Review

Cell PRESS

Feature Review

The neural mechanisms of inter-temporal decision-making: understanding variability

Jan Peters and Christian Büchel

Department of Systems Neuroscience, University Medical Centre Hamburg-Eppendorf, Martinistraße 52, 20246 Hamburg, Germany

Humans and animals prefer immediate over delayed rewards (delay discounting). This preference for smaller-but-sooner over larger-but-later rewards shows substantial interindividual variability in healthy subjects. Moreover, a strong bias towards immediate reinforcement characterizes many psychiatric conditions such as addiction and attention-deficit hyperactivity disorder. We discuss the neural mechanisms underlying delay discounting and describe how interindividual variability (trait effects) in the neural instantiation of subprocesses of delay discounting (such as reward valuation, cognitive control and prospection) contributes to differences in behaviour. We next discuss different interventions that can partially remedy impulsive decision-making (state effects). Although the precise neural mechanisms underlying many of these modulating influences are only beginning to be unravelled, they point towards novel treatment approaches for disorders of impulse control.

The subjective nature of preferences

Experience tells us that preferences are subjective. Some people are patient, others impatient, some take risks and others tend to avoid them. In recent years, many areas of decision science, including psychology, behavioural economics, psychiatry and cognitive and systems neuroscience, have adopted approaches that focus on subjective aspects of choice and valuation. One area of research that has been extremely fruitful in the study of subjective choice and valuation is intertemporal decision making (see Glossary). In intertemporal choice problems, agents are required to compute a trade-off between time and gains or losses. Typically, future outcomes are devalued as a function of delay [1] and this process is referred to as temporal discounting or delay discounting (DD). The subjective value of a reward of €50 is greater when delivered today than when expected in a month's time. This highly interdisciplinary area of research has shown remarkable success and rapid progress in the past few years for a number of reasons. The issue is of high ecological relevance, because intertemporal decisions are abundant in everyday life, such as in the areas of education, health, retirement savings, investment and so forth. The issue is also of high clinical relevance, because impairments in DD characterize a range of psychiatric conditions, including substance abuse, addiction and attention-deficit hyperactivity disorder. Finally, formal models of intertemporal choice can describe individual preferences with high accuracy, which facilitates the detection of subtle differences in preferences both within and between individuals.

In this review, we start with a brief introduction on modelling of DD and then summarize sources of variability between individuals. We draw a core distinction between trait differences (i.e. differences in decision-making between individuals, e.g. because of genetic factors) and state differences (i.e. context-dependent changes in preferences within the same individual). We then examine what cognitive neuroscience has contributed to our understanding of the neural mechanisms underlying intertemporal decision-making. We first identify component processes of DD (e.g. reward valuation, cognitive control and prospection) and examine how variability in these processes at the neural level accounts for interindividual differences in behaviour. We then turn to the state dependency of DD and highlight recent attempts to modulate discounting within subjects using behavioural, pharmacological and training-based interventions.

Glossary

Delay (or temporal) discounting: the phenomenon that agents typically devalue rewards as a function of the delay to their delivery.
Dynamic inconsistency: Consistent delay discounting entails that adding a common constant delay to the available options does not change which option is preferred by an individual. The fact that human preferences are typically not consistent in this fashion is referred to as dynamic inconsistency. For example, an individual may prefer 20€ in 1 week over 25€ in 2 weeks, but 25€ in 10 weeks over 20€ in 9 weeks.
Framing effect: a modulation of decision-making due to the way in which a decision problem is stated.
Indifference point: a magnitude-delay combination of a larger-but-later reward which is of equal subjective value as a particular smaller-but-sooner reward.
Inter-temporal choice: choosing between options associated with outcomes at different points in the future.
State-difference: a difference in behaviour in an individual that depends on short-term situational factors, such as a pharmacological intervention or a particular framing effect.
Trait-difference: a difference in behaviour between groups of subjects (e.g. psychiatric patients and healthy subjects) that is relatively stable over time, and thus similar to a personality variable.

Corresponding author: Peters, J. (j.peters@uke.uni-hamburg.de).

  doi:10.1016/j.tics.2011.03.002

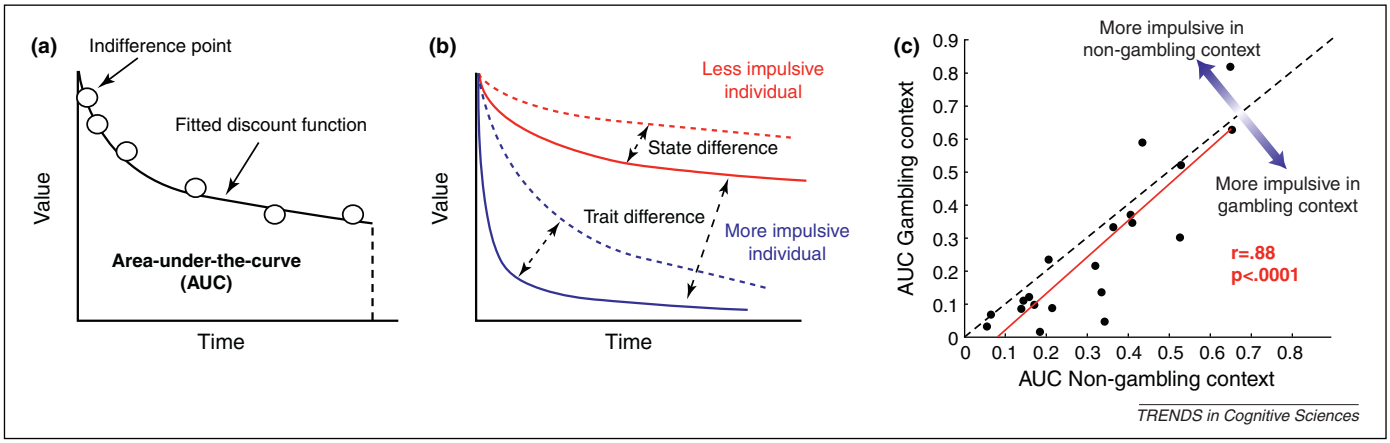

Figure 1. (**a**) Exemplary discount curve. Indifference points correspond to magnitude-delay combinations of delayed rewards that, for one particular subject, are subjectively equivalent to some smaller-but-sooner reward. Different model functions can be fitted to these points (see the main text). The area under the empirical discount curve (AUC) constitutes a model-free measure of the degree of discounting. (**b**) Prototypical discount functions for a more impulsive subject (blue) and a less impulsive subject (red). The difference in these curves corresponds to a trait difference. Preferences in both individuals can be modulated by contextual or situational factors (dashed lines), corresponding to state differences. (**c**) State and trait differences in delay discounting in pathological gamblers (data from [17]). Delay discounting was assessed using the model-free AUC measure in a gambling context (y axis) and in a non-gambling context (x axis). The test–retest reliability was very high (r=0.88, p<0.001), indicating trait-like stability of discounting. At the same time, the vast majority of gamblers discounted less when tested in a non-gambling context (most points are below the dashed diagonal), indicating a state-dependent change in preferences.

Computational models of DD

Standard models

Computational models of DD aim to develop functions that capture the relationship between temporal proximity and subjective value (Figure 1a). Two models have dominated the field of temporal discounting for the last decades and both include a single free parameter, the discount rate k. The decay of subjective value (SV) over time is modelled as an exponential (i.e. $SV=Ae^{-kD}$ [2]) or hyperbolic (i.e. $SV=A/(1+kD)$ [3]) function of delay, where A is the objective amount of the reward, D is the delay and k is the subject-specific discount rate. In both models, lower values of k indicate that a subject is relatively patient and willing to wait for a longer time, even for a delayed payoff that is only moderately larger than the available smaller-but-sooner option. Greater values of k, conversely, reflect the fact that a subject is impatient and refuses to wait, even for relatively large rewards in the proximal future. Typically, the hyperbolic model is preferred over the exponential model [1] because of a superior fit to most data sets [4] and because, unlike the exponential model, it can account for temporal discounting phenomena such as dynamic inconsistency [1]. Finally, a model-free measure of DD can be derived by simply calculating the area under the empirically derived curve (AUC; Figure 1a) [5]. Larger AUC values correspond to less discounting, whereas smaller values correspond to greater discounting.

Two-parameter extensions

More recent research indicates that an additional parameter might be required to accurately model temporal discounting, at least in human subjects [1]. Two-parameter extensions of both the exponential and hyperbolic models have been suggested. For instance, a prominent extension of the exponential model, the β–δ model, introduces an additional parameter (β) that specifically weights immediate rewards [6]. Unlike the single-parameter exponential function, this two-parameter model can account for dynamic inconsistency. Two-parameter extensions of the hyperbolic model are often referred to as quasi-hyperbolic models and introduce an additional scaling exponent, either applied to the entire denominator ($SV=A/(1+kD)^s$ [7]) or only to the delay ($SV=A/(1+kD^s)$ [8]). There is some evidence that two-parameter models provide an even better fit than single-parameter models [4] even when accounting for increased model complexity [9]. The additional scaling exponent in the latter model might also have a psychological interpretation as the scaling of subjective time, which is often highly non-linear (Box 1) [10].

The success of these models can be attributed to both their simplicity and the fact that the discount rate (or AUC) facilitates a direct psychological interpretation as a measure of impulsivity or impatience. The degree of discounting seems to be a trait-like characteristic of an individual that is stable within subjects for periods from weeks or months [11–14] to years [15,16]. To illustrate this effect, Figure 1c shows the stability of temporal discounting (assessed using the model-free AUC measure) for pathological gamblers tested once in a gambling context (y axis) and once in a non-gambling context (x axis) [17]. The test–

Box 1. Subjective time perception and discounting

Delay discounting might partly be attributable to a dilated subjective time perception [10]. If an agent perceives delays as subjectively longer than they actually are, this might in part account for an increased tendency to choose smaller but sooner rewards, because subjectively the future will seem to be more distant. Interestingly, there is some evidence of overestimation of temporal durations in addicts that is partly accounted for by differences in impulsivity [132]. Addicts typically show particularly steep delay discounting, which suggests a link between discounting, impulsivity and time perception [109]. Although the time scale investigated in this study was in the range of seconds to minutes rather than days or months (as is typical in studies of delay discounting), subjective overestimation of durations might be an additional factor contributing to increased discounting in addiction.

retest reliability (a measure of consistency of a particular assessment over time) was highly significant, reflecting the high long-term (trait-like) stability of temporal discounting.

Such model-based analyses of decision-making facilitate the detection of even relatively subtle changes in preferences, both between and within individuals. In addition, subjective values derived from these computational models can be used as explanatory variables in electrophysiological [18] and human functional neuroimaging studies [11,12,19,20], facilitating the characterization of neural activity that co-varies with these subjectively discounted values.

Individual differences in DD

The trait–state distinction

An important question that arises in decision research is whether certain differences observed in choice and valuation (e.g. between different individuals or experimental conditions) are caused by state or trait differences. In particular with respect to DD, it has recently been suggested that both factors might affect decision-making [21]. In this view, preferences are flexible and dependent on the decision context or current requirements of the organism. These factors might thus induce a state-dependent shift in the value function that reflects the ability of the organism to adapt preferences and choices to a changing environment or changing internal states or goals (Figure 1b). At the same time, such state-dependent changes might occur at different baseline levels in different individuals, and these different baseline levels of preferences reflect the trait component. Figure 1c shows how the degree of discounting in a group of pathological gamblers is stable across multiple testing sessions [17] (trait component). In fact, there is even some evidence that the trait-like stability of DD might be partly determined by genetic factors (Box 2). However, the data shown in Figure 1c also reveal a state-dependent shift in preferences: the vast majority of gamblers were more impulsive (i.e. smaller AUC) when tested in a gambling context compared to a non-gambling context. In the following sections on trait differences, we focus on addiction and the crucial period of adolescence (Box 4) as two well-studied examples of trait differences in valuation processes.

Box 2. Evidence of a genetic basis of DD

A number of recent findings corroborated the idea that DD might be a trait-like characteristic of the individual that is at least partly attributable to genetic differences in the dopaminergic system. For example, a recent study examined polymorphisms in genes that code for D2 and D4 dopamine receptors, *DRD2* and *DRD4* [133]. Increased DD was associated with specific polymorphisms in these genes, but the overall level of variance explained by genetic differences was relatively low. The Val158Met polymorphism of the catechol-*O*-methyltransferase (*COMT*) gene, affecting mainly prefrontal dopamine levels, was also examined in a small sample of nineteen subjects [52]. Met/Met carriers for this enzyme are thought to have higher tonic dopamine concentrations, predominantly in the PFC, but also in subcortical regions, compared to Val/Val carriers [134]. Compared to Met/Met carriers, Val/Val carriers showed increased discounting [52].

More recently, a longitudinal study in twins revealed significant heritability of DD at the ages of both 12 and 14 years [15]. Here, the proportion of variance explained by genetic factors was substantially greater (~30% and ~50% at age 12 and 14 years, respectively), which suggests that a considerable variety of genes (rather than just dopamine-related genes) might contribute to the interindividual variability of DD. Convergent cross-species evidence comes from a study in rodents that revealed that different strains of rats also show distinct patterns of DD, compatible with a role of genetic factors [135]. Thus, there is mounting overall evidence of a genetic influence on interindividual differences in DD.

DD in addiction

The rate of DD is a reliable trait marker for addiction, because addicts typically discount delayed rewards much more steeply than control subjects [21,22]. This has been observed for opioid-dependent subjects [23,24], methamphetamine users [25], smokers [26–31] and alcoholics [32,33], and thus seems to be largely independent of the particular drug of abuse. In fact, similar effects have been reported for pathological gambling [34–37], a non-substance-based addiction [38]. Additional evidence indicates that impulsive discounting in addiction is observed for both non-drug rewards such as money and the drug of abuse, although discounting for the latter might be even steeper [26,39,40].

The association of DD with addiction raises the typical question of causality: is increased discounting a consequence or cause of addiction? One possibility is that common genetic factors might result in an impulsive personality (which is reflected in steeper discounting) and at the same time increase the likelihood of drug use [41]. Alternatively, impulsive discounting might arise as a consequence of long-term drug use, which could induce changes at the neural level that bias an individual to make short-sighted decisions. A recent longitudinal study addressed this issue in a large cohort of adolescents [32], a population that is often considered particularly vulnerable to addiction [42,43]. No association between changes in DD over time and changes in smoking behaviour was observed. That is, subjects who smoked more over time did not exhibit an increase in DD over time. DD might therefore constitute a risk factor for smoking, rather than being a consequence of long-term nicotine use. This view is also compatible with the finding that even mild adolescent smokers show increased DD, in conjunction with reduced striatal reward anticipation responses [31]. Similar observations have been made in rats that were pre-screened for differences in DD [44]. Steeply discounting animals acquired a cocaine self-administration habit significantly faster and at higher dosages than rats who discounted less, in line with the view that DD reflects a risk factor for substance abuse.

At the same time, effects of chronic exposure might differ between drugs. For example, prior exposure to cocaine induces long-term increases in DD in rats [45,46] and leads to long-term neural changes such as a reduction in dopamine D2 receptor availability in monkeys [47]. Along similar lines, acute administration of D-amphetamine (a drug that increases extracellular dopamine levels) in rats decreases discounting, whereas chronic administration increases discounting [48]. Thus, depending on the specific drug or substance in question, effects on DD can be chronic and/or related to acute exposure (or withdrawal).

The cognitive neuroscience of DD: trait effects

Recent theoretical accounts distinguish between at least two general processing stages in decision-making [49]: valuation, which is the neural computation and representation of the subjective values of available decision options, and choice, which comprises processes leading to and supporting action selection. Following this taxonomy, we first focus on the neural mechanisms underlying reward valuation processes in DD. We then address the role of processes related to conflict monitoring and cognitive control, and finally consider the role of prospection in intertemporal decision-making. In all cases, we highlight how alterations in the processes might contribute to trait differences in DD.

The valuation network

Domain-general and domain-specific valuation

Overwhelming evidence implicates the ventral striatum (VS) and orbitofrontal cortex (OFC), in particular its ventromedial part (often referred to as ventromedial prefrontal cortex, vmPFC, or medial OFC) in the representation of the incentive value of a broad range of different classes of rewards [49–52]. The VS is a projection region of dopaminergic neurons in the substantia nigra (SN) and the ventral tegmental area (VTA), which have been implicated in reinforcement learning and reward processing [53]. The VS and vmPFC are strongly interconnected and have extensive connections to other regions such as the amygdala and hippocampus [54]. Overlapping regions of the vmPFC and mOFC seem to represent the value of primary sensory reinforcers, such as pleasant tastes, smells or images, abstract secondary rewards such as money, and even more complex subjective values in which multiple dimensions of a stimulus, such as different decision costs, are integrated [51], which suggests that the VS–OFC network (Figure 2) forms a domain-general valuation network [12,49,50,52,55]. In particular, the basolateral amygdala (BLA) seems to be crucial for the acquisition of value representations in the vmPFC [56].

In line with these observations, it has been repeatedly shown that activity in the ventral striatum and/or vmPFC correlates with the discounted value of future rewards in DD paradigms [11,12,14,19,20,57,58]. Electrophysiological studies have also revealed neurons that code for discounted value in monkey dorsolateral PFC [18] and the avian analogue of the PFC [59]. In addition, at least in humans, there are regions in which valuation-related activity is somewhat specific to delayed rewards, for example when compared to probabilistic rewards [12,60] or rewards associated with physical effort [57]. These delay-specific signals are found in medial PFC, lateral parietal cortex and subregions of the posterior cingulate cortex (PCC). Thus, although a range of different rewards (including temporally discounted delayed rewards) are represented in overlapping regions of the vmPFC and/or ventral striatum [51], at the neural level, some signatures of value might be specific to DD to a certain extent.

Single versus dual valuation accounts

An early debate concerned the question of single versus dual valuation systems for immediate and delayed rewards. In line with the behavioural two-parameter β–δ model of intertemporal choice (see previous section), McClure and colleagues reported that distinct neural systems are recruited during DD, depending on whether a particularly tempting immediate reward option is present or not [6,61]. In their view, immediate rewards recruit a limbic system including the striatum and vmPFC, whereas the value of more delayed rewards is represented in prefrontal control regions such as the dorsolateral PFC (DLPFC). By contrast, others have argued that a single neural system (medial PFC, ventral striatum and PCC) represents the value of all rewards, regardless of delay [11]. Methodological differences between the two sets of studies make direct comparison of the findings somewhat difficult. Nonetheless, recent data might help to resolve this debate, and lend some support to the single valuation account. First, medial PFC and PCC might signal the presence of an immediate reward in an all-or-none fashion, in other words, without enhancing a neural value correlation [58]. Second, when the subjective values of delayed rewards are increased to a level comparable to a situation in which choices are made relative to a fixed immediate reward, medial PFC, ventral striatum and PCC represent

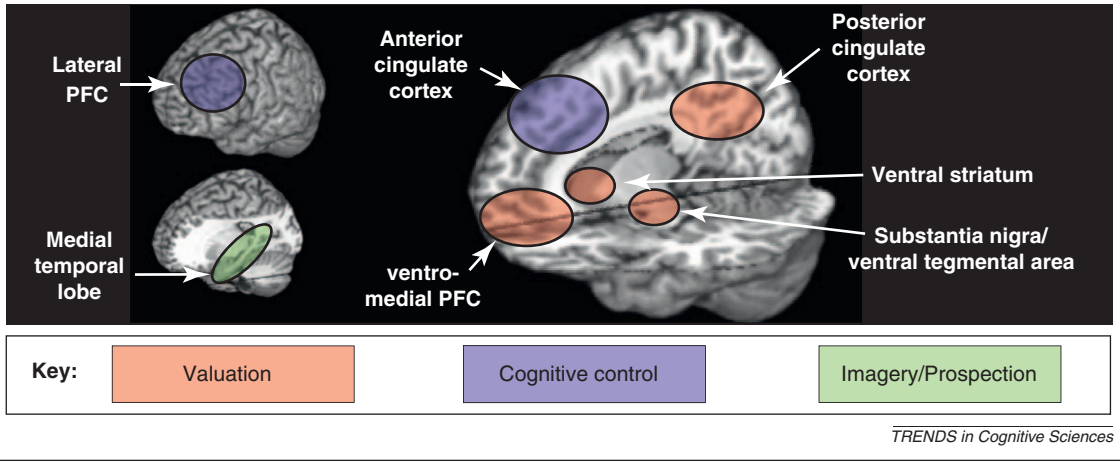

Figure 2. Networks implicated in different component processes of temporal discounting: cognitive control (blue), reward valuation (red) and imagery or prospection (green). Ventromedial PFC and posterior cingulate cortex are involved in both prospection and valuation.

subjective value, even in the absence of immediate rewards [19]. This is inconsistent with the notion that these regions represent a specific immediacy signal. Furthermore, the lateral PFC might reflect deployment of self-control during decision-making not because an alternative (i.e. delayed) value signal is represented in this structure, but because lateral PFC might modulate a value signal encoded in the vmPFC [62]. There is also recent evidence that immediate rewards might carry greater incentive value than delayed rewards, even when they are preference-matched [63], because they result in greater activation in the valuation network. Finally, a recent study observed increased discounting in mOFC or vmPFC lesion patients [64]. If mOFC activity biases individuals to make short-sighted impulsive choices, as suggested by the β–δ model, mOFC damage would be expected to reduce, not increase, discounting.

Addiction is associated with altered neural value representations

It is well established that drug-related cues induce an increased response in the reward system of addicts [65]. Fewer studies have addressed the question of whether addiction is associated with more general alterations in reward processing. This is of particular interest because it might constitute a risk factor for the development of drug use. An early positron emission tomography (PET) study assessed neural responses to monetary and non-monetary reinforcement in control subjects and opiate addicts [66] and observed reduced striatal responses to non-monetary reinforcement in the addicted group. Another study found that in a simple probabilistic guessing task, pathological gamblers showed a marked reduction in gain-related activation of the VS and vmPFC [40], and this reduction in reward sensitivity was correlated with gambling severity. Along similar lines, cocaine addicts showed reduced orbitofrontal cortex activation to monetary rewards of different magnitude [67] whereas control subjects exhibited increased OFC activation with increasing reward amount; this pattern was considerably less pronounced in the addicted group. Finally, both adolescent [31] and adult smokers [68] show reduced striatal responses during reward processing. Thus, addiction might be associated with a reduced neural response to non-drug rewards [69], which might be associated with a decrease in VS dopamine release [70].

However, because addiction is associated with steeper reward discounting, the rewards under consideration in some of these studies were probably not matched for subjective value between groups, and this might partly account for the differences observed in neural reward responses. Findings from a PET study in smokers and non-smokers argue against this possibility [71]. During the course of this experiment, subjects rated the subjective value of rewards on an 11-point scale. Even though the ratings revealed a similar valuation of monetary rewards in smokers and non-smokers, smokers nonetheless showed reduced reward-related responses in the VS. In addition, there is recent evidence that the neural valuation response in adult smokers might be particularly reduced for delayed compared to immediate monetary rewards, even when these rewards are preference-matched [72]. Thus, the overall data are compatible with the view that addiction is associated with reduced responses of the VS and orbitofrontal cortex, including vmPFC, during the processing of non-drug rewards, consistent with findings in animal models (Box 3).

Box 3. The valuation network and addiction: evidence from animal models

The finding in humans of an association between addiction and functional alterations in the valuation network is compatible with data from animal models, and we highlight just two examples. Rats that are more behaviourally impulsive show increased levels of cocaine self-administration [76]. At the same time, these animals also have reduced availability of dopamine D2/3 receptors in the VS [76]. Similar effects have been observed in a study that examined cocaine self-administration in monkeys. Monkeys with lower baseline dopamine D2 receptor availability showed increased levels of self-administration compared to monkeys with higher D2 receptor levels [47]. These observations confirm findings in humans that interindividual differences in the dopaminergic system are associated with differences in vulnerability to drug use.

Interindividual differences in neural valuation predict differences in discounting

The literature on addiction summarized above suggests the possibility that individual differences in DD correlate with changes in reward-related neural responses in the valuation network. Although a first analysis of the relationship between DD (tested behaviourally outside the scanner) and striatal responses during positive versus negative reward feedback revealed a positive correlation [73] – individuals who discounted more steeply showed stronger feedback-related VS responses – a more recent study revealed reduced VS responses to the magnitude of delayed rewards in steep discounters in a healthy population [14]. In line with this finding, lateral OFC activation is negatively correlated with impulsive discounting [74] – that is, less discounting is associated with greater lateral OFC activity – which is consistent with the link between discounting and reduced responses in the reward system in addiction. The latter results are also consistent with the observation that lesions to the nucleus accumbens, but not to the anterior cingulate or medial PFC, increase DD in rats [75], which strongly suggests that striatal dysfunction contributes to impulsive decision-making [76]. Although additional research and replications are clearly needed, preliminary evidence therefore points towards a link between a behavioural focus on short-term reinforcement and a reduction in sensitivity of regions involved in the valuation stage of DD. This association might characterize addiction, but might also contribute to interindividual differences in healthy subjects.

The cognitive control network

Conflict monitoring, strategy adaptation and the anterior cingulate cortex

In addition to effects of subjective reward value, decision-making is affected by another important variable, decision conflict. Decisions are difficult when options are of similar value, whereas decisions are easier when option values are clearly different. The degree of decision conflict in such situations is correlated with activity in prefrontal control regions, in particular the anterior cingulate cortex (ACC)

[77]. In intertemporal choice, this effect is typically examined by comparing choices close to a subject's indifference point (i.e. situations in which the smaller-but-sooner reward has a similar subjective value to the larger-but-later reward). ACC activity [78–80] and lateral PFC activity [6,80] are typically greater during hard compared to easy intertemporal choices. ACC activity also reflects increases in conflict-induced response times during DD [79]. More generally, recent findings suggest that distinct types of conflict, such as between different decision options, responses or decision strategies, are reflected in ACC activation, possibly involving distinct subregions [81]. The function of ACC conflict signals are debated, but one proposal is that they might serve to bias future behaviour towards more efficient (i.e. cognitively less demanding) processing modes or strategies [82]. Support for such a role of the ACC during DD comes from a recent study that found that valuation signals in bilateral ACC correlated with degree of change in impulsivity between contextually different experimental conditions [20], which is compatible with a role of the ACC in mediating context-dependent changes in decision strategy.

Cognitive control and the anterior-lateral PFC

It has been suggested that maturation of prefrontal regions is one factor underlying the development of self-control during adolescence (Box 4). However, an important role for the PFC in cognitive control during intertemporal choice in adults was also suggested by McClure and colleagues [6]. In this study, whenever subjects chose the delayed reward, relative activation in regions comprising the delta-network (i.e. circuits in the PFC and lateral parietal cortex) were more active than when subjects chose the immediate reward, which is consistent with a role of these regions in exerting cognitive control to support harvesting of greater long-term benefits. A more recent study examined the hypothesis that value signals in the vmPFC are modulated by top-down control of the lateral PFC [62]. In this study, dieters performed three different tasks during fMRI: health ratings of food items, taste ratings of food items, and choices between different foods and a reference food item. Based on their choices, subjects were either classified as self-controllers (SCs, subjects who made their choices based on both taste and health) and non-self-controllers (NSCs, subjects who chose based on taste alone). Only in trials in which SCs successfully used self-control was the value signal in the vmPFC significantly modulated by the DLPFC (see Box 5 for more information on advanced fMRI analyses). Interestingly, this modulatory influence of the DLPFC was indirect via functional connectivity with a more ventral PFC region, which in turn showed connectivity with the vmPFC. Based on these data, we could hypothesize a similar role of the DLPFC in self-control during intertemporal decision-making (i.e. biasing behaviour towards choosing the larger-but-later rather than the smaller-but-sooner reward) [6]. This hypothesis was examined by Figner and colleagues, who applied transcranial magnetic stimulation (TMS) over the left or right DLPFC during an intertemporal choice task [83]. Disruption of left DLPFC increased impulsive choices, specifically in trials in which a particularly tempting immediate reward option was available. Importantly, TMS did not affect the valuation of decision options presented in isolation, which is compatible with the idea that DLFPC modulates value signals in other regions rather than contributing to the actual valuation process *per se*.

Steep discounters show reduced prefrontal activation

In addition to functional changes in reward processing, addiction is also characterized by changes in cognitive control processes predominantly mediated by the PFC [69,84]. For example, during simple response-inhibition paradigms, addicts show marked impairments compared to healthy comparison subjects, and these impairments are associated with reduced neural responses in PFC and ACC [85]. There is some evidence that prefrontal activity during difficult intertemporal choices might be less pronounced in methamphetamine addicts [25]. One function of the PFC during DD might be the exertion of cognitive control to overrule short-sighted choices [83], so it could be hypothesized that there is an association between the degree of impulsive discounting and the functional involvement of the PFC. In line with this idea, two neuroimaging studies revealed greater activity in an anterior medial PFC region in less impulsive subjects, which was interpreted in terms of enhanced imagery processes [86] or enhanced executive control [58]. Activity in a more ventrolateral PFC region showed a similar correlation with discount rates in a mixed sample of control subjects and methamphetamine users [25]. Another study revealed dorsolateral PFC deactivation that was correlated with reward delay [14], and this deactivation was more pronounced in impulsive than in less-impulsive subjects. Finally, greater anterior PFC activity measured during an unrelated working memory task predicted less discounting [87]. Taken together, these

Box 4. Delay discounting across the lifespan

DD shows considerable variability in healthy young adults, but considerable individual differences in the ability to delay gratification can already be observed in pre-schoolers, in whom self-control is a good predictor of later academic performance [136]. The degree of DD decreases throughout childhood and adolescence [137–142] and only reaches levels comparable to those in young adulthood around the age of 16 years [139]. Thus, impulsive discounting might be one behavioural correlate of the highly impulsive period of adolescence [143]. Older adults, conversely, tend to discount delayed rewards comparable to [144] or less steeply than younger adults [145]. On a neural level, increased impulsivity in adolescents might be due to continuing maturation of prefrontal cortical regions throughout adolescence and well into the early twenties [146]. At the same time, limbic regions implicated in incentive processing mature much earlier, possibly leading to an imbalance between prefrontal control and lower-level incentive-based behaviour [147], which might contribute to the finding that adolescents can be at particularly high risk of developing addiction [43]. For example, adolescents show increased striatal responses and decreased prefrontal impulse control during the processing of appetitive cues [148]. Along similar lines, the magnitude of neural reward-prediction errors peaks during adolescence [149]. It has been shown that in adults, DD correlates with lateral PFC volume [150]. In line with this, the developmental trajectory of DD is associated with distinct changes in brain structure. For example, reduced white matter integrity in the PFC was associated with greater DD in a sample of 9- to 23-year-old volunteers [141], which is compatible with the view that maturation of prefrontal circuits contributes to the development of self-control.

findings support the notion that interindividual differences in the degree of PFC recruitment contribute to interindividual variability in discounting, with greater PFC involvement probably reflecting enhanced cognitive control and, as a result, less impulsive decision-making.

The medial temporal lobe (MTL) network: predictions and affect

MTL contributions to DD

Two regions in the MTL, the hippocampus and the amygdala, have repeatedly been implicated in DD, although their precise contributions are poorly understood. Damage to the hippocampus increases DD in rats [88–90], although it is unclear whether this constitutes a selective impairment in DD or generalizes to other forms of cost–benefit decision-making. Amygdala damage in rodents, conversely, is known to impair performance in a range of cost–benefit choice tasks, including probability discounting, effort discounting and DD [91–93]. However, the precise role of the amygdala in these processes is unclear. One possibility is that the amygdala contributes through memory-related processes [56,91] and/or through activation of somatic markers of emotional states associated with rewards, in particular with respect to immediate reinforcement [94]. Amygdala activation during imagery in humans might also reflect positive affect [95], which in turn might contribute to reductions in DD in conditions promoting episodic imagery, which were associated with increased ACC–amygdala coupling [20].

A hippocampal representation of decision outcomes?

In rats, hippocampal activation at decision points during maze traversion represents potential forward paths that could be taken by the animal [96,97], which is consistent with a role in the evaluation of decision outcomes. In humans, the hippocampus is part of an extended system representing past and future events [98,99], in particular vivid details associated with event episodes [100], and recent data indicate that hippocampal damage in humans can also lead to impairments in decision-making [101]. One possibility is therefore that the role of the hippocampus in decision-making (including DD) might be a representation of decision outcomes [20,102]. In addition to the hippocampus, vmPFC, mOFC and PCC are part of an extended imagery or prospection network [20,98]. There is some recent evidence that damage to the mOFC increases discounting in humans [64], a finding that is compatible with a role of this region in supporting future-minded decision-making through mechanisms of episodic prospection. This extended prospection network is also strongly implicated in the valuation stage of DD (see previous sections), so one important open question is how imagery and valuation processes interact in these regions [103]. For example, do overlapping regions of the vmPFC, mOFC and PCC process imagery- and value-related information? How do patients with hippocampal amnesia, who show marked impairments in prospection [104], evaluate future rewards? If the hippocampus reduces DD through its role in episodic imagery [20], hippocampal patients would be expected to show increased DD similar to mOFC patients [64]. A related issue is whether increased impulsivity in DD is associated with impairments in episodic imagery. Variability in imagery might constitute an additional factor underlying the considerable variability of DD in healthy subjects. At the same time, it is possible that an inability to use episodic predictions to guide choices might contribute to the steep discounting observed in addiction.

Interim conclusions

We have shown that at least three distinct networks contribute to intertemporal decision-making. A valuation network comprising vmPFC, mOFC, ventral striatum and PCC represents the subjective discounted value of future rewards. The lateral PFC and ACC are involved in DD, predominantly through their role in cognitive control, conflict monitoring and strategy adaptation. Finally, although still poorly understood, MTL regions including the hippocampus might contribute to DD through representing potential future outcomes of decisions (prospection). Interindividual differences in DD might therefore arise from processing differences in these neural systems, such as from an inability to accurately represent the incentive value of future rewards (valuation deficit) and/or from an inability to exert top-down modulatory control over a disadvantageous choice tendency (self-control deficit) and/or, a rarely addressed issue, a deficit in using mental representations of decision outcomes to guide choice (prospection deficit).

With respect to valuation deficits, samples that show impulsive discounting are characterized by processing differences in core regions involved in the valuation process [50,51], but both hyper- (adolescents) and hyporesponsivity (addiction) have been reported, which suggests that different underlying mechanisms exist. At the same time, whether reward anticipation or feedback processing is examined might also play an important role, a point that we have not addressed [105]. Differences in neural valuation processes might also underlie the observed effects of genetic (e.g. dopaminergic) polymorphisms [106] on DD. When it comes to the role of the executive control network in DD, trait differences might arise because of between-subject differences in the ability to exert self-control, and findings indicate that prefrontal down-regulation might underlie impairments in self-control. This has been observed during development, in psychiatric conditions such as addiction and in analyses focussing on individual differences in healthy adults. An additional (albeit understudied) factor that might drive the considerable degree of interindividual differences in DD is variability in episodic imagery, which could contribute to interindividual differences in both healthy subjects and psychiatric populations. Further studies are required to explore this possibility.

A range of open questions remain regarding the neurobiological underpinnings of individual differences in DD. Interactions between the proposed networks have rarely been examined (but see [20,62,107]) and future studies will benefit from the use of advanced fMRI analysis techniques (Box 5) to examine how differences in the functional interactions between these different networks contribute to trait differences in behaviour. The idea of a top-down modulation of the valuation system through prefrontal

cognitive control is appealing [62] but requires replication in other decision-making contexts. Finally, a better process-based understanding of mechanisms underlying trait differences can be achieved if potential contributing psychological constructs are routinely measured. This could include standardized assessments of prospection [108] and/or time perception [109] (Box 1) in DD studies.

Contextual modulations in DD: state effects

In light of the consistent association of DD with substance abuse and addiction, it is of high clinical relevance to identify mechanisms or interventions that reduce impulsive discounting. At the same time, a better understanding of modulating factors could enhance our understanding of the psychological (and neural) processes underlying DD. We address three basic types of state modulation that provide insight into the psychological and neural mechanisms of DD, as well as into the potential for intervention.

Behavioural state effects: framing and context

Behavioural state effects occur, for example, on a trial-by-trial or condition-by-condition basis, as a result of differences in the context or framing of decision options. Framing effects are a central component of prospect theory [110], which indicates that valuation and/or choice are highly dependent on the decision context. Recently, a range of contextual manipulations specific to the domain of DD have been discovered that shed light on the psychological processes involved. First, context manipulations that might affect the way that time or delay is represented by a subject seem to modulate DD. Framing a delayed reward in terms of accelerating its arrival reduces DD, whereas framing in terms of delaying its arrival increases DD [111]. Along similar lines, expressing a delay in terms of the date of reward delivery reduces discounting compared to purely delay-based (i.e. interval) processing [112]. Thus, highlighting the waiting duration increases reward discounting whereas putting the focus on the outcome delivery time point decreases discounting.

A more recent observation in intertemporal decision-making is that delayed rewards that are paired with subject-specific real episodic cues reduce the rate of reward discounting [20]. In particular, this effect of episodic cues on preferences was significantly affected by interindividual differences in episodic imagery, as assessed through post-scan ratings, which suggests that the better one imagines the future, the more one also values the future. This fits well with previous theoretical considerations of the potential evolutionary advantage of the human ability to (mentally) time travel into the future [113]. Functional neuroimaging revealed that the effect of episodic thinking on DD was correlated with the degree of hippocampal–ACC coupling (see Box 5 for methodological considerations). This strongly suggests that brain regions involved in episodic memory and future thinking such as the hippocampus [98] functionally interact with prefrontal decision-making circuits during imagery-dependent alterations in DD.

More generally, construal level theory (CLT) suggests that time itself modulates the way that a particular future event is mentally represented, which can in turn affect preferences [114]. People evaluate events in the more distant future with greater weight placed on more abstract features of those events (high-level construal), whereas more proximal events are evaluated with respect to concrete aspects (low-level construal) [115]. In line with CLT, there is evidence that positive mental representations of abstract event features increase the value of more distal events, whereas positive representations of concrete event features increase the value of more proximal events [115]. Alterations of temporal construal might therefore affect DD, a possibility that could be explored in future studies.

Box 5. Methodological considerations

How do different brain circuits interact during decision-making?

More advanced analysis methods in functional neuroimaging can help to address this issue. For example, using psychophysiological interaction analyses (PPI, also referred to as functional connectivity analyses) researchers can examine how interregional correlations in the MR signal change as a function of an experimental manipulation [151]. Importantly, PPI analyses examine correlation, not causation, and therefore some caution is warranted for interpretations in terms of neural interactions between regions. Nonetheless, interactions consistent with primate neuroanatomy have frequently been observed. Hare and colleagues observed functional connectivity between PFC and vmPFC, specifically in trials involving successful self-control [62], which is compatible with a modulatory top-down influence of the PFC on valuation-related activity in the vmPFC. Similar coupling effects have been observed between PFC and ventral striatum [107]. In a recent study by Peters and Büchel, functional connectivity between the hippocampus and the ACC increased as the effect of episodic imagery on subjects' choices increased [20]. Both studies show that such analyses can be used to test anatomically motivated hypotheses of functional interactions between regions. Using more elaborate approaches such as dynamic causal modelling (DCM), specific anatomically motivated models, including hypothesis about the directionality of interactions, can be tested and different competing models can be compared [152]. Finally, carefully designed disconnection studies in rodents [92,153] can be informative regarding the inter-regional communication required in a specific task.

Which networks play a causal role in a given process?

In contrast to functional neuroimaging, transcranial magnetic stimulation (TMS, a technique that facilitates reversible partial disruption or enhancement of neural processing in specific cortical regions in healthy subjects) and studies in brain-damaged patients and lesion studies in experimental animals provide opportunities to directly examine the causal role of a given brain region for a particular task. For example, TMS revealed a role for lateral PFC in cognitive control during intertemporal and risky choice [83,154] and during valuation of food rewards [155]. Relatively few studies have investigated decision-making deficits following circumscribed brain lesions, and most of these have focussed on patients with vmPFC, insula and amygdala damage, using the Iowa Gambling Task or variations thereof [94,156–161], whereas one study that examined DD observed no effects of medial PFC damage [162]. By contrast, a recent study on patients with more inferior lesions including the mOFC revealed a marked increase in impulsive discounting [64]. Such experimental studies can be complemented by neural network simulations that compare the performance of intact and lesioned models [163].

At the same time, a large body of animal literature describes impairments in cost–benefit decision-making in rodents following lesions to the amygdala, hippocampus and medial PFC [88,91–93,153], but how these findings relate to human data remains unclear. Therefore, the use of convergent tasks for neuroimaging, patient studies and TMS would add to our knowledge and could lead to much firmer conclusions regarding the causal necessity of activations observed in neuroimaging for specific subprocesses of DD, such as valuation, cognitive control and conflict monitoring.

The general testing context can also modulate discount functions (Figure 1c). Pathological gamblers show increased impulsive choices when discount functions are tested in a gambling compared to a non-gambling context [17]. This finding provides strong support for the distinction between state and trait effects on DD, because gamblers typically discount more steeply (see the previous section). This finding is also compatible with the view that general contextual cues might affect decision-making through activation of learned behavioural patterns. In addition, in men, but less so in women, viewing attractive faces of the opposite sex increases DD [116], possibly through an arousal-related mechanism.

Finally, factors that have not been investigated with respect to DD are the effects of environmental enrichment and social hierarchy. Social hierarchy influences the behavioural effects of cocaine administration in monkeys, whereas environmental enrichment can increase cocaine abstinence [117], which suggests that both factors might also play a role in human impulsive choice such as DD.

Physiological states

Individuals can be in different physiological states, for example because of deliberate pharmacological intervention, drug intoxication or withdrawal, or dietary interventions. Dopamine plays a pivotal role in reward processing and addiction [118], and changes in dopaminergic signalling might also underlie other psychiatric disorders such as attention-deficit hyperactivity disorder that are also associated with alterations in DD [119]. Furthermore, interindividual differences in dopamine autoreceptor availability in the SN and VTA predict trait impulsivity [120]. In line with these findings, pharmacological alterations of DD have been linked to both direct and indirect state modulations in dopaminergic processing. Pine and colleagues administered the dopamine precursor L-DOPA, haloperidol or placebo in a within-subject design during functional neuroimaging while participants performed a DD task [121]. Pharmacological enhancement of dopamine activity through L-DOPA administration increased reward DD in 12 out of 13 subjects. This observation is in agreement with the finding of increased impulsive behaviour in Parkinson's disease patients on L-DOPA medication [122].

By contrast, dopamine levels in the ventral striatum are reduced during acute nicotine withdrawal [123,124]. At the same time, nicotine and opioid deprivation increases discounting of both drug rewards and money [39,40], which is compatible with a general reduction in reward sensitivity during periods of nicotine withdrawal [125], but at odds with the previously described hyperimpulsivity following enhancement of dopaminergic signalling. Acute administration of D-amphetamine, which increases dopamine release and reduces dopamine reuptake, reduces impulsive discounting in rats [126] and humans [127]. State modulations in dopaminergic processing therefore clearly affect DD, but dose–response relationships might be affected by a range of factors, including genetic differences in baseline dopaminergic signalling [106]. Dopamine might also support distinct functions in the PFC and striatum [105].

Finally, human subjects showed reduced DD (in a within-subject design) after consuming a sugar-containing soft drink compared with subjects who consumed a drink containing artificial sweetener [128]. Thus, choice between immediate and delayed rewards might be affected by current caloric requirements, such that in a state of relatively lower energy supply, organisms might focus more on immediate rewards, whereas a state of high energy supply biases more towards long-term reward harvesting.

Training interventions to reduce impulsive discounting

The previous sections examined trial-by-trial alterations in reward discounting through behavioural manipulations or effects of pharmacological interventions, but a few recent studies have examined specific training procedures aimed at reducing impulsive discounting. In conditional discrimination training, neutral stimuli acquire affective value through repeated association with positive (e.g. larger sums of money, better letter grades, etc.) or negative (less money, lower letter grades) stimuli. For example, participants learn over a number of trials that, for example, yellow is associated with positive stimuli whereas green is associated with negative stimuli. In gamblers, this training procedure alters preferences for otherwise identical slot machines that are associated with the trained colours [129], such that the positively associated slot machine is preferred following training. A similar effect occurs in DD, whereby delayed rewards that are presented together with the positive colour are preferred after training [130], which results in a reduction in discounting. Although the time course of this training-related effect is unclear, it nonetheless shows that learning of contextual associations can transfer and modulate choices in unrelated decision-making settings.

In light of the relationship between discounting and episodic memory or imagery [20] and working memory [87], an interesting question is whether memory training can reduce the degree of DD. This was recently assessed in two groups of stimulant addicts, one of which received working memory training whereas the other received similar cognitive training without specific memory demands [131]. Only in the memory training group was discounting of hypothetical money significantly reduced following training. However, the mechanism by which training induced changes in preferences remains a matter of speculation. For example, DD depends partly on working memory functions (i.e. decision options need to be actively maintained in memory to make accurate choices) and this might have affected decision-making.

Interim conclusions

The findings summarized in the preceding sections show that DD is a considerably stable trait within individuals, but one that is also subject to modulation on various levels. Behavioural framing and context effects suggest an important role for mental representation of the decision problem: how subjects represent delay and/or outcome seems to be a crucial factor in the valuation of that outcome. The overall decision context might also activate learned behavioural patterns, which might play a role in the impulsive behaviour observed in specific disorders such as pathological gambling [17]. A more complex picture emerges regarding changes in the dopaminergic system, because interindividual

differences in dopaminergic signalling (e.g. due to genetic factors, Box 2) probably interact with state-dependent changes in dopamine functioning in a region-specific manner [105]. Furthermore, environmental factors such as social hierarchy and environmental enrichment might interact with genetic predispositions [117] to determine the degree of impulsivity of an individual in a given situation. Finally, initial tests of training interventions specifically aimed at increasing future-minded choice have yielded promising results, and feasible future targets of such interventions might include training of imagery processes, temporal construal and self-control.

Concluding remarks

A basic model of the functional neuroanatomy of intertemporal choice is beginning to take shape. This model includes neural circuits that support different aspects of intertemporal decisions: vmPFC, VS and PCC are involved in the representation of subjective discounted value [49], and hyposensitivity of these regions might contribute to impulsive discounting in psychiatric conditions. PFC and ACC are part of a network that exerts cognitive control during decision-making, and in DD might bias behaviour towards overcoming of short-sighted (impulsive) choice tendencies. Reduced prefrontal control might be an additional mechanism contributing to highly impulsive discounting. By contrast, although clearly implicated in DD, the specific contributions of the hippocampus and amygdala are much less well studied, but might depend on the involvement of these regions in memory, prospection and affect. In our view, an important but rarely addressed hypothesis is that the hippocampus contributes to DD through the mental representation of future decision outcomes. If we view DD as arising from memory decay into the future, a contribution of the hippocampus follows quite naturally from its well-established role in episodic memory.

Although strongly determined by personality and genetic factors, impulsive discounting is not carved in stone. Despite strong trait-like interindividual differences, DD can be modulated by behavioural and pharmacological interventions. A better understanding of the neural mechanisms underlying these contextual modulations will therefore not only enhance our understanding of the neural and psychological processes contributing to DD, but also inform the development of novel treatment approaches based on the idea that people may be able to learn to mind the future in their choices.

Acknowledgements

We thank Markus Staudinger and Sebastian Gluth for helpful comments on a previous version of this manuscript.

References

1 Green, L. and Myerson, J. (2004) A discounting framework for choice with delayed and probabilistic rewards. *Psychol. Bull.* 130, 769–792
2 Samuelson, P.A. (1937) A note on measurement of utility. *Rev. Econ. Stud.* 4, 155–161
3 Mazur, J.E. (1987) An adjusting procedure for studying delayed reinforcement. In *The Effect of Delay and of Intervening Events on Reinforcement Value Quantitative Analyses of Behavior* (Vol. 5) (Commons, M.L. *et al.*, eds), In pp. 55–73, Lawrence Erlbaum
4 McKerchar, T.L. *et al.* (2009) A comparison of four models of delay discounting in humans. *Behav. Process* 81, 256–259
5 Myerson, J. *et al.* (2001) Area under the curve as a measure of discounting. *J. Exp. Anal. Behav.* 76, 235–243
6 McClure, S.M. *et al.* (2004) Separate neural systems value immediate and delayed monetary rewards. *Science* 306, 503–507
7 Myerson, J. and Green, L. (1995) Discounting of delayed rewards: models of individual choice. *J. Exp. Anal. Behav.* 64, 263–276
8 Rachlin, H. (2006) Notes on discounting. *J. Exp. Anal. Behav.* 85, 425–435
9 Takahashi, T. *et al.* (2008) Psychophysics of time perception and intertemporal choice models. *Phys. A* 387, 2066–2074
10 Zauberman, G. *et al.* (2009) Discounting time and time discounting: subjective time perception and intertemporal preferences. *J. Marketing Res.* XLVI, 543–556
11 Kable, J.W. and Glimcher, P.W. (2007) The neural correlates of subjective value during intertemporal choice. *Nat. Neurosci.* 10, 1625–1633
12 Peters, J. and Büchel, C. (2009) Overlapping and distinct neural systems code for subjective value during intertemporal and risky decision making. *J. Neurosci.* 29, 15727–15734
13 Ohmura, Y. *et al.* (2006) Three-month stability of delay and probability discounting measures. *Exp. Clin. Psychopharmacol.* 14, 318–328
14 Ballard, K. and Knutson, B. (2009) Dissociable neural representations of future reward magnitude and delay during temporal discounting. *Neuroimage* 45, 143–150
15 Anokhin, A.P. *et al.* (2011) Heritability of delay discounting in adolescence: a longitudinal twin study. *Behav. Genet.* 41, 175–183
16 Kirby, K.N. (2009) One-year temporal stability of delay-discount rates. *Psychon. Bull. Rev.* 16, 457–462
17 Dixon, M.R. *et al.* (2006) Contextual control of delay discounting by pathological gamblers. *J. Appl. Behav. Anal.* 39, 413–422
18 Kim, S. *et al.* (2008) Prefrontal coding of temporally discounted values during intertemporal choice. *Neuron* 59, 161–172
19 Kable, J.W. and Glimcher, P.W. (2010) An "as soon as possible" effect in human intertemporal decision making: behavioral evidence and neural mechanisms. *J. Neurophysiol.* 103, 2513–2531
20 Peters, J. and Büchel, C. (2010) Episodic future thinking reduces reward delay discounting through an enhancement of prefrontal–mediotemporal interactions. *Neuron* 66, 138–148
21 Bickel, W.K. *et al.* (2007) Behavioral and neuroeconomics of drug addiction: competing neural systems and temporal discounting processes. *Drug Alcohol Depend.* 90 (Suppl. 1), S85–91
22 Businelle, M.S. *et al.* (2010) A comparison of delay discounting among smokers, substance abusers, and non-dependent controls. *Drug Alcohol Depend.* 12, 247–250
23 Kirby, K.N. *et al.* (1999) Heroin addicts have higher discount rates for delayed rewards than non-drug-using controls. *J. Exp. Psychol. Gen.* 128, 78–87
24 Madden, G.J. *et al.* (1997) Impulsive and self-control choices in opioid-dependent patients and non-drug-using control participants: drug and monetary rewards. *Exp. Clin. Psychopharmacol.* 5, 256–262
25 Monterosso, J.R. *et al.* (2007) Frontoparietal cortical activity of methamphetamine-dependent and comparison subjects performing a delay discounting task. *Hum. Brain Mapp.* 28, 383–393
26 Bickel, W.K. *et al.* (1999) Impulsivity and cigarette smoking: delay discounting in current, never, and ex-smokers. *Psychopharmacology (Berl.)* 146, 447–454
27 Bickel, W.K. *et al.* (2008) Cigarette smokers discount past and future rewards symmetrically and more than controls: is discounting a measure of impulsivity? *Drug Alcohol Depend.* 96, 256–262
28 Mitchell, S.H. (1999) Measures of impulsivity in cigarette smokers and non-smokers. *Psychopharmacology (Berl.)* 146, 455–464
29 Peters, J. *et al.* (2011) Lower ventral striatal activation during reward anticipation in adolescent smokers. *Am. J. Psychiatry* DOI: 10.1176/appi.ajp.2010.10071024
30 Audrain-McGovern, J. *et al.* (2009) Does delay discounting play an etiological role in smoking or is it a consequence of smoking? *Drug Alcohol Depend.* 103, 99–106
31 Johnson, M.W. *et al.* (2007) Moderate drug use and delay discounting: a comparison of heavy, light, and never smokers. *Exp. Clin. Psychopharmacol.* 15, 187–194

32 Petry, N.M. (2001) Delay discounting of money and alcohol in actively using alcoholics, currently abstinent alcoholics, and controls. *Psychopharmacology (Berl.)* 154, 243–250
33 Mitchell, J.M. *et al.* (2005) Impulsive responding in alcoholics. *Alcohol Clin. Exp. Res.* 29, 2158–2169
34 Alessi, S.M. and Petry, N.M. (2003) Pathological gambling is associated with impulsivity in a delay discounting procedure. *Behav. Process.* 64, 345–354
35 Petry, N.M. (2001) Pathological gamblers, with and without substance use disorders, discount delayed rewards at high rates. *J. Abnorm. Psychol.* 110, 482–487
36 Petry, N.M. and Casarella, T. (1999) Excessive discounting of delayed rewards in substance abusers with gambling problems. *Drug Alcohol Depend.* 56, 25–32
37 Dixon, M.R. *et al.* (2003) Delay discounting by pathological gamblers. *J. Appl. Behav. Anal.* 36, 449–458
38 Reuter, J. *et al.* (2005) Pathological gambling is linked to reduced activation of the mesolimbic reward system. *Nat. Neurosci.* 8, 147–148
39 Giordano, L.A. *et al.* (2002) Mild opioid deprivation increases the degree that opioid-dependent outpatients discount delayed heroin and money. *Psychopharmacology (Berl.)* 163, 174–182
40 Field, M. *et al.* (2006) Delay discounting and the behavioural economics of cigarette purchases in smokers: the effects of nicotine deprivation. *Psychopharmacology (Berl.)* 186, 255–263
41 Wills, T.A. *et al.* (1994) Novelty seeking, risk taking, and related constructs as predictors of adolescent substance use: an application of Cloninger's theory. *J. Subst. Abuse.* 6, 1–20
42 Paus, T. *et al.* (2008) Why do many psychiatric disorders emerge during adolescence? *Nat. Rev. Neurosci.* 9, 947–957
43 Chambers, R.A. *et al.* (2003) Developmental neurocircuitry of motivation in adolescence: a critical period of addiction vulnerability. *Am. J. Psychiatry* 160, 1041–1052
44 Perry, J.L. *et al.* (2005) Impulsivity (delay discounting) as a predictor of acquisition of IV cocaine self-administration in female rats. *Psychopharmacology (Berl.)* 178, 193–201
45 Mendez, I.A. *et al.* (2010) Self-administered cocaine causes long-lasting increases in impulsive choice in a delay discounting task. *Behav. Neurosci.* 124, 470–477
46 Roesch, M.R. *et al.* (2007) Previous cocaine exposure makes rats hypersensitive to both delay and reward magnitude. *J. Neurosci.* 27, 245–250
47 Nader, M.A. *et al.* (2006) PET imaging of dopamine D2 receptors during chronic cocaine self-administration in monkeys. *Nat. Neurosci.* 9, 1050–1056
48 Richards, J.B. *et al.* (1999) Effects of methamphetamine on the adjusting amount procedure, a model of impulsive behavior in rats. *Psychopharmacology (Berl.)* 146, 432–439
49 Kable, J.W. and Glimcher, P.W. (2009) The neurobiology of decision: consensus and controversy. *Neuron* 63, 733–745
50 Chib, V.S. *et al.* (2009) Evidence for a common representation of decision values for dissimilar goods in human ventromedial prefrontal cortex. *J. Neurosci.* 29, 12315–12320
51 Peters, J. and Büchel, C. (2010) Neural representations of subjective reward value. *Behav. Brain Res.* 213, 135–141
52 Kringelbach, M.L. and Rolls, E.T. (2004) The functional neuroanatomy of the human orbitofrontal cortex: evidence from neuroimaging and neuropsychology. *Prog. Neurobiol.* 72, 341–372
53 Schultz, W. *et al.* (1997) A neural substrate of prediction and reward. *Science* 275, 1593–1599
54 Haber, S.N. and Knutson, B. (2010) The reward circuit: linking primate anatomy and human imaging. *Neurosci.* 35, 4–26
55 Rangel, A. *et al.* (2008) A framework for studying the neurobiology of value-based decision making. *Nat. Rev. Neurosci.* 9, 545–556
56 Schoenbaum, G., Setlow, B., Saddoris, M.P. and Gallagher, M. (2003) Encoding predicted outcome and acquired value in orbitofrontal cortex during cue sampling depends upon input from basolateral amygdala. *Neuron* 39, 855–867
57 Prevost, C. *et al.* (2010) Separate valuation subsystems for delay and effort decision costs. *J. Neurosci.* 30, 14080–14090
58 Sripada, C.S. *et al.* (2010) The neural correlates of intertemporal decision-making: contributions of subjective value, stimulus type, and trait impulsivity. *Hum. Brain Mapp.* DOI: 10.1002/hbm.21136
59 Kalenscher, T. *et al.* (2005) Single units in the pigeon brain integrate reward amount and time-to-reward in an impulsive choice task. *Curr. Biol.* 15, 594–602
60 Weber, B.J. and Huettel, S.A. (2008) The neural substrates of probabilistic and intertemporal decision making. *Brain Res.* 1234, 104–115
61 McClure, S.M. *et al.* (2007) Time discounting for primary rewards. *J. Neurosci.* 27, 5796–5804
62 Hare, T.A. *et al.* (2009) Self-control in decision-making involves modulation of the vmPFC valuation system. *Science* 324, 646–648
63 Luo, S. *et al.* (2009) Behavioral and neural evidence of incentive bias for immediate rewards relative to preference-matched delayed rewards. *J. Neurosci.* 29, 14820–14827
64 Sellitto, M. *et al.* (2010) Myopic discounting of future rewards after medial orbitofrontal damage in humans. *J. Neurosci.* 30, 16429–16436
65 Diekhof, E.K. *et al.* (2008) Functional neuroimaging of reward processing and decision-making: a review of aberrant motivational and affective processing in addiction and mood disorders. *Brain Res. Rev.* 59, 164–184
66 Martin-Soelch, C. *et al.* (2001) Changes in reward-induced brain activation in opiate addicts. *Eur. J. Neurosci.* 14, 1360–1368
67 Goldstein, R.Z. *et al.* (2007) Is decreased prefrontal cortical sensitivity to monetary reward associated with impaired motivation and self-control in cocaine addiction? Am. *J. Psychiatry* 164, 43–51
68 Buhler, M. *et al.* (2010) Nicotine dependence is characterized by disordered reward processing in a network driving motivation. *Biol. Psychiatry* 67, 745–752
69 Kalivas, P.W. and Volkow, N.D. (2005) The neural basis of addiction: a pathology of motivation and choice. *Am. J. Psychiatry* 162, 1403–1413
70 Volkow, N.D. *et al.* (1997) Decreased striatal dopaminergic responsiveness in detoxified cocaine-dependent subjects. *Nature* 386, 830–833
71 Martin-Soelch, C. *et al.* (2003) Neural activity related to the processing of increasing monetary reward in smokers and nonsmokers. *Eur. J. Neurosci.* 18, 680–688
72 Luo, S. *et al.* (2010) Striatal hyposensitivity to delayed rewards among cigarette smokers. *Drug Alcohol Depend.* DOI: 10.1016/j.drugalcdep.2010.11.012
73 Hariri, A.R. *et al.* (2006) Preference for immediate over delayed rewards is associated with magnitude of ventral striatal activity. *J. Neurosci.* 26, 13213–13217
74 Boettiger, C.A. *et al.* (2007) Immediate reward bias in humans: fronto-parietal networks and a role for the catechol-*O*-methyltransferase 158(Val/Val) genotype. *J. Neurosci.* 27, 14383–14391
75 Cardinal, R.N. *et al.* (2001) Impulsive choice induced in rats by lesions to the nucleus accumbens core. *Science* 292, 2499–2501
76 Dalley, J.W. *et al.* (2007) Nucleus accumbens D2/3 receptors predict trait impulsivity and cocaine reinforcement. *Science* 315, 1267–1270
77 Pochon, J.B. *et al.* (2008) Functional imaging of decision conflict. *J. Neurosci.* 28, 3468–3473
78 Marco-Pallares, J. *et al.* (2010) Brain activations reflect individual discount rates in intertemporal choice. *Brain Res.* 1320, 123–129
79 Pine, A. *et al.* (2009) Encoding of marginal utility across time in the human brain. *J. Neurosci.* 29, 9575–9581
80 Hoffman, W.F. *et al.* (2008) Cortical activation during delay discounting in abstinent methamphetamine dependent individuals. *Psychopharmacology (Berl.)* 201, 183–193
81 Venkatraman, V. *et al.* (2009) Resolving response, decision, and strategic control: evidence for a functional topography in dorsomedial prefrontal cortex. *J. Neurosci.* 29, 13158–13164
82 Botvinick, M.M. (2007) Conflict monitoring and decision making: reconciling two perspectives on anterior cingulate function. *Cogn. Affect. Behav. Neurosci.* 7, 356–366
83 Figner, B. *et al.* (2010) Lateral prefrontal cortex and self-control in intertemporal choice. *Nat. Neurosci.* 13, 538–539
84 Miller, E.K. and Cohen, J.D. (2001) An integrative theory of prefrontal cortex function. *Annu. Rev. Neurosci.* 24, 167–202
85 Hester, R. and Garavan, H. (2004) Executive dysfunction in cocaine addiction: evidence for discordant frontal, cingulate, and cerebellar activity. *J. Neurosci.* 24, 11017–11022
86 Luhmann, C.C. *et al.* (2008) Neural dissociation of delay and uncertainty in intertemporal choice. *J. Neurosci.* 28, 14459–14466

87 Shamosh, N.A. *et al.* (2008) Individual differences in delay discounting: relation to intelligence, working memory, and anterior prefrontal cortex. *Psychol. Sci.* 19, 904–911
88 Cheung, T.H. and Cardinal, R.N. (2005) Hippocampal lesions facilitate instrumental learning with delayed reinforcement but induce impulsive choice in rats. *B.M.C. Neurosci.* 6, 36
89 Mariano, T.Y. *et al.* (2009) Impulsive choice in hippocampal but not orbitofrontal cortex-lesioned rats on a nonspatial decision-making maze task. *Eur. J. Neurosci.* 30, 472–484
90 Rawlins, J.N. *et al.* (1985) The effects of delaying reward on choice preference in rats with hippocampal or selective septal lesions. *Behav. Brain Res.* 15, 191–203
91 Winstanley, C.A. *et al.* (2004) Contrasting roles of basolateral amygdala and orbitofrontal cortex in impulsive choice. *J. Neurosci.* 24, 4718–4722
92 Floresco, S.B. and Ghods-Sharifi, S. (2007) Amygdala-prefrontal cortical circuitry regulates effort-based decision making. *Cereb. Cortex* 17, 251–260
93 Ghods-Sharifi, S. *et al.* (2009) Fundamental contribution by the basolateral amygdala to different forms of decision making. *J. Neurosci.* 29, 5251–5259
94 Gupta, R. *et al.* (2010) The amygdala and decision-making. *Neuropsychologia* DOI: 10.1016/j.neuropsychologia.2010.09.029
95 Sharot, T. *et al.* (2007) Neural mechanisms mediating optimism bias. *Nature* 450, 102–105
96 Johnson, A. and Redish, A.D. (2007) Neural ensembles in CA3 transiently encode paths forward of the animal at a decision point. *J. Neurosci.* 27, 12176–12189
97 van der Meer, M.A. *et al.* (2010) Triple dissociation of information processing in dorsal striatum, ventral striatum, and hippocampus on a learned spatial decision task. *Neuron* 67, 25–32
98 Schacter, D. *et al.* (2007) Remembering the past to imagine the future: the prospective brain. *Nat. Rev. Neurosci.* 8, 657–661
99 Bar, M. (2009) The proactive brain: memory for predictions. *Philos. Trans. R. Soc. Lond. B. Biol. Sci.* 364, 1235–1243
100 Addis, D.R. and Schacter, D.L. (2008) Constructive episodic simulation: temporal distance and detail of past and future events modulate hippocampal engagement. *Hippocampus* 18, 227–237
101 Gupta, R. *et al.* (2009) Declarative memory is critical for sustained advantageous complex decision-making. *Neuropsychologia* 47, 1686–1693
102 Johnson, A. *et al.* (2007) Integrating hippocampus and striatum in decision-making. *Curr. Opin. Neurobiol.* 17, 692–697
103 Bar, M. (2010) Wait for the second marshmallow? Future-oriented thinking and delayed reward discounting in the brain. *Neuron* 66, 4–5
104 Hassabis, D. *et al.* (2007) Patients with hippocampal amnesia cannot imagine new experiences. *Proc. Natl. Acad. Sci. U.S.A.* 104, 1726–1731
105 Cools, R. (2008) Role of dopamine in the motivational and cognitive control of behavior. *Neuroscientist* 14, 381–395
106 Yacubian, J. *et al.* (2007) Gene–gene interaction associated with neural reward sensitivity. *Proc. Natl. Acad. Sci. U.S.A.* 104, 8125–8130
107 Diekhof, E.K. and Gruber, O. (2010) When desire collides with reason: functional interactions between anteroventral prefrontal cortex and nucleus accumbens underlie the human ability to resist impulsive desires. *J. Neurosci.* 30, 1488–1493
108 Addis, D.R. *et al.* (2008) Age-related changes in the episodic simulation of future events. *Psychol. Sci.* 19, 33–41
109 Wittmann, M. and Paulus, M.P. (2008) Decision making, impulsivity and time perception. *Trends Cogn. Sci.* 12, 7–12
110 Tversky, A. and Kahneman, D. (1981) The framing of decisions and the psychology of choice. *Science* 211, 453–458
111 Weber, E.U. *et al.* (2008) Asymmetric discounting in intertemporal choice: a query theory account. *Psychol. Sci.* 18, 516–523
112 Read, D. *et al.* (2005) Four score and seven years from now: the date/delay effect in temporal discounting. *Manag. Sci.* 51, 1326–1335
113 Boyer, P. (2008) Evolutionary economics of mental time travel? *Trends Cogn. Sci.* 12, 219–224
114 Trope, Y. and Liberman, N. (2003) Temporal construal. *Psychol. Rev.* 110, 403–421
115 Trope, Y. and Liberman, N. (2000) Temporal construal and time-dependent changes in preference. *J. Pers. Soc. Psychol.* 79, 876–889
116 Wilson, M. and Daly, M. (2004) Do pretty women inspire men to discount the future? *Proc. Biol. Sci.* 271 (Suppl. 4), S177–S179
117 Nader, M.A. *et al.* (2008) Positron emission tomography imaging studies of dopamine receptors in primate models of addiction. *Philos. Trans. R. Soc. Lond. B. Biol. Sci.* 363, 3223–3232
118 Robbins, T.W. and Everitt, B.J. (1999) Drug addiction: bad habits add up. *Nature* 398, 567–570
119 Luman, M. *et al.* (2010) Identifying the neurobiology of altered reinforcement sensitivity in ADHD: a review and research agenda. *Neurosci. Biobehav. Rev.* 34, 744–754
120 Buckholtz, J.W. *et al.* (2010) Dopaminergic network differences in human impulsivity. *Science* 329, p532
121 Pine, A. *et al.* (2010) Dopamine, time, and impulsivity in humans. *J. Neurosci.* 30, 8888–8896
122 Cools, R. *et al.* (2003) L-Dopa medication remediates cognitive inflexibility, but increases impulsivity in patients with Parkinson's disease. *Neuropsychologia* 41, 1431–1441
123 Rada, P. *et al.* (2001) Effects of nicotine and mecamylamine-induced withdrawal on extracellular dopamine and acetylcholine in the rat nucleus accumbens. *Psychopharmacology (Berl.)* 157, 105–110
124 Natividad, L.A. *et al.* (2010) Nicotine withdrawal produces a decrease in extracellular levels of dopamine in the nucleus accumbens that is lower in adolescent versus adult male rats. *Synapse* 64, 136–145
125 Epping-Jordan, M.P. *et al.* (1998) Dramatic decreases in brain reward function during nicotine withdrawal. *Nature* 393, 76–79
126 Wade, T.R. *et al.* (2000) Effects of dopaminergic drugs on delayed reward as a measure of impulsive behavior in rats. *Psychopharmacology (Berl.)* 150, 90–101
127 de Wit, H. *et al.* (2002) Acute administration of d-amphetamine decreases impulsivity in healthy volunteers. *Neuropsychopharmacology* 27, 813–825
128 Wang, X.T. and Dvorak, R.D. (2010) Sweet future: fluctuating blood glucose levels affect future discounting. *Psychol. Sci.* 21, 183–188
129 Zlomke, K.R. and Dixon, M.R. (2006) Modification of slot-machine preferences through the use of a conditional discrimination paradigm. *J. Appl. Behav. Anal.* 39, 351–361
130 Dixon, M.R. and Holton, B. (2009) Altering the magnitude of delay discounting by pathological gamblers. *J. Appl. Behav. Anal.* 42, 269–275
131 Bickel, W.K. *et al.* (2011) Remember the future: working memory training decreases delay discounting among stimulant addicts. *Biol. Psychiatry* 69, 260–265
132 Wittmann, M. *et al.* (2007) Impaired time perception and motor timing in stimulant-dependent subjects. *Drug Alcohol Depend.* 90, 183–192
133 Eisenberg, D.T. *et al.* (2007) Examining impulsivity as an endophenotype using a behavioral approach: a DRD2 TaqI A and DRD4 48-bp VNTR association study. *Behav. Brain Funct.* 3, p2
134 Bilder, R.M. *et al.* (2004) The catechol-*O*-methyltransferase polymorphism: relations to the tonic-phasic dopamine hypothesis and neuropsychiatric phenotypes. *Neuropsychopharmacology* 29, 1943–1961
135 Wilhelm, C.J. and Mitchell, S.H. (2009) Strain differences in delay discounting using inbred rats. *Genes Brain Behav.* 8, 426–434
136 Mischel, W. *et al.* (1989) Delay of gratification in children. *Science* 244, 933–938
137 Scheres, A. *et al.* (2006) Temporal and probabilistic discounting of rewards in children and adolescents: effects of age and ADHD symptoms. *Neuropsychologia* 44, 2092–2103
138 Olson, E.A. *et al.* (2007) Adolescents' performance on delay and probability discounting tasks: contributions of age, intelligence, executive functioning, and self-reported externalizing behavior. *Pers. Individ. Diff.* 43, 1886–1897
139 Steinberg, L. *et al.* (2009) Age differences in future orientation and delay discounting. *Child Dev.* 80, 28–44
140 Christakou, A. *et al.* (2011) Maturation of limbic corticostriatal activation and connectivity associated with developmental changes in temporal discounting. *Neuroimage* 54, 1344–1354
141 Olson, E.A. *et al.* (2009) White matter integrity predicts delay discounting behavior in 9- to 23-year-olds: a diffusion tensor imaging study. *J. Cogn. Neurosci.* 21, 1406–1421
142 Prencipe, A. *et al.* (2011) Development of hot and cool executive function during the transition to adolescence. *J. Exp. Child Psychol.* 108, 621–637

143 Arnett, J.J. (1999) Adolescent storm and stress, reconsidered. *Am. Psychol.* 54, 317–326
144 Green, L. *et al.* (1996) Temporal discounting in choice between delayed rewards: the role of age and income. *Psychol. Aging* 11, 79–84
145 Green, L. *et al.* (1994) Discounting of delayed rewards: a life-span comparison. *Psychol. Sci.* 5, 33–36
146 Giedd, J.N. (2004) Structural magnetic resonance imaging of the adolescent brain. *Ann. N. Y. Acad. Sci.* 1021, 77–85
147 Casey, B.J. *et al.* (2008) The adolescent brain. *Ann. N. Y. Acad. Sci.* 1124, 111–126
148 Somerville, L.H. *et al.* (2010) Frontostriatal maturation predicts cognitive control failure to appetitive cues in adolescents. *J. Cogn. Neurosci.* DOI: 10.1162/jocn.2010.21572
149 Cohen, J.R. *et al.* (2010) A unique adolescent response to reward prediction errors. *Nat. Neurosci.* 13, 669–671
150 Bjork, J.M. *et al.* (2009) Delay discounting correlates with proportional lateral frontal cortex volumes. *Biol. Psychiatry* 65, 710–713
151 Friston, K.J. *et al.* (1997) Psychophysiological and modulatory interactions in neuroimaging. *Neuroimage* 6, 218–229
152 Friston, K.J. and Dolan, R.J. (2010) Computational and dynamic models in neuroimaging. *Neuroimage* 52, 752–765
153 Churchwell, J.C. *et al.* (2009) Interactions between the prefrontal cortex and amygdala during delay discounting and reversal. *Behav. Neurosci.* 123, 1185–1196
154 Knoch, D. *et al.* (2006) Disruption of right prefrontal cortex by low-frequency repetitive transcranial magnetic stimulation induces risk-taking behavior. *J. Neurosci.* 26, 6469–6472
155 Camus, M. *et al.* (2009) Repetitive transcranial magnetic stimulation over the right dorsolateral prefrontal cortex decreases valuations during food choices. *Eur. J. Neurosci.* 30, 1980–1988
156 Bechara, A. *et al.* (1994) Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition* 50, 7–15
157 Bechara, A. *et al.* (1999) Different contributions of the human amygdala and ventromedial prefrontal cortex to decision-making. *J. Neurosci.* 19, 5473–5481
158 Bechara, A. *et al.* (2000) Characterization of the decision-making deficit of patients with ventromedial prefrontal cortex lesions. *Brain* 123, 2189–2202
159 Clark, L. *et al.* (2008) Differential effects of insular and ventromedial prefrontal cortex lesions on risky decision-making. *Brain* 131, 1311–1322
160 Tranel, D. *et al.* (2002) Asymmetric functional roles of right and left ventromedial prefrontal cortices in social conduct, decision-making, and emotional processing. *Cortex* 38, 589–612
161 Naccache, L. *et al.* (2005) Effortless control: executive attention and conscious feeling of mental effort are dissociable. *Neuropsychologia* 43, 1318–1328
162 Fellows, L.K. and Farah, M.J. (2005) Dissociable elements of human foresight: a role for the ventromedial frontal lobes in framing the future, but not in discounting future rewards. *Neuropsychologia* 43, 1214–1221
163 Frank, M.J. and Claus, E.D. (2006) Anatomy of a decision: striato-orbitofrontal interactions in reinforcement learning, decision making, and reversal. *Psychol. Rev.* 113, 300–326