conflict* (Harvard University Press, Cambridge, MA, 1960).
2. R. H. Frank, *Passions within reason: the strategic role of the emotions* (Norton, New York, 1988).
3. S. Pinker, *How The Mind Works* (Allen Lane - The Penguin Press, London, 1997).
4. R. Trivers, *Social evolution* (Benjamin/Cummings, Reading, MA, 1985).
5. M. Ridley, *The Red Queen: Sex and the Evolution of Human Nature* (Viking, London, 1993).
6. C. Darwin, *The Expression of the Emotions in Man and Animals with photographic and other illustrations* (J. Murray, London, 1872).
7. P. Ekman, W. V. Friesen, P. Ellsworth, *Emotion in the Human Face: Guidelines for Research and an Integration of Findings* (Pergamon, New York, 1972).
8. P. Ekman, W. V. Friesen, *Unmasking the Face* (Prentice-Hall, Englewood Cliffs, NJ, 1975).
9. W. James, *Mind* **9**, 188-205 (1884).
10. C. G. Lange, in *The Emotions* K. Dunlap, Ed. (Hafner, London, 1885 / 1967).
11. W. B. Cannon, *American Journal of Psychology* **39**, 106-124 (1927).
12. G. Marañon, *Revue Française d'Endocrinologie* **2**, 301-325 (1924).
13. P. Bard, in *A Handbook of General Experimental Psychology* C. Murchison, Ed. (Clark University Press, Worcester, MA, 1934) pp. 264-311.
14. G. W. Hohmann, *Psychophysiology* **3**, 143-156 (1966).
15. A. F. Ax, *Psychosomatic Medicine* **15**, 433-442 (1953).
16. P. Ekman, R. W. Levenson, W. V. Friesen, *Science* **221**, 1208-10 (1983).
17. J. D. Laird, *Journal of Personality and Social Psychology* **29**, 475-486 (1974).
18. S. Schachter, in *Advances in Experimental Social Psychology, Volume 1* L. Berkowitz, Ed. (Academic Press, New York, 1964).
19. R. S. Lazarus, *American Psychologist* **37**, 1019-1024 (1982).
20. S. Schachter, J. E. Singer, *Psychological Review* **69**, 379-399 (1962).
21. G. D. Marshall, P. G. Zimbardo, *Journal of Personality and Social Psychology* **37**, 970-988 (1979).
22. J. C. Speisman, R. S. Lazarus, A. M. Mordkoff, L. A. Davidson, *Journal of Abnormal and Social Psychology* **68**, 397-398 (1964).
23. S. Schachter, *Science* **161**, 751-756 (1968).
24. J. Slochower, *Psychosomatic Medicine* **38**, 131-139 (1976).
25. D. C. Dutton, A. P. Aron, *Journal of Personality and Social Psychology* **30**, 510-517 (1974).
26. S. Valins, *Journal of Personality and Social Psychology* **4**, 400-408 (1966).
27. J. H. Martin, *Neuroanatomy: Text and Atlas* (Appleton & Lange, East Norwalk, CT, 1989).
28. P. Broca, *Revue Anthropologique (Paris)* **1**, 456-498 (1878).
29. J. W. Papez, *Archives of Neurology and Psychiatry* **38**, 725-743 (1937).
30. P. D. MacLean, *Psychosomatic Medicine* **11**, 338-353 (1949).
31. W. B. Cannon, S. W. Britton, *American Journal of Physiology* **72**, 283-294 (1925).
32. P. Bard, *American Journal of Physiology* **84**, 490-515 (1928).
33. W. R. Hess, *Beitrage zur Physiologie des Hirnstammes* (Georg Thième, Leipzig, 1932).
34. P. Bard, V. B. Mountcastle, *Res. Pub. Assoc. Nervous Mental Diseases* **31**, 362-404 (1948).
35. H. Klüver, P. C. Bucy, *Archives of Neurology and Psychiatry* **42**, 979-997 (1939).
36. H. Klüver, P. C. Bucy, *American Journal of Physiology* **119**, 352-353 (1937).
37. S. Brown, E. A. Schaefer, *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences* **179**, 303-327 (1888).
38. H. Terzian, G. Dalle Ore, *Neurology* **5**, 373-380 (1955).
39. W. B. Marlowe, E. L. Mancall, J. J. Thomas, *Cortex* **11**, 53-59 (1975).
40. J. P. Aggleton, R. C. Saunders, in *The amygdala: a functional analysis* J. P. Aggleton, Ed. (Oxford University Press, New York, 2000) pp. 1-30.
41. A. Bechara, et al., *Science* **269**, 1115-8 (1995).
42. A. Bechara, H. Damasio, A. R. Damasio, G. P. Lee, *Journal of Neuroscience* **19**, 5473-81 (1999).
43. R. Adolphs, D. Tranel, H. Damasio, A. Damasio, *Nature* **372**, 669-72 (1994).
44. L. Cahill, in *The amygdala: a functional analysis* J. P. Aggleton, Ed. (Oxford University Press, New York, 2000) pp. 425-445.
45. R. N. Cardinal, J. A. Parkinson, J. Hall, B. J. Everitt, *Neuroscience and Biobehavioral Reviews* **26**, 321-352 (2002).
46. M. Numan, T. P. Sheehan, *Ann N Y Acad Sci* **807**, 101-25 (1997).
47. K. Stern, M. K. McClintock, *Nature* **392**, 177-9 (1998).
48. J. E. LeDoux, *Annual Review of Neuroscience* **23**, 155-184 (2000).
49. M. Davis, in *The amygdala: a functional analysis* J. P. Aggleton, Ed. (Oxford University Press, New York, 2000) pp. 213-287.
50. J. L. McGaugh, B. Ferry, A. Vazdarjanova, B. Roozendaal, in *The amygdala: a functional analysis* J. P. Aggleton, Ed. (Oxford University Press, New York, 2000) pp. 391-423.
51. J. L. McGaugh, *Science* **287**, 248-51 (2000).
52. L. Cahill, B. Prins, M. Weber, J. L. McGaugh, *Nature* **371**, 702-4 (1994).
53. L. Cahill, R. Babinsky, H. J. Markowitsch, J. L. McGaugh, *Nature* **377**, 295-6 (1995).
54. K. C. Liang, R. G. Juler, J. L. McGaugh, *Brain Res* **368**, 125-33 (1986).
55. J. M. Harlow, *Boston Medical and Surgical Journal* **39**, 389-393 (1848).
56. J. M. Harlow, *Publications of the Massachusetts Medical Society* **2**, 327-47 (1868).
57. H. Damasio, T. Grabowski, R. Frank, A. M. Galaburda, A. R. Damasio, *Science* **264**, 1102-5 (1994).
58. A. R. Damasio, *Descartes' Error* (Grosset/Putnam, New York, 1994).
59. A. Bechara, A. R. Damasio, H. Damasio, S. W. Anderson, *Cognition* **50**, 7-15 (1994).
60. O. Devinsky, M. J. Morrell, B. A. Vogt, *Brain* **118**, 279-306 (1995).
61. L. C. Maas, et al., *American Journal of Psychiatry* **155**, 124-126 (1998).
62. N. D. Volkow, G. J. Wang, J. S. Fowler, *Ann N Y Acad Sci* **820**, 41-54; discussion 54-5 (1997).
63. A. R. Childress, et al., *American Journal of Psychiatry* **156**, 11-18 (1999).
64. H. Garavan, et al., *American Journal of Psychiatry* **157**, 1789-1798 (2000).
65. C. J. Bench, et al., *Psychological Medicine* **22**, 607-15 (1992).
66. W. C. Drevets, *Biological Psychiatry* **48**, 813-829 (2000).
67. H. S. Mayberg, *Journal of Neuropsychiatry and Clinical Neurosciences* **9**, 471-481 (1997).
68. H. S. Mayberg, et al., *Neuroreport* **8**, 1057-1061 (1997).
69. H. S. Mayberg, et al., *Biological Psychiatry* **48**, 830-843 (2000).
70. H. S. Mayberg, et al., *American Journal of Psychiatry* **156**, 675-682 (1999).
71. A. Maslow, *Motivation and Personality* (Harper & Row, New York, 1954).
72. B. F. Skinner, *The behavior of organisms: an experimental analysis* (Appleton, New York, 1938).
73. H. C. Wilcoxon, in *Reinforcement and Behavior* J. T. Tapp, Ed. (Academic Press, New York, 1969) pp. 1-46.
74. E. L. Thorndike, *The Elements of Psychology* (Seiler, New York, 1905).
75. B. F. Skinner, *Science and Human Behavior* (Macmillan, New York, 1953).
76. F. Toates, *Motivational systems* (Cambridge University Press, Cambridge, 1986).
77. C. P. Richter, *Quarterly Review of Biology* **2**, 307-343 (1927).
78. E. D. Ferguson, *Motivation: a biosocial and cognitive integration of motivation and emotion* (Oxford University Press, Oxford, 2000).
79. R. J. Erwin, E. D. Ferguson, *American Journal of Psychology* **92**, 611-626 (1979).
80. C. L. Hull, *Principles of behavior* (Appleton-Century-Crofts, New York, 1943).
81. W. B. Cannon, *Bodily Changes in Pain, Hunger, Fear, and Rage* (Appleton, New York, 1929).
82. J. K. Elmquist, E. Maratos-Flier, C. B. Saper, J. S. Flier, *Nature Neuroscience* **1**, 445-450 (1998).
83. J. K. Elmquist, C. F. Elias, C. B. Saper, *Neuron* **22**, 221-32 (1999).
84. B. J. Rolls, E. T. Rolls, *Thirst* (Cambridge University Press, Cambridge, 1982).
85. C. T. Montague, et al., *Nature* **387**, 903-8 (1997).
86. B. K. Anand, J. R. Brobeck, *Yale Journal of Biology and Medicine* **24**, 123-140 (1951).
87. A. W. Hetherington, S. W. Ranson, *Journal of Comparative Neurology* **76** (1942).
88. A. W. Hetherington, S. W. Ranson, *Proceedings of the Society for Experimental Biology and Medicine* **41**, 465-466 (1939).
89. J. T. Fitzsimons, J. Kucharczyk, *Journal of Physiology* **276**, 419-434 (1978).
90. C. W. Malsbury, D. W. Pfaff, A. M. Malsbury, *Brain Research* **181**, 267-284 (1980).
91. B. J. Everitt, P. Stacey, *Journal of Comparative Psychology* **101**, 407-19 (1987).
92. D. B. Adams, *Nature* **232**, 573-574 (1971).
93. H. J. Carlisle, *Journal of Comparative and Physiological Psychology* **69**, 391-402 (1969).
94. J. A. Boulant, *Clin Infect Dis* **31 Suppl 5**, S157-61 (2000).
95. T. L. Powley, R. E. Keesey, *Journal of Comparative and Physiological Psychology* **70**, 25-36 (1970).
96. B. J. Everitt, M. Cador, T. W. Robbins, *Neuroscience* **30**, 63-75 (1989).
97. R. D. Gross, *Psychology: the Science of Mind and Behaviour* (Hodder & Stoughton, London, ed. Fourth, 2001).
98. J. Olds, P. Milner, *Journal of Comparative and Physiological Psychology* **47**, 419-427 (1954).
99. R. W. Doty, J. F. Bosma, *Journal of Neurophysiology* **19**, 44-60 (1956).
100. F. H. Gawin, *Science* **251**, 1580-1586 (1991).
101. S. T. Tiffany, D. J. Drobes, *Addict Behav* **15**, 531-9 (1990).
102. C. P. O'Brien, A. R. Childress, R. Ehrman, S. J. Robbins, *Journal of Psychopharmacology* **12**, 15-22 (1998).
103. T. E. Robinson, K. C. Berridge, *Brain Research Reviews* **18**, 247-91 (1993).
104. R. N. Cardinal, B. J. Everitt, *Curr Opin Neurobiol* **14**, 156-62 (2004).
105. D. K. Dodd, R. B. Stalling, J. Bedell, *International Journal of Obesity* **1**, 43-47 (1977).
106. D. J. Mela, J. I. Aaron, S. J. Gatenby, *Physiol Behav* **60**, 1331-5 (1996).
107. H. Rachlin, L. Green, J. Kagel, R. Battalio, in *The Psychology of Learning and Motivation* G. Bower, Ed. (Academic Press, New York, 1976) pp. 129-154.
108. J. Allison, *Behavioral Science* **24**, 403-415 (1979).
109. J. von Neumann, O. Morgenstern, *Theory of games and economic behavior* (Princeton University Press, Princeton, New Jersey, 1947).
110. S. J. Russell, P. N. Norvig, *Artificial Intelligence: a modern approach* (Prentice-Hall, Upper Saddle River, New Jersey, 1995).
111. D. Kahneman, P. Slovic, A. Tversky, Eds., *Judgement Under Uncertainty: Heuristics and Biases* (Cambridge University Press, New York, 1982).
112. V. M. Chase, R. Hertwig, G. Gigerenzer, *Trends in Cognitive Sciences* **2**, 206-214 (1998).
113. D. E. Heckerman, E. J. Horvitz, B. N. Nathwani, *Methods of Information in Medicine* **31**, 90-105 (1992).
114. G. M. Heyman, K. Gendel, J. Goodman, *Psychopharmacology (Berl)* **144**, 213-9 (1999).
115. G. M. Heyman, *Alcohol Res Health* **24**, 132-9 (2000).
116. T. E. Keeler, T. W. Hu, P. G. Barnett, W. G. Manning, *J Health Econ* **12**, 1-18 (1993).
117. G. J. Madden, W. K. Bickel, *Addiction* **94**, 577-88 (1999).
118. F. J. Chaloupka, S. Emery, L. Liang, in *Choice, Behavioral Economics and Addiction* N. Heather, R. E. Vuchinich, Eds. (Elsevier, Oxford, 2003) pp. 71-89.
119. H. Rachlin, in *Choice, Behavioral Economics and Addiction* N. Heather, R. E. Vuchinich, Eds. (Elsevier, Oxford, 2003) pp. 129-149.
120. K. E. McCollister, M. T. French, *Addiction* **98**, 1647-59 (2003).