units in visual word recognition. *Q. J. Exp. Psychol.* 54A, 439–467
7 Humphreys, G.W. and Mayall, K. (2001) A peripheral reading deficit under conditions of diffuse visual attention. *Cogn. Neuropsychol.* 18, 551–576
8 Allport, D.A. (1977) On knowing the meaning of words we are unable to report: the effects of visual masking. In *Attention and Performance VI* (Dornic, S., ed.), pp. 505–533, MIT Press
9 Shallice, T. and McGill, J. (1978) The origins of mixed errors. In *Attention and Performance VII* (Requin, J., ed.), pp. 193–208, MIT Press
10 Mozer, M.C. (1983) Letter migration in word perception. *J. Exp Psychol. Hum. Percept. Perform.* 9, 531–546
11 McClelland, J.L. and Mozer, M.C. (1986) Perceptual interactions in two-word displays: familiarity and similarity effects. *J. Exp Psychol. Hum. Percept. Perform.* 12, 18–35
12 Treisman, A. and Souther, J. (1986) Illusory words: the roles of attention and of top-down constraints in conjoining letters to form words. *J. Exp Psychol. Hum. Percept. Perform.* 12, 3–17
13 Shallice, T. (1988) *From Neuropsychology To Mental Structure*, Cambridge University Press
14 Mozer, M.C. and Behrmann, M. (1992) Reading with attentional impairments: a brain-damaged model of neglect and attentional dyslexias. In *Connectionist Approaches to Natural Language Processing* (Reilly, R.G. and Sharkey, N.E., eds), pp. 409–460, Erlbaum
15 Mayall, K. and Humphreys, G.W. (2002) Presentation and task effects on migration errors in attentional dyslexia. *Neuropsychologia* 40, 1506–1515
16 Friedmann, N. and Gvion, A. (2001) Letter position dyslexia. *Cogn. Neuropsychol.* 18, 673–696

Colin J. Davis
Max Coltheart
Macquarie Centre for Cognitive Science (MACCS), Macquarie University, Sydney, NSW 2109, Australia.
e-mail: colin@maccs.mq.edu.au

Decision-making deficits in drug addiction

Luke Clark and Trevor W. Robbins

Core aspects of addictive behaviour can be explained in terms of abnormal decision-making. Using recording of autonomic function during performance of two gambling tasks, Bechara *et al.* have recently identified three distinct neuropsychological subtypes in individuals with substance dependence. These subtypes may reflect dissociable patterns of disruption in limbic brain circuitry.

Characterization of the cognitive mechanisms involved in chronic substance abuse has clear implications for pharmacological and rehabilitative treatment strategies, and also impacts upon our understanding of cognitive and motivational processing in the healthy brain. The relationship of decision-making to addiction has received particular attention recently. Decision-making involves, first, the assessment of reward and punishment associations to the available response options, and second, the selection of the option calculated to be optimal. In chronic substance abuse, decision-making appears to be altered in terms of the trade-off between short-term reward and the long-term negative consequences of drug abuse on health, employment and family life [1].

Neuropsychology of decision-making

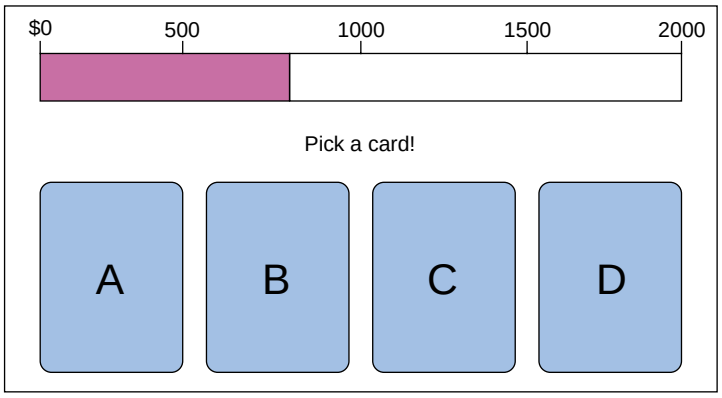
Two recent studies by Bechara and colleagues [2,3] have investigated the decision-making profile in substance abuse, using a neuropsychological measure known as the Gambling Task (see Fig. 1). In this task, subjects are presented with four decks of cards and must make a long series of decisions, picking from any deck on each go without knowing that there are 'safe' and 'risky' decks. Over 100 choices, healthy subjects typically develop a preference for the 'safe' decks (C and D) over the 'risky' decks (A and B). This learning has a physiological correlate in the development of an 'anticipatory' skin conductance response (SCR) prior to selection from the risky decks [4], which is assumed to reflect some awareness that the decision could result in high punishment.

Patients with brain damage in the ventromedial region of prefrontal cortex (PFC) perform poorly on the Gambling Task [4]. They continue to select from the risky decks even after accruing considerable financial debt, and fail to develop anticipatory SCRs to the risky choices, despite showing normal post-choice autonomic responses to reward and punishment. Their decision-making deficit has been labelled 'myopia for the future' – these patients are unable to use ongoing feedback to guide future responses, and therefore evaluate each decision in terms only of the immediate reward available. This pattern is consistent with the real-life cognitive difficulties seen in patients with lesions in this area. However, ventromedial PFC is unlikely to function in isolation: in particular, the ventral striatum and amygdala are known to be part of an extended neural network involved in motivational processing and goal-driven behaviour [5]. Amygdala damage also impairs performance on the Gambling Task, but is associated with a distinct autonomic profile, with blunted responses to task punishment and to aversive noise [6].

Decision-making heterogeneity in substance-dependent individuals

Grant *et al.* have previously tested a group of multiple-drug users recruited from the community on the Gambling Task, and reported increased selection from the risky decks relative to controls [7]. Bechara *et al.* [2] extended these findings in a larger and more clinically severe group by administering the task with physiological monitoring to a group of 46 individuals, who were undergoing drug rehabilitation at an inpatient centre and who met DSM-IV criteria for alcohol or substance dependence. The group consisted of approximately similar numbers of alcohol-, cocaine-, and amphetamine-preferring poly-drug users. Performance was compared against a healthy control group and 10 patients with ventromedial PFC damage. Gambling performance in the substance-dependent group fell midway between the control and ventromedial groups, and differing significantly from both. This pattern might plausibly reflect a learning deficit, which causes subjects to persist with the risky decks for longer at the start of the task, before eventually acquiring the successful strategy – this would be compatible with the mild deficit reported previously in mania [8], for example. By contrast, the profile in the substance-dependent group resembled more closely a bimodal distribution: 63% of

 1364-6613/02/$ – see front matter PII: S1364-6613(02)01960-5



	Decks A and B	Decks C and D
Original task	High reward ($100 per go). Intermittent high losses. Net loss.	Lower reward ($50 per go). Intermittent low losses. Net profit.
Variant task	High loss ($100 per go). Intermittent high reward. Net profit.	Lower loss ($50 per go). Intermittent low reward. Net loss.

TRENDS in Cognitive Sciences

Fig. 1. Schematic representation of the display from the Gambling Task, showing the reward and punishment contingencies in the original and variant versions.

the group showed gambling task deficits consistent with ventromedial PFC dysfunction, preferring the risky decks for the entire duration of the task. The remaining 37% behaved like the controls from the start of the task. Critically, the subgrouping was unrelated to the substance abused, and was supported by the physiological measurements: the impaired substance-dependent group showed no evidence of an anticipatory SCR whereas the non-impaired group clearly developed this effect.

A follow-up study used a modified version of the Gambling Task in the same substance-dependent group [3]. The variant task was designed to differentiate hypersensitivity to immediate reward from insensitivity to long-term punishment. These are conceptually independent factors, which can both impair performance and contribute to addictive behaviour. The variant task separates these processes by reversing the reward and punishment contingencies (see Fig. 1). Substance-dependent individuals who performed well on the original task also performed well on the modified task. However, within the group that were impaired on the original task, a further division became evident. Roughly a third of that group were also impaired on the variant task, indicating that they were insensitive to future consequences regardless of the emotional valency. This effect has previously been shown in patients with ventromedial PFC damage [9]. The remaining two-thirds of the group acquired the successful strategy on the modified task, despite showing impairment on the original task. This indicated that feedback about reward, but not about punishment, was able to guide long-term decision-making in these individuals. Moreover, this subgroup showed a distinctive physiological profile on the modified task. Firstly, their SCR to reward was exaggerated, and secondly, the anticipatory SCR on the safe decks became larger over time, whereas in control subjects the anticipatory SCR to the risky decks became larger as the preference developed. This subgroup, which constituted the largest proportion of the substance-dependent individuals, displayed hypersensitivity to reward coupled with hyposensitivity to punishment. The amygdala is known to have a critical role in processing the incentive value of stimuli [6], but is also activated by punishment [10,11], and an imbalance in the amygdala could produce this decision-making bias [3].

Methodological issues in addiction research

Abnormalities in ventromedial PFC and amygdala therefore appear to be associated with distinct manifestations of decision-making impairment. Functional neuroimaging potentially provides a further step for confirming these dissociable neuroanatomical substrates, and the clinical and rehabilitative significance of the heterogeneity is another target for research. However, the precise nature of neuropsychological dysfunction in addiction remains unclear. Chronic exposure to substances of abuse might first cause neurotoxic damage [12] with subsequent concomitant effects upon cognition. Animal research has repeatedly demonstrated examples of this model, revealing pathological and behavioural changes following chronic administration of stimulants [13], which frequently persist after prolonged abstinence. The alternative is a diathetic model, where developmental or genetic abnormalities in decision-making circuitry predispose the individual to addictive behaviour to a range of substances [14]. Assessment of background neuropsychological functioning in Bechara's group revealed largely intact memory, attention and executive functioning [2]. A relatively selective impairment in decision-making in a mixed group of chronic substance abusers is perhaps more compatible with a diathetic model than with exposure-induced damage. Exposure also seems unlikely given that the impaired and unimpaired subgroups in their first study were comparable in terms of years of abuse and length of time in treatment.

The issue of cause and effect in addiction research is approached more directly through research on experimental animals, where developmental and environmental factors can be carefully controlled, and the confounding effect of poly-drug use can be avoided. Further methodological obstacles for research on substance-dependent groups are psychiatric co-morbidity and abstinence effects. Although a policy of excluding any subjects with psychiatric co-morbidity could be criticized for 'throwing the baby out with the bathwater', subjects in the Bechara *et al.* studies were given a full psychiatric screening and a points system for each diagnosis; subjects scoring above 3 were excluded. Participants in the two studies had also been abstinent for at least 15 days, which is pertinent given neuroimaging data showing ventromedial PFC modulation during both acute drug craving and short-term withdrawal [15,16].

Component processes in decision-making

The learning context of the Gambling Task complicates its use in functional neuroimaging, where a carefully-matched control task is needed for subtraction analysis. A recent PET study by Ernst *et al.* [17] contrasted Gambling Task performance with a control condition using a specified order of card selection (i.e. A, B, C, D – A, B, C, D, etc…). Both dorsal and ventral aspects of PFC were activated in this subtraction, associated with the volitional aspects of decision-making. However, both conditions in this study involved evaluating the reward and punishment associations of the different decks, which might be more relevant to the deficits in some patient populations than others. It is possible to remove the learning element of the Gambling Task by fully specifying the variables in the gamble on a trial-by-trial basis. A PET study using the 'Risk Task' [18] demonstrated activations in three distinct regions of ventral PFC (Brodmann areas 10, 11, and 47) during a decision-making conflict between a large but uncertain reward, and a smaller but more likely reward. Another decision-making test has been developed that further separates probabilistic reasoning in decision-making from actual risk-taking behaviour, and there is accumulating evidence that these two factors might be doubly-dissociable [14,19].

The Gambling Task also confounds a topical theoretical distinction between delay and uncertainty. Temporal- (or delay-) discounting tasks assess how subjects prioritise a small immediate reward over a larger but delayed reward. Opiate addicts have been shown to discount large delayed rewards more than control subjects do [20]. A probabilistic discounting task, by contrast, assesses how subjects prioritise a small but *certain* reward over a larger but *uncertain* reward. The framework of the Gambling Task emphasizes the dimension of uncertainty; the larger rewards carry a concomitant risk of high punishment. However, the task also has an delay component, because the successful strategy involves prioritising a slow but steady approach over fast short-term gain, and indeed performance on the Gambling Task has been shown to correlate with that on a delay-discounting task, in a group of cocaine addicts [21]. Meanwhile, the validity of this distinction remains controversial, with theorists such as Rachlin arguing that delay and uncertainty are inherently linked and processed in a unified manner [22]. Temporal and probabilistic discounting indices often do correlate closely [23], and orbitofrontal cortex lesions in the rat increase discounting of both variables [24]. Against a unified model, however, Green *et al.* report opposing effects of the manipulation of reward on temporal and probabilistic discounting [25], and serotonergic lesions in the rat selectively disrupt temporal but not probabilistic discounting [26]. Consensus is still to be found, therefore, in this dynamic field.

Characterization of the decision-making deficit in chronic substance abuse is thus constrained by current theoretical models of decision-making, as well as by limited understanding of the underlying neuroanatomy and neurochemistry. The findings of the two Bechara studies are important because they highlight behavioural and physiological subtypes in substance abuse, using a single task believed to tap a core construct in addictive behaviour. This heterogeneity could account for inconsistencies in the existing literature, but must also be taken into account in future research if its full clinical significance is to be understood.

References

1 Rahman, S. *et al.* (2001) Decision making and neuropsychiatry. *Trends Cogn. Sci.* 5, 271–277
2 Bechara, A. and Damasio, H. (2002) Decision-making and addiction (Part I): impaired activation of somatic states in substance-dependent individuals when pondering decision with negative future consequences. *Neuropsychologia* 40, 1675–1689
3 Bechara, A. *et al.* (2002) Decision-making and addiction (Part II): myopia for the future or hypersensitivity to reward? *Neuropsychologia* 40, 1690–1705
4 Bechara, A. *et al.* (1996) Failure to respond autonomically to anticipated future outcomes following damage to prefrontal cortex. *Cereb. Cortex* 6, 215–225
5 Cador, M. *et al.* (1989) Involvement of the amygdala in stimulus-reward associations: interaction with the ventral striatum. *Neuroscience* 30, 77–86
6 Bechara, A. *et al.* (1999) Differential contributions of human amygdala and ventromedial prefrontal cortex to decision-making. *J. Neurosci.* 19, 5473–5481
7 Grant, S. *et al.* (2000) Drug abusers show impaired performance in a laboratory test of decision making. *Neuropsychologia* 38, 1180–1187
8 Clark, L. *et al.* (2001) A neuropsychological investigation of prefrontal cortex involvement in acute mania. *Am. J. Psychiatry* 158, 1605–1611
9 Bechara, A. *et al.* (2000) Characterization of the decision-making impairment of patients with ventromedial prefrontal cortex lesions. *Brain* 123, 2189–2202
10 Killcross, S. *et al.* (1997) Different types of fear-conditioned behaviour mediated by separate nuclei within amygdala. *Nature* 388, 377–380
11 Zalla, T. *et al.* (2000) Differential amygdala responses to winning and losing: a functional magnetic resonance imaging study in humans. *Eur. J. Neurosci.* 12, 1764–1770
12 Wilson, J.M. *et al.* (1996) Striatal dopamine nerve terminal markers in human, chronic methamphetamine users. *Nat. Med.* 2, 699–703
13 Ricaurte, G.A. *et al.* (1984) Long-term effects of repeated methamphetamine administration on dopamine and serotonin neurons in the rat brain: a regional study. *Brain Res.* 193: 153–163
14 Rogers, R.D. *et al.* (1999) Dissociable deficits in the decision-making cognition on chronic amphetamine abusers, opiate abusers, patients with focal damage to prefrontal cortex, and tryptophan-depleted normal volunteers: evidence for monoaminergic mechanisms. *Neuropsychopharmacology* 20, 322–329
15 Childress, A.R. *et al.* (1999) Limbic activation during cue-induced cocaine craving. *Am. J. Psychiatry* 156, 11–18
16 Volkow, N.D. and Fowler, J.S. (2000) Addiction, a disease of compulsion and drive: involvement of the orbitofrontal cortex. *Cereb. Cortex* 10, 318–325
17 Ernst, M. *et al.* (2002) Decision-making in a risk-taking task: a PET study. *Neuropsychopharmacology* 26, 682–691
18 Rogers, R.D. *et al.* (1999) Choosing between small, likely rewards and large, unlikely rewards activates inferior and orbital prefrontal cortex. *J. Neurosci.* 20, 9029–9038
19 Manes, F. *et al.* (2002) Decision-making processes following damage to the prefrontal cortex. *Brain* 125, 624–639
20 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
21 Monterosso, J. *et al.* (2001) Three decision-making tasks in cocaine-dependent patients: do they measure the same construct? *Addiction* 96, 1825–1837
22 Rachlin, H. *et al.* (1991) Subjective probability and delay. *J. Exp. Anal. Behav.* 55, 233–244
23 Richards, J.B. *et al.* (1999) Delay or probabilistic discounting in a model of impulsive behavior: effect of alcohol. *J. Exp. Anal. Behav.* 71, 121–143
24 Mobini, S. *et al.* (2002) Effects of lesions of the orbitofrontal cortex on sensitivity to delayed and probabilistic reinforcement. *Psychopharmacology* 160, 290–298
25 Green, L. *et al.* (1999) Amount of reward has opposite effects on the discounting of delayed and probabilistic outcomes. *J. Exp. Psychol. Learn. Mem. Cogn.* 25, 418–427
26 Mobini, S. *et al.* (2000) Effects of central 5-hydroxytryptamine depletion on sensitivity to delayed and probabilistic reinforcement. *Psychopharmacology* 152, 390–397

Luke Clark
Trevor W. Robbins*
Dept of Experimental Psychology, University of Cambridge, Downing Site, Cambridge, UK CB2 3EB.
*e-mail: twr2@cus.cam.ac.uk.