Available online at www.sciencedirect.com
ScienceDirect
Drug and Alcohol Dependence 94 (2008) 82–91
DRUG and ALCOHOL DEPENDENCE
www.elsevier.com/locate/drugalcdep

Neuropsychological predictors of clinical outcome in opiate addiction

F. Passetti [a,*], L. Clark [b], M.A. Mehta [c], E. Joyce [d], M. King [a]

[a] *Department of Mental Health Sciences, University of London, London NW3 2PF, UK*
[b] *Department of Experimental Psychology, University of Cambridge, Cambridge CB2 3EB, UK*
[c] *Institute of Psychiatry, University of London, London SE5 8AF, UK*
[d] *Institute of Neurology, University of London, London WC1N 3BG, UK*

Received 23 April 2007; received in revised form 15 October 2007; accepted 17 October 2007
Available online 11 December 2007

Abstract

A growing literature supports a role for neurocognitive deficits such as impaired decision-making in the development and maintenance of addictive behaviour. On the basis of these findings, it has been suggested that measures of neurocognitive functioning may be applied to the task of predicting clinical outcome in drug addiction. This in turn may have relevance for differentiating treatment based on individual patient needs. To explore this hypothesis we obtained neurocognitive measures of planning, impulsivity and decision-making from 37 opiate dependent individuals within 6 weeks of starting a community drug treatment programme and we followed them up 3 months into the programme. Performance on two tests of decision-making, but not on tests of planning, motor inhibition, reflection impulsivity or delay discounting, was found to predict abstinence from illicit drugs at 3 months with high specificity and moderate sensitivity. In particular, two thirds of the participants performing normally on the Cambridge Gamble Task and the Iowa Gambling Task, but none of those impaired on both, were abstinent from illicit drugs at follow up. Other neuropsychological, psychiatric or psychosocial factors measured in this sample did not explain this finding. The results are discussed in terms of the brain circuitry involved and the potential implications for the planning of treatment services for opiate dependence.

Keywords: Neuropsychology; Decision-making; Impulsivity; Opiate; Outcome; Predictors

1. Introduction

Several recent large cohort studies support the effectiveness of treatment programmes for drug addiction, including addiction to opiates. Thus, treatment programmes have been shown to reduce drug use (e.g. Hubbard et al., 1997; Gossop et al., 2000a), improve harm associated with injecting practices (Darke et al., 2005) and decrease drug-related crime (Gossop et al., 2000b). However, addiction to opiates remains a remarkably persistent condition (Hser et al., 2001). Studies show that only a small proportion of individuals entering treatment become abstinent for sustained periods of time (Sheehan et al., 1993; Darke et al., 2005). Thus, understanding whether there are specific aspects of treatment or client characteristics that are associated with favourable outcome is of major clinical importance, because a better knowledge of these factors may help improve abstinence rates. The availability of reliable methods for predicting clinical outcome might help identify those clients who require specific types of intervention in order to achieve and maintain abstinence.

Addictive behaviour change is a complex process that is affected by treatment-related and client-centred factors ranging from the severity and length of addiction (Hser et al., 1999; Joe et al., 1999; Flynn et al., 2003), to the presence of co-morbid psychopathology (Joe et al., 1999), the treatment length and perception (Hubbard et al., 1997; Gossop et al., 1999; Flynn et al., 2003) and the environment of the recovering addict (Hser et al., 1999; Flynn et al., 2003). Neural and neuropsychological mechanisms, particularly those related to decision-making, are also probably important, but have been investigated less extensively. Drug dependent individuals tend to guide their behaviour based on the available short-term gains rather than on careful consideration of the long-term effects of their choices (Kirby et al., 1999; Bechara, 2005). This cognitive style may hinder the effectiveness of treatment in several ways. For example, it may interfere

* Corresponding author at: Section of Addictive Behaviour, Division of Mental Health, St George's University of London, Cranmer Terrace, London SW17 0RE, London, UK. Fax: +44 208 725 2914.
E-mail address: fpassett@sgul.ac.uk (F. Passetti).

0376-8716/$ – see front matter © 2007 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.drugalcdep.2007.10.008

with the ability of dependent individuals to forego using drugs for the sake of long-term benefits, or it may hinder attempts to develop effective strategies to avoid situations in which they may experience drug craving. Thus, measures of neurocognitive functioning may be valuable for predicting clinical outcome in drug addiction (Bechara, 2005).

Paulus et al. (2005) used brain imaging techniques to look at patterns of brain activation in recovering methamphetamine-dependent individuals during performance of a decision-making task. Discriminant function analysis showed that combined activation patterns in frontal and temporal regions predicted the likelihood of relapse at 1 year with high sensitivity and specificity. These findings support the notion that individual variability in brain mechanisms engaged in decision-making may contribute to individual differences in treatment effectiveness in drug-dependent individuals. However, the decision-making task employed in that study was a simple guessing task that was designed to activate relevant networks, not to capture the neuropsychological profile associated with relapse. Thus, although these results support the usefulness of a neural perspective on addictive behaviour change, they do not provide any direct information regarding the specific neuropsychological processes involved in maintaining abstinence from illicit drugs. In addition, the use of imaging techniques makes it unlikely that these results will have direct implications for assessment or treatment.

The neuropsychology of drug addiction has been a burgeoning area of research in recent years. A number of novel neuropsychological tasks have been developed, which are sensitive to the neurocognitive changes associated with drug addiction. Tasks of affective decision-making, including the Iowa Gambling Task (IGT), the Cambridge Gamble Task (CGT) and the Delay Discounting Task (DDT) (for review see Monterosso et al., 2001; Clark and Robbins, 2003; Kirby and Petry, 2004), as well as tasks measuring aspects of motor (Fillmore and Rush, 2002; Monterosso et al., 2005; Verdejo-Garcia et al., 2007) and cognitive impulsivity (Clark et al., 2006) have been used to characterise such changes. These tasks reliably distinguish drug users and non-drug using controls. However, only one study has looked at these neurocognitive variables as predictors of clinical outcome in a prospective cohort design (Bowden-Jones et al., 2005). It was found that the performance of recovering alcohol-dependent individuals on decision-making tasks was poorer in those who would relapse within 3 months of completing a 21-day inpatient treatment programme, compared to those who would remain abstinent throughout the same period.

The present study employed tasks of decision-making, impulsivity and planning in a group of opiate (polydrug) users at intake into a community drug addiction treatment programme, to investigate the possibility of using neuropsychological measures to predict abstinence from illicit drugs at 3 months. This is to our knowledge the first study to look at the early stages of treatment in a relatively unselected sample of drug users. Our prediction was that, in line with the findings of studies with recovering individuals (Paulus et al., 2005; Bowden-Jones et al., 2005) poorer outcome would be associated with poorer performance on some or most of these tasks. To facilitate investigating the potential for clinical application of measures of task performance on these tasks, we established criteria for impaired and unimpaired performance on these tasks, and we used a similar discriminant function analysis to that used by Paulus et al. (2005).

2. Methods

2.1. Participants and treatment program

Forty-three opiate dependent individuals were recruited from a drug service in central London on the basis of the following criteria: age 18–55, opiate dependence syndrome as defined by DSM-IV criteria, no other current non-substance related DSM-IV Axis I diagnosis and no history of: any non-substance related psychotic disorder, major depressive disorder, dementia or mental retardation. Additional exclusion criteria were: acute intoxication, being on a drug treatment order, inability to communicate in English and being pregnant. They were interviewed and tested 30 ± 3 days from starting treatment (range 7–60 days), i.e. as soon as they had been stabilised on substitute opiate prescription. Nearly everyone who was offered to take part in the study agreed. Drug use and severity of drug-related problems were assessed using a modified version of the Maudsley Assessment Protocol (MAP, Marsden et al., 1999). IQ was estimated using the Wechsler Test of Adult Reading (WTAR; Wechsler, 2001). Assessment of current and past psychiatric history was based on the DSM-IV Structured Clinical Interview as well as on the Brief Psychiatric Rating Scale, the Beck's Depression Inventory and the Young Mania Rating Scale (Young et al., 1978). Participants provided written informed consent prior to testing and received a small amount of money in shop vouchers as token of gratitude for their participation. The study was approved by the Local NHS Research Ethics Committee.

The treatment program included substitute opiate administration under supervision either at the treatment centre or at a nearby pharmacy registered with the National Health Service supervised daily dispensing scheme. Clients were required to meet with a keyworker at least weekly. In addition, they had access to a psychologist and to a Crack Cocaine guided discussion group. Keyworkers encouraged reduced illicit drug use and discussed with clients the need for adjustment of prescribed opiate dose, as well as monitoring their illicit drug use by means of random urine drug screen tests. The client's failure to reduce illicit drug use resulted in a review by one of the centre doctors, for psychiatric assessment and to re-negotiate the opiate prescription as needed (Quirk et al., 2004). Breath alcohol readings were obtained daily for alcohol dependent individuals and as clinically indicated (but at least weekly) for non-alcohol dependent individuals.

Participants were followed up opportunistically at various points during the follow up period and formally interviewed 3 months into treatment. A small group of individuals achieved abstinence shortly after commencing treatment and remained abstinent for most of the follow-up period (A group), while a larger group continued to take illicit drugs on at least a weekly basis (NA group). Few individuals fell in between these two patterns (three remained illicit drug-free for more than 1 week, but less than two). For the purpose of this study, abstinence at follow up was defined as not using any illicit drugs for at least the previous 30 days and was based on self-report and on one or more confirmatory urine drug screen results. On the second interview, participants also completed the Treatment Perception Questionnaire (TPQ, Marsden et al., 1998). At follow-up two participants were in prison and four had disengaged from the service without leaving a valid contact address. The demographics of the remaining 37 participants are presented in Table 1.

2.2. Neuropsychological testing

Computerised tasks were administered in a quiet room using a laptop PC with mounted touch-sensitive monitor. Two tasks (Tower of London and Cambridge Gambling Task) were part of a larger neuropsychological test battery (CANTAB, Cambridge Cognition Ltd). Participants were allowed a brief break in between tests, during which they could smoke tobacco if they wished to.

2.2.1. Decision-making. The Iowa Gambling Task and Cambridge Gamble Task are two computerised tasks of decision-making that require individuals to

Table 1
Characteristics of the abstinent and non-abstinent groups

	Abstinent ($n = 10$)	Non-abstinent ($n = 27$)	Statistic[a]
Age (years)[b]	37.7 ± 2.6	37.3 ± 1.5	0.14, NS
M:F	7:3	19:8	0.01, NS
Ethnicity (White:other)	5:5	21:6	2.69, NS
Verbal IQ[b]	100.5 ± 2.7	97.7 ± 2.1	0.67, NS
BPRS[b]	28.3 ± 1.1	28.4 ± 0.9	0.04, NS
BDI[b]	13.8 ± 3.4	17.7 ± 2.2	0.88, NS
Young mania rating scale[b]	0.3 ± 0.1	0.9 ± 0.3	1.21, NS
Education (% no qualification)	30.0%	59.2%	2.50, NS
% Homeless	60.0%	59.2%	0.01, NS
Parental occupation (% unskilled)	22.2%	40.0%	0.92, NS

[a] Independent samples Student's *t*-test or Pearson's Chi square.
[b] Mean ± S.E.M.

select between alternative choices associated with uncertain rewards and punishments. The IGT requires individuals to choose from four decks of cards each characterised by a different reward-punishment profile. Unbeknownst to the players, two decks (A′ and B′, the risky decks) are associated with large wins and even larger losses, resulting in net loss, while the other two decks (C′ and D′, the safe decks) are associated with smaller wins and even smaller penalties, resulting overall in profit. The main measure of performance is the difference between the number of choices from the safe decks minus the number of choices from the risky decks ('net' score). In previous literature, individuals with a drug addiction had lower scores for this parameter, compared with matched controls (reviewed in Bechara, 2005), suggesting a tendency for risk-taking.

The CGT requires individuals to bet on the occurrence of either of two mutually exclusive events differing in their probability. Subjects were presented with an array of ten boxes at the top of the screen, some of which were red and some were blue. They were told that the computer had hidden a yellow token randomly inside one of the boxes and their task was to guess the colour of this box. Subjects bet on their choice by selecting from a series of available bets that were presented sequentially at the right hand side of the screen. In order to isolate the effects of impulsivity from genuine risk seeking, bets were presented in ascending order on half of the trials and in descending order in the other half. The ratio of red to blue boxes varied from trial to trial, in order to permit assessment of subjects' decision-making across a range of odds of winning. For example, for some ratios contingencies were very unequal (e.g. 1 red:9 blue), while for others (e.g. 4 red:6 blue) they were more equally balanced. It is important to note that in this task choosing the least likely outcome was not associated with any premium in terms of the rewards to be won. Subjects simply won or lost the amount of points they chose to bet on each trial. Thus, consistently choosing the least likely outcome in this task indicates poor decision-making. Measures of performance included the quality of decision-making (i.e. the percentage of times subjects bet on the most likely outcome), the decision latency and the proportion of points bet. Previous studies have shown performance of individuals with a drug addiction to be characterised by suboptimal decisions and/or slower speed of decision-making (see Rogers and Robbins, 2001, for review).

The Delay Discounting Task is a decision-making task that measures the ability of individuals to tolerate a delay in order to obtain a larger reward instead of a smaller reward available immediately. Subjects were presented with a list of choices between larger delayed and smaller immediate rewards and were required to select their preferred option for each. To enhance validity, subjects were told that one of the choice items would be selected at the end of the task and they would receive the reward they chose for this item, at the stated delay. Choices on the DDT were used to calculate for each participant a discounting rate parameter k for the discounting function described by the following formula:

$$V = \frac{A}{(1 + kD)}$$

where V is the current value of the reward A at delay D (see Kirby et al., 1999 for more detailed description). This parameter has been shown to be higher in individuals with a drug addiction compared to non-addicted controls (Kirby et al., 1999; Kirby and Petry, 2004).

2.2.2. Planning. A computerised version of the Tower of London was used as a measure of planning and problem-solving. In this task subjects were required to match two arrangements of coloured balls by moving one set of balls on a touch-sensitive screen. The balls had to be moved according to a set of rules, imposing a requirement to plan the moves in advance in order to correctly solve the problem (see Owen et al., 1990; Owen et al., 1995). Problems were graded in difficulty, ranging from easy (2 moves), to difficult (5 moves). A total of 12 problems were presented. Measures of performance were the average number of moves taken to solve the harder problems and the overall number of problems solved in the minimum number of moves ("perfect solutions"). Previous studies found impairments of performance on this task in current and former opiate users compared to controls (Ornstein et al., 2000; Ersche et al., 2006).

2.2.3. Reflection impulsivity. Impulsivity is not a unitary construct, but includes at least two broad aspects, motor and cognitive impulsivity (see Evenden, 1999). One aspect of cognitive impulsivity is the extent to which relevant information is sampled prior to making a decision. Impulsive individuals may make poor decisions due to inadequate 'reflection' (Kagan, 1966). Using the Information Sampling Task (IST), Clark et al. (2006) demonstrated disrupted reflection in current and former users of opiates or amphetamines, compared to matched controls. Subjects were presented with a 5 × 5 grid of grey boxes, which they could open one by one by touching them, to reveal an underlying distribution of two colours. They were told that they could open as many boxes as they wanted and their task was to decide which colour would be in the majority. There were two conditions, which were presented across subjects in counterbalanced order. In the fixed reward condition subjects won or lost always the same amount (100 points) regardless of the number of boxes opened. In the other condition (decreasing reward) the amount that could be won decreased by 10 points with each successive opening of boxes. The main measures of performance on this task were the average number of boxes opened and the probability of being correct at the point of decision [p(correct)] in each condition (see Clark et al., 2006, for further details).

2.2.4. Motor impulsivity. Motor impulsivity has been associated with addiction to drugs, particularly stimulants, in studies using the Stop-Signal Task and Go/No-go tasks (Fillmore and Rush, 2002; Monterosso et al., 2005; Verdejo-Garcia et al., 2007). Here we used a Go/No-go task in which the load on motor inhibitory processes could be manipulated by varying the number of Go stimuli preceding every No-go stimulus (based on Durston et al., 2002). In approximately half of the participants (50% of NA participants and 62.5% of A participants) the task was not administered together with the rest of the battery, but in a subsequent session. Subjects were presented with a series of yellow patterns appearing briefly on a blue background. They were asked to press a button in response to Go stimuli, but to withhold responding to an infrequent No-go stimulus. Subjects had to press a different button to signal that they had detected the presentation of No-go stimuli. A total of 336 trials included 25% No-go stimuli. Measures of performance were the probability of hits and false alarms, and the reaction times to Go and No-go stimuli. The effect of preceding context was examined by comparing the trials in which the No-go stimulus was preceded by another No-go stimulus with the trials in which No-go stimuli were preceded by one or more Go stimuli.

2.2.5. Categorical measures of performance. While it is important to demonstrate differences in neuropsychological tests scores between two groups with different likelihood of responding to treatment, the availability of a cut-off defining "unimpaired" and "impaired" performance increases the clinical value of any study on outcome. Previous literature has determined a cut-off score that appears to discriminate between substance dependent individuals and individuals without an addiction for the IGT (Bechara and Damasio, 2002). In the present study we used normative data to calculate cut-off scores (defined as mean ± 2 S.D. from the mean) also for the other tasks. These criterion scores were used to achieve two groups, "impaired" versus "unimpaired" at intake, in order to test the hypothesis that performance on each task be associated to clinical outcome. The criterion scores for unimpaired performance thus determined were: (i) a net

score of 10 or above, for the IGT (Bechara and Damasio, 2002); (ii) a quality of decision-making score of 0.897 or above, for the CGT (normative data from Rogers et al., 1999); (iii) a discounting parameter k score of 0.0523 or lower, for the DDT (normative data from Kirby and Petry, 2004); and a *p*(correct) value of 0.616, for the IST (normative data from Clark et al., 2006). For the Tower of London we used the comparison with normative data automatically performed by the CANTAB battery computer program (Cambridge Cognition Ltd.), which highlighted performance falling in the bottom 5–10% of the normal distribution. For the Go/No-go task, for which no published normative data were available, participants were divided in two groups using a median split.

2.3. Statistical analysis

Two groups of individuals, abstinent and non-abstinent from illicit drugs at 3 months, were compared in these analyses. Data for continuous variables were analysed using Student's *t*-test or repeated measures analysis of variance (ANOVA). Post-hoc analysis was carried out using the Student–Newman–Keuls test (S–N–K). Prior to ANOVA or *t*-test, data were plotted and exploratory analyses using box plots, tests of skewness and tests of homogeneity of variance were performed. Based on these preliminary analyses, skewed data, which violate the assumption of normality were subjected to arcsine, square root or logarithmic transformation as recommended by Howell (1997). The Greenhouse–Geisser Epsilon correction for degrees of freedom was used whenever appropriate (significant Mauchly's 'sphericity' test). Data for categorical variables were analysed using the Chi square test. To determine the degree to which neuropsychological performance predicted relapse a stepwise linear discriminant function analysis (F_{enter}: $p < 0.05$) was computed with non-abstinence at 3 months as the dependent measure and factors that differed across the two groups as independent measures. A cross validation procedure using a leave-1-out classification method was used to determine sensitivity and specificity of the neurocognitive measures to predict non-abstinence. Statistical analyses were conducted using the SPSS 11.0 statistical package.

3. Results

3.1. Participants

Three months into the treatment programme 10 individuals had become abstinent from illicit drugs ("Abstinent" group, A), while 24 were taking heroin at least on a weekly basis on top of their prescribed opiate medication ("Non-Abstinent" group, NA; individuals in this group had also taken on one or more occasions cocaine ($n = 14$), benzodiazepines ($n = 7$), cannabis ($n = 6$), MDMA ($n = 2$), ketamine ($n = 2$)). Three individuals who had achieved abstinence for more than 1 week, but less than two were included in the NA group. The two groups of participants had received approximately the same amount of treatment (similar numbers of keyworking sessions; in addition to these, three (11%) participants in the NA group and one (10%) in the A group also attended psychotherapy sessions). Only one participant (NA) was no longer in treatment. A and NA participants did not differ in terms of their scores on the Treatment Perception Questionnaire ($t = 1.0$, NS).

Table 2 shows the drug histories of the two groups. NA individuals tended to report having used larger amounts of heroin and for longer, although these differences were not significant. A and NA participants did not differ in terms of BDI, YMRS or BPRS scores, or in terms of the physical or psychological problem scores on the Maudsley Addiction Questionnaire ($t < 1.21$, NS). Five individuals in the NA group and one individual in the A group satisfied the criteria for alcohol dependence. It should be noted that alcohol dependence was uncommon and of mild severity in this sample, as participants were excluded from the study if at the time of testing their breath alcohol level was above zero or if they showed any clinical signs of withdrawal. One individual in the NA group and two in the A group were on prescribed buprenorphine (6-mg daily for the NA individual and 6-mg daily or 2-mg daily for the two A individuals). None of the participants was HIV positive, while in each group, approximately half had antibodies for blood borne hepatitis viruses.

Table 2
Drug histories of the abstinent and non-abstinent groups

	Abstinent ($n = 10$)	Non-abstinent ($n = 27$)	Statistic[a]
Mean years of abuse[b]	10.2 ± 1.7	15.8 ± 2.0	1.47, NS
Heroin daily amount (g)[b]	0.67 ± 0.10	0.88 ± 0.08	1.62, NS
IV:smokers	7:3	17:10	0.16, NS
Mean methadone dose[b,c]	40.0 ± 3.8	50.0 ± 3.0	1.70, $p = 0.1$
No. of cocaine dependent (%)	5 (50)	12 (44)	0.09, NS
No. of alcohol dependent (%)	1 (10)	5 (18.5)	0.39, NS
No. of tobacco smokers (%)	10 (100)	27 (100)	

[a] Independent samples Student's *t*-test or Pearson's Chi square.
[b] Mean ± S.E.M.
[c] Stabilisation dose; three participants (two A, one NA) who were prescribed buprenorphine not included.

3.2. Iowa Gambling Task

Across groups, performance on the IGT was comparable to that of drug-dependent individuals reported in previous studies (Bechara and Damasio, 2002). When the A and NA groups were compared in terms of their deck preference across four blocks of 25 trials (Fig. 1), repeated-measures ANOVA found a significant effect of block ($F(3,105) = 3.55$, $p < 0.02$). Post-hoc analysis found higher overall scores in blocks 2 and 3 compared to block 1 (S–N–K, $p < 0.05$), indicating that in this part of the session subjects developed a preference for the safe over the risky decks, as they learned about the task contingencies. There

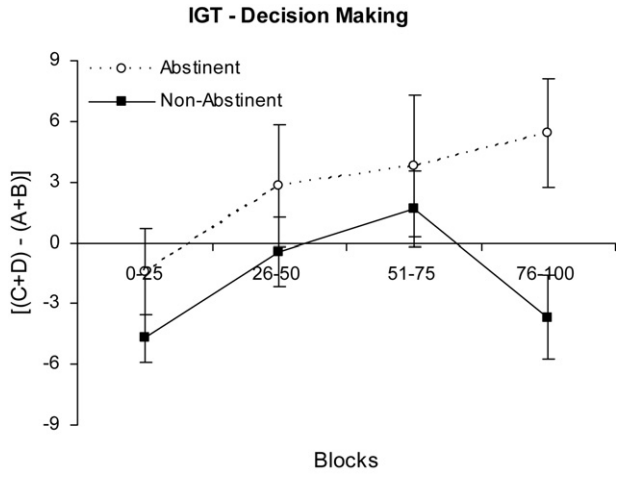

Fig. 1. Compared to individuals in the NA group, individuals in the A group tended to pick more cards from the "safe" decks (C and D) than from the "risky" decks (A and B), although this difference did not reach statistical significance.

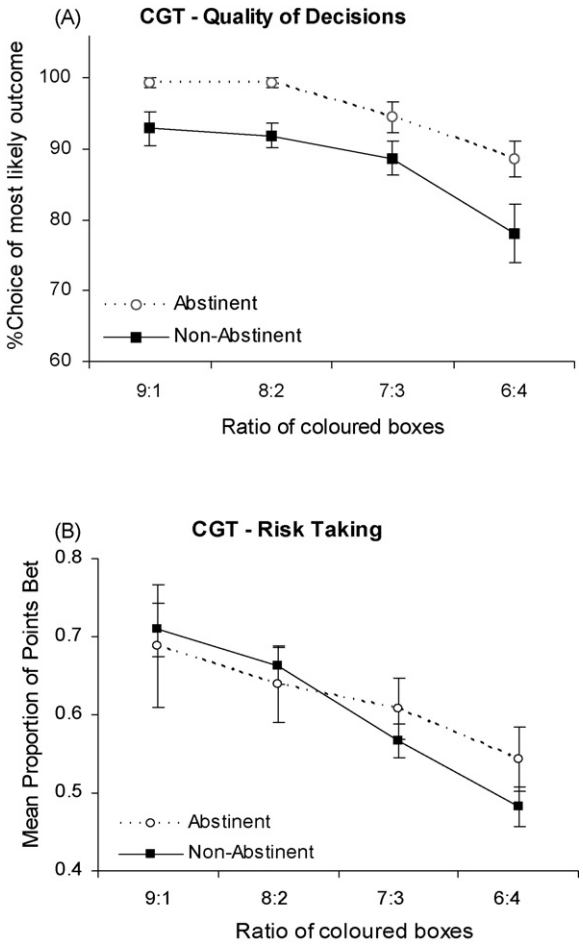

Fig. 2. Quality of decision-making (A) and risk-taking (B) across four conditions differing in the relative likelihood of two outcomes. All subjects were sensitive to decreasing likelihood of the most favourable outcome, as suggested by the reductions in the average proportion of points bet on each trial (B). However, compared to individuals in the A group, individuals in the NA group more often chose the least favourable outcome (A; $F(1,34) = 4.54$, $p < 0.05$).

was no significant main effect of group ($F(1,35) = 3.19$, $p = 0.08$) or group × block interaction ($F(3,105) = 1.44$, NS). However, using a criterion net score of 10 to define impairment (see Bechara and Damasio, 2002), individuals in the NA group were more likely to be impaired, compared to subjects in the A group (Chi square = 6.01, $p < 0.02$), suggesting that normal IGT performance was associated with abstinence from illicit drugs at 3 months.

3.3. Cambridge Gamble Task

Performance on the CGT was comparable to that of opiate users in the study by Rogers et al. (1999) both in terms of the quality of decision-making (89.8 ± 1.5% versus 92% in Rogers et al., 1999) and the decision latencies (3413 ± 225 ms in this study versus 3766 ms in Rogers et al., 1999). Fig. 2A shows the percentage of trials on which subjects chose the most likely outcome (i.e. the colour in the majority of boxes), across the different ratios of coloured boxes. There was a significant main effect of ratio ($F(2,80) = 15.90$, $p < 0.001$), as subjects chose the likely outcome more often at the greater odds. In addition, there was a main effect of group ($F(1,34) = 4.54$, $p < 0.05$), indicating that subjects in the A group more consistently chose the most likely outcome. There was no significant group x ratio interaction ($F(2,80) < 1$, NS). The two groups did not differ in terms of speed of decision-making (A = 3169 ± 389; NA = 3869 ± 449; $t = 0.9$, NS) or risk taking ($t = 0.5$, NS; Fig. 2B). To investigate whether the two groups differed in terms of the ability of each individual to withhold responding while waiting for the desired bet size to appear on the screen, we compared the overall proportion of points bet in the ascending versus descending condition. ANOVA found a robust main effect of condition ($F(1,35) = 56.18$, $p < 0.001$), but no significant main effect of group or group × condition interaction ($F(1,35) < 1$, NS), suggesting that both groups were similarly impatient when waiting for the desired bet to be offered.

When participants were divided into impaired and unimpaired based on the percentage of trials on which they chose the more likely outcome (with cut-off set at 89.7%, see Section 2), there were clear differences between the groups. All the A individuals were classified as unimpaired, but only 13 out of 27 NA individuals scored in the unimpaired range (Chi square = 8.34, $p < 0.01$).

3.4. Delay Discounting Task

Across all participants' choices, nearly 99% were consistent with the assigned discount rate, with only one participant having a mean consistency lower than 92% (this participant was excluded from the following analyses; in addition, one NA participant who chose the delayed reward for all the items was also excluded from the analyses). *K* parameters were similar to those reported previously in opiate users ($k = 0.074 \pm 0.011$ versus 0.083 in Kirby and Petry, 2004). Discount rates were not significantly different across the two groups, although NA participants tended to have higher discount rates than A participants (NA = 0.0869 ± 0.0142; A = 0.0435 ± 0.0126; $t(1,33) = 1.82$, $p = 0.078$). When discount rates at the three reward sizes were compared between the A and NA groups, ANOVA found a robust effect of reward size ($F(2,66) = 5.83$, $p < 0.01$), but no significant interaction between group and reward size ($F(2,66) < 1$, NS). Dividing participants into impaired and unimpaired (with $k = 0.0523$ as cut-off, see Section 2) yielded no evidence of association between DDT performance and clinical outcome. Whilst numerically it was more common for NA participants to score above this criterion compared to individuals in the A group (52% versus 30%), this difference was not statistically significant (Pearson's Chi square = 1.39, $p = 0.238$).

3.5. Tower of London

Data for this task were available for 26 out of 27 NA participants and 8 out of 10 A participants. There was no difference between the A and NA groups on any measure of performance of this task. A subjects solved on average 6.9 ± 0.6 and NA subjects 7.4 ± 0.4 problems in the minimum number of moves

($t(1,32) < 1$, NS). In each group, similar proportions of participants fell in the bottom 10% of the normal distribution (A = 37.5%; NA = 34.6%). Repeated-measures ANOVA found a significant effect of difficulty ($F(2,67) = 37.36$, $p < 0.001$) on initial thinking times (the time taken to plan the moves necessary to solve each problem), with all subjects taking longer to solve the difficult problems. There was no significant main effect of group ($F(1,32) < 1$, NS) or group × difficulty interaction ($F(2,67) < 1$, NS) on the initial thinking times.

3.6. Information Sampling Task

Data for this task were available for 17 out of the 27 NA participants and 10 of 10 A participants. A and NA subjects opened similar numbers of boxes in each condition (fixed reward: A = 11.3 ± 1.5; NA = 11.4 ± 1.5; decreasing reward: A = 7.2 ± 0.6; NA = 7.7 ± 0.8) and at the time of decision they were equally likely to be correct (fixed reward: A = 0.77 ± 0.03; NA = 0.76 ± 0.03; decreasing reward: A = 0.69 ± 0.01; NA = 0.69 ± 0.01). There were no significant differences for any of these measures ($t(1,25) < 1$, NS). Although most subjects had comparatively low p(correct) scores (in both groups, 80% of subjects scored below mean minus 1-SD of normal controls data from Clark et al., 2006), using a cut-off of 0.616 (mean minus 2 S.D.) only one NA subject was classified as impaired on this task and thus performance on this task did not predict clinical outcome.

3.7. Go/No-go Task

Data for this task were available for 20 out of 27 NA participants and 8 out of 10 A participants. There was no difference between A and NA subjects in terms of the probability of false alarms ($t(1,26) = 1.71$, NS) or in terms of the speed of responding to Go or No-Go stimuli ($t(1,26) < 1$, NS), suggesting that the two groups did not differ in terms of motor impulsivity, as measured by performance on this task. A participants achieved significantly more hits than NA (probability of hits, A = 0.993 ± 0.003; NA = 0.985 ± 0.003; $t(1,26) = 2.10$, $p < 0.05$), suggesting a relative deficit of sustained or selective attention in the latter group. In the analyses looking at the effect of manipulating the preceding context, ANOVA of the probability of false alarms found a significant effect of preceding context ($F(2,40) = 6.63$, $p < 0.01$), as subjects made more errors when No-go stimuli were preceded by a No-go stimulus, compared to when the No-go stimuli were preceded by one or more Go stimuli. There was no significant main effect of group ($F(1,26) < 1$, NS) or group × context interaction ($F(2,40) < 1$, NS), suggesting that the two groups of participants were similarly affected by this manipulation. ANOVA of the reaction times to No-go stimuli yielded similar results (significant main effect of preceding context, $F(1,31) = 3.25$, $p < 0.05$; no significant effect of group or group × context interaction). When participants were split into two groups based on the median for the probability of false alarms, 11 out of 20 NA participants and 2 out of 8 A participants scored in the lower half, but this difference was not significant (Pearson's Chi square = 2.07, $p = 0.150$).

Table 3
Discriminant function analysis results and cross-validation predictions[a]

	Predicted group membership, *n* (%)		Negative/positive predictive value
	Non-abstinent	Abstinent	
Original grouped cases			
Non-abstinent	24 (88.9)	4 (40.0)	0.86
Abstinent	3 (11.1)	6 (60.0)	0.67

[a] Of original grouped cases, 81.1% were correctly classified.

3.8. Relationship between neurocognitive performance and abstinence from street drugs at 3 months

In terms of predicting abstinence, for the two gambling tasks sensitivity and specificity were 60.0% and 81.5% (IGT), and 100.0% and 51.9% (CGT), respectively. The stepwise discriminant function revealed that performance on the CGT and IGT best differentiated opiate dependent individuals who were abstinent or not abstinent from illicit drugs at 3 months (Wilks $\lambda = 0.69$, Chi square = 12.54, $p < 0.01$). Table 3 presents the results of the discriminant function analysis. Cross validation analysis was able to correctly predict all 6 of the 10 original grouped cases who were abstinent at 3 months and all 24 of the 27 who were not (60% sensitivity; 89% specificity).

4. Discussion

4.1. Decision-making and clinical outcome

The main result of the present study is that performance on two tasks of affective decision-making, the CGT and IGT, predicted clinical outcome in a group of drug users undergoing community drug treatment. Thus, most of the participants who were abstinent from illicit drugs at 3 months, but only three of those who were not, scored above the criteria for impairment on both tasks. This finding suggests that after deciding to undergo treatment for drug dependence, intact decision-making processes may be crucial to achieve and maintain abstinence, at least in the short term. These differences were specific to decision-making processes, as the two groups did not differ in estimated IQ or on measures of planning, delay discounting, reflection impulsivity or motor impulsivity. These results are in keeping with previous studies suggesting a correlation between activation of neural networks involved in decision-making and likelihood of relapse after drug treatment (Paulus et al., 2005). Both CGT and IGT are associated with the functional integrity of the orbitofrontal cortex, a region that is integral to these networks and that has been widely implicated in neurobiological models of the breakdown of self-control processes in drug addiction (Goldstein and Volkow, 2002).

The most striking differences between the individuals with good and poor short-term outcome were found on the CGT. In contrast to the IGT, this task does not require participants to learn about task contingencies in order to guide behaviour, as the parameters for each decision are presented on the screen on each trial (Rogers et al., 1999; Clark et al., 2004). In addition, perfor-

mance on the CGT depends less on working memory processes (Bechara and Martin, 2004; Clark et al., 2004) and reversal learning (Fellows and Farah, 2005). Participants with poor short-term outcome were less likely than those with good clinical outcome to choose the favourable option (i.e. the box colour in the majority) on each trial. It is unlikely that NA individuals did so because of impaired comprehension of the task or because they were too hasty in making their selection. NA and A subjects both showed a subtle effect of ratio on quality of decision-making (Fig. 2A), and comparable tendency to reduce their bets as the ratio of boxes became less favourable (Fig. 2B). Taken together, these features suggest that NA subjects understood as well as individuals in the A group that incorrect decisions would lead to point deduction. In addition, A and NA subjects showed comparable latencies to make their red–blue decision and comparable tendency to bet higher proportions of their accumulated points in the descending compared to ascending condition, suggesting that their behaviour was not differentially affected by impulsivity. This is also supported by performance on the Go/No-go task and Information Sampling Task, which showed no evidence of differential impulsivity in the NA group compared to the A subjects. Thus, the difference between the performance of NA and A participants on the CGT appears to relate directly to affective decision-making, for example to faulty processing of reward or punishment cues (Bechara et al., 2002; Rogers et al., 2003, 2004) or to a detrimental effect of negative feedback received on preceding trials (Ersche et al., 2005).

The groups of A and NA participants did not differ in their performance on another decision-making task on which opiate dependent individuals tend to perform differently from controls, the Delay Discounting Task. It is possible that this negative finding reflected insufficient power of the test to detect the deficits associated with poor short-term outcome. However, it is also plausible that among the decision-making tasks used in this study, the gambling tasks were better suited to capture such neurocognitive changes. The Delay Discounting Task requires a comparison of different rewards across different delay periods. Unlike the gambling tasks, the Delay Discounting Task does not require the evaluation of trade-offs between uncertain rewards and punishments. The inclusion of punishment (lost outcomes) in the gambling tasks may increase their ecological validity to the kinds of decisions faced by drug users, and may underlie their superior association with short-term abstinence in the present data.

A and NA individuals did not differ in terms of the probability of false alarms in the Go/No-go task, suggesting that motor impulsivity is also unrelated to clinical outcome. The manipulation of preceding context in the Go/No-go task affected performance in both groups of participants, suggesting that the lack of effect was not simply explained by a "floor" effect. However, since in half of our cohort the task was administered closer to follow-up than the rest of the battery, these results remain inconclusive as to the potential role of motor inhibition deficits in processes leading to achieving and maintaining abstinence. A subjects stopped using illicit drugs shortly after the initial assessment, while NA subjects did not, and thus it is possible that at the time of testing with the Go/No-go task performance of some NA subjects was affected by continued use of illicit drugs. Recent drug taking may also explain the finding of marginally more accurate detection of Go stimuli in the A group, compared to NA subjects.

4.2. Neurocognitive performance as outcome predictor

The identification of outcome predictors is an area of research that has potentially important implications for clinical practice. While there is a wide array of treatment options available to individuals seeking help with their addiction, including pharmacological (methadone maintenance, methadone reduction, buprenorphine reduction, etc.) and psychological (12 steps facilitation, cognitive behavioural interventions, motivational interviewing, etc.) approaches, as well as a variety of treatment environments (community treatment, day programmes, residential programmes, etc.), there is currently no evidence-based method for choosing the most appropriate options for each individual. In addition, there is controversy over what aspects of treatment are most strongly associated with treatment response (Gossop et al., 2003). Previous studies seeking to identify predictors of outcome in drug addiction have looked at factors such as gender, ethnicity, psychiatric comorbidity, severity of addiction, readiness to change, social network and personality features (Filstead et al., 1983; Rounsaville et al., 1986; Hser et al., 1990; Saxon et al., 1996; Miller et al., 1997; Alterman et al., 1998, 2000; Harrison and Asche, 1999; Pettinati et al., 1999). Although this research has identified a range of risk factors for relapse or poor engagement with treatment, none has proved sufficiently robust to inform management strategies. We believe that the emphasis on neurocognitive factors might be more fruitful, in terms of its potential for identifying clinically useful predictors of outcome.

In addition to decision-making differences, A and NA subjects may also have differed in some other respects, in line with previous research on outcome predictors. For example, NA individuals tended to have more complex and severe drug histories (Table 2) and more deprived backgrounds, e.g. spending fewer years in education (Table 1). However, none of these differences reached statistical significance, suggesting that in isolation these were less robust predictors of clinical outcome. Individuals with good and poor short-term outcome might have also differed in terms of a more general disturbance of behaviour, emotion and thinking such as it is normally described by the notion of abnormal personality. In this study, we did not include direct measures of personality, such as borderline or antisocial personality traits. However, it is unlikely that antisocial or borderline personality disorder measures might be preferable to decision-making measures as predictors of clinical outcome. Diagnosing these personality disorders requires the demonstration of features such as impulsivity, affective instability and difficulties in interpersonal problems (APA, 1994), which are difficult to establish reliably and objectively, and more importantly are all affected by substance misuse (see discussion of co-morbidity in Trull et al., 2000). Thus, a wide range of prevalence figures of these disorders has been reported in the addiction literature (e.g. 11–65% for borderline personality disorder and 28–71%

for antisocial personality disorder, see Trull et al., 2000; Grant et al., 2004; Darke et al., 2004) and research on the outcome prediction validity of personality disorder has included approximately as many studies supporting its value (Woody et al., 1985; Alterman and Cacciola, 1991; Alterman et al., 1998), as those refuting it (Carroll et al., 1994; Cacciola et al., 1995; McKay et al., 1998; Darke et al., 2004), at least when abstinence from illicit drugs is the outcome of interest.

Several previous studies have supported the possibility that neuropsychological mechanisms contribute to clinical outcome in addiction psychiatry (McCrady and Smith, 1986; Fals-Stewart and Schafer, 1992; Teichner et al., 2001; Bowden-Jones et al., 2005; Paulus et al., 2005; Aharanovich et al., 2006). Extending those previous findings, the present study identified criteria for predicting clinical outcome in the early stages of treatment. This is an important aspect of treatment, because research suggests that the largest drop-out from treatment tends to be early on (Simpson and Joe, 1993) and that early engagement is a predictor of later engagement (e.g. Gossop et al., 2003). Neurocognitive measures could be usefully added to the range of clinical information that is collected during the initial assessment of drug users presenting to treatment, to inform treatment planning. Together with other clinical measures, these tools may be thus used to identify individuals who might require some form of specific cognitive rehabilitation. In addition, since treatment options for opiate dependence vary widely in cost and intensity, these tools could be used to ensure that the more expensive treatments are reserved to those individuals who are most likely to benefit from them. In the UK, where publicly-funded residential rehabilitation programmes are gradually disappearing (NTORS, 2001), this approach if successful might help retain a treatment option that may benefit greatly particular individuals.

The present study has begun to investigate the potential of neuropsychological measures as clinically useful predictors of early outcome in a group of opiate dependent poly-drug users treated at an inner city community treatment centre (not unlike the population described in National Treatment Outcome Research Study, see NTORS, 2001; our sample was more likely to be homeless and less likely to be alcohol dependent). A limitation of the study was that all participants were treated within a single treatment modality, a low-intensity community treatment. In addition, the context of the study did not permit controlling for environmental variables that may have exerted their influence outside the clinic (the variability in the time required to become stabilised on substitute opiate prescription suggests that our cohort might have been heterogeneous in terms of some of these influences). In future studies, we will aim to extend these findings to more selected subgroups of drug users (e.g. for age of onset of drug problems and for illicit substances used) and to other clinical settings, including inpatient, residential rehabilitation and intensive community treatment programmes.

Conflict of interest

LC is a consultant for Cambridge Cognition. There are no conflicts of interest for any of the other authors.

Acknowledgements

The authors would like to thank Professors Kris Kirby and Antoine Bechara for supplying the Delay Discounting and Iowa Gambling Tasks, Dr Paul Davis for help with setting up the project at the Margarete Centre, Dr Robert Blizard for his suggestions on statistical analyses and Mr Jeff Dalton for developing the program for the Go/No-Go Task.

Role of funding source: Funding for this study was provided by the North Central London Research consortium (NoCLoR) and by University College London (UCL); neither organisation had any further role in study design; in the collection, analysis and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

Contributors: FP, MK and EJ designed the study and wrote the protocol. FP collected the data, undertook the statistical analysis and wrote the first draft of the manuscript, including his summary of previous related work. LC and MAM provided two of the neuropsychological tasks and were advisers on the interpretation of the findings from these tests. All authors contributed to and have approved the final manuscript.

References

Aharanovich, E., Hasin, D.S., Brooks, A.C., Liu, X., Bisaga, A., Nunes, E.V., 2006. Cognitive deficits predict low treatment retention in cocaine dependent patients. Drug Alcohol Depend. 81, 313–322.

Alterman, A.I., Cacciola, J.S., 1991. The antisocial personality disorder diagnosis in substance abusers: problems and issues. J. Nerv. Ment. Dis. 179, 401–409.

Alterman, A.I., Rutherford, M.J., Cacciola, J.S., McKay, J.R., Boardman, C.R., 1998. Prediction of 7 months methadone maintenance treatment response by four measures of antisociality. Drug Alcohol Depend. 49, 217–223.

Alterman, A.I., McKay, J.R., Mulvaney, F.D., Cnaan, A., Cacciola, J.S., Tourian, K.A., Rutherford, M.J., Merikle, E.P., 2000. Baseline prediction of 7-month cocaine abstinence for cocaine dependence patients. Drug Alcohol Depend. 59, 215–221.

American Psychiatric Association (APA), 1994. Diagnostic and statistical manual of mental disorders, fourth ed. DSM-IV. American Psychiatric Association, Washington, DC.

Bechara, A., 2005. Decision making, impulse control and loss of willpower to resist drugs: a neurocognitive perspective. Nat. Neurosci. 8 (11), 1458–1463.

Bechara, A., Damasio, H., 2002. Decision-making and addiction (part I): impaired activation of somatic states in substance dependent individuals when pondering decisions with negative future consequences. Neuropsychologia 40, 1675–1689.

Bechara, A., Dolan, S., Hindes, A., 2002. Decision-making and addiction (part II): myopia for the future or hypersensitivity to reward? Neuropsychologia 40, 1690–1705.

Bechara, A., Martin, E.M., 2004. Impaired decision making related to working memory deficits in individuals with substance addictions. Neuropsychology 18 (1), 152–162.

Bowden-Jones, H., McPhillips, M., Rogers, R., Hutton, S., Joyce, E., 2005. Risk-taking on tests sensitive to ventromedial prefrontal cortex dysfunction predicts early relapse in alcohol dependency: a pilot study. J. Neuropsychiatry Clin. Neurosci. 17 (3), 417–420.

Cacciola, J.S., Alterman, A.I., Rutherford, M.J., Snider, E.C., 1995. Treatment response and problem severity of antisocial personality substance abusers. J. Nerv. Ment. Dis. 183, 166–171.

Carroll, K.M., Rounsaville, B.J., Gordon, L., Nich, C., Jatlow, P., Bisighini, R.M., Gawin, F.H., 1994. Psychotherapy and pharmacotherapy for ambulatory cocaine abusers. Arch. Gen. Psychiatry 51, 177–187.

Clark, L., Robbins, T.W., 2003. Decision making deficits in drug addiction. Trends Cogn. Sci. 6 (9), 361–363.

Clark, L., Cools, R., Robbins, T.W., 2004. The neuropsychology of ventral prefrontal cortex: decision-making and reversal learning. Brain Cogn. 55, 41–53.

Clark, L., Robbins, T.W., Ersche, K.D., Sahakian, B.J., 2006. Reflection impulsivity in current and former substance users. Biol. Psychiatry 60, 515–522.

Darke, S., Ross, J., Williamson, A., Teesson, M., 2004. The impact of borderline personality disorder on 12-month outcomes for the treatment of heroin dependence. Addiction 100, 1121–1130.

Darke, S., Ross, J., Teesson, M., Ali, R., Cooke, R., Ritter, A., Lynskey, M., 2005. Factors associated with 12 months continuous heroin abstinence: findings from the Australian Treatment Outcome Study (ATOS). J. Subst. Abuse Treatm. 28, 255–263.

Durston, S., Thomas, K.N., Worden, M.S., Yang, Y., Casey, B.J., 2002. The effect of preceding context on inhibition: an event-related fMRI study. NeuroImage 16, 449–453.

Ersche, K.D., Roiser, J.P., Clark, L., London, M., Robbins, T.W., Sahakian, B.J., 2005. Punishment induces risky decision-making in methadone-maintained opiate users but not in heroin users or healthy volunteers. Neuropsychopharmacology 30, 2115–2124.

Ersche, K.D., Clark, L., London, M., Robbins, T.W., Sahakian, B.J., 2006. Profile of executive and memory function associated with amphetamine and opiate dependence. Neuropsychopharmacology 31 (5), 1036–1047.

Evenden, J.L., 1999. Varieties of impulsivity. Psychopharmacology (Berl.) 146, 348–361.

Fals-Stewart, W., Schafer, J., 1992. The relationship between neurocognitive functioning and length of stay in drug-free therapeutic communities. J. Clin. Psychol. 48, 539–543.

Fellows, L.K., Farah, M.J., 2005. Different underlying impairments in decision-making following ventromedial and dorsolateral frontal lobe damage in humans. Cereb. Cortex 15 (1), 58–63.

Fillmore, M.T., Rush, C.R., 2002. Impaired inhibitory control of behavior in chronic cocaine users. Drug Alcohol Depend. 66 (3), 265–273.

Filstead, W.J., Drachman, D.A., Rossi, J.J., Getsinger, S.A., 1983. The relationship of MMPI subtype membership to demographic variables and treatment outcome among substance misusers. J. Stud. Alcohol 44 (5), 917–922.

Flynn, P.M., Joe, G.W., Broome, K.M., Simpson, D.D., Brown, B.S., 2003. Recovery from opioid addiction in DATOS. J. Subst. Abuse Treatm. 25, 177–186.

Goldstein, R.Z., Volkow, N., 2002. Drug addiction and its underlying neurobiological basis: neuroimaging evidence for the involvement of the frontal cortex. Am. J. Psychiatry 159, 1642–1652.

Gossop, M., Marsden, J., Stewart, D., Rolfe, A., 1999. Treatment retention and 1 year outcomes for residential programmes in England. Drug Alcohol Depend. 57, 89–98.

Gossop, M., Marsden, J., Stewart, D., Rolfe, A., 2000a. Patterns of improvement after methadone treatment: 1-year follow-up results from the National Treatment Outcome Research Study (NTORS). Drug Alcohol Depend. 60, 275–286.

Gossop, M., Marsden, J., Stewart, D., Rolfe, A., 2000b. Reductions in acquisitive crime and drug use after treatment of addiction problems: 1-year follow-up outcomes. Drug Alcohol Depend. 58, 165–172.

Gossop, M., Stewart, D., Marsden, J., 2003. Treatment process component and heroin use outcome among methadone patients. Drug Alcohol Depend. 71, 93–102.

Grant, B.F., Stinson, F.S., Dawson, D.A., Chou, P., Ruan, W.J., Pickering, R.P., 2004. Co-occurrence of 12-month alcohol and drug use disorders and personality disorders in the United States. Arch. Gen. Psychiatry 61, 361–368.

Harrison, P.A., Asche, S.E., 1999. Comparison of substance abuse treatment outcomes for inpatients and outpatients. J. Subst. Abuse Treatm. 17 (3), 207–220.

Howell, D.C., 1997. Statistical Methods for Psychology, fourth ed. Duxbury Press, London.

Hser, Y.I., Anglin, M.D., Liu, Y., 1990. A survival analysis of gender and ethnic differences in responsiveness to methadone maintenance treatment. Int. J. Addict. 25 (11A), 1295–1315.

Hser, Y., Grella, C.E., Hsieh, S., Anglin, M.D., Brown, B., 1999. Prior treatment experience related to process and outcomes in DATOS. Drug Alcohol Depend. 57, 137–150.

Hser, Y., Hoffman, V., Grella, C., Anglin, M.D., 2001. A 33-year follow-up of narcotic addicts. Arch. Gen. Psychiatry 58, 503–508.

Hubbard, R.L., Craddock, S.G., Flynn, P.M., Anderson, J., Etheridge, R.M., 1997. Overview of one year follow-up outcomes in the Drug Abuse Treatment Outcome Study (DATOS). Psychol. Addict. Behav. 11, 261–278.

Joe, G.W., Broome, K.M., Simpson, D.D., 1999. Retention and patient engagement in models for different treatment modalities in DATOS. Drug Alcohol Depend. 57, 113–125.

Kagan, J., 1966. Reflection–impulsivity: the generality and dynamics of conceptual tempo. J. Abnorm. Psychol. 71 (1), 17–24.

Kirby, K.N., Petry, N.M., 2004. Heroin and cocaine abusers have higher discount rates for delayed rewards than alcoholics or non-drug-using controls. Addiction 99 (4), 461–471.

Kirby, K.N., Petry, N.M., Bickel, W.K., 1999. Heroin addicts have higher discount rates for delayed rewards than non-drug-using controls. J. Exp. Psychol. Gen. 128 (1), 78–87.

Marsden, J., Bacchus, L., Stewart, D., Griffiths, P., Clarke, K., Gossop, M., Strang, J., 1998. The Treatment Perceptions Questionnaire (TPQ): a brief questionnaire for assessing service satisfaction, Unpublished manuscript. National Addiction Centre, London.

Marsden, J., Gossop, M., Stewart, D., Best, D., Farrell, M., Lehmann, P., Edwards, C., Strang, J., 1999. The Maudsley Addiction Profile (MAP): a brief instrument for assessing treatment outcome. Addiction 93 (12), 1857–1867.

McCrady, B.S., Smith, D.E., 1986. Implications of cognitive impairment for the treatment of alcoholism. Alcohol Clin. Exp. Res. 10, 145–149.

McKay, J.R., Alterman, A.I., Cacciola, J.S., Rutherford, M.R., O'Brien, C.P., Koppenhaver, J., 1998. A comparison of group counseling vs. individualized relapse prevention aftercare following intensive outpatient treatment for cocaine dependence: initial results. J. Consul. Clin. Psychol. 65, 778–788.

Miller, N.S., Ninonuevo, F., Hoffman, N.G., Astrachan, B.M., 1997. Prediction of treatment outcomes: lifetime depression versus the continuum of care. Am. J. Addict. 8 (3), 243–253.

Monterosso, J.R., Ehrman, R., Napier, K.L., O'Brien, C.P., Childress, A.R., 2001. Three decision-making tasks in cocaine-dependent patients: do they measure the same construct? Addiction 96, 1825–1837.

Monterosso, J.R., Aron, A.R., Cordova, X., Xu, J., London, E.D., 2005. Deficits in response inhibition associated with chronic methamphetamine abuse. Drug Alcohol Depend. 79 (2), 273–277.

NTORS after five years (National Treatment Outcome Research Study), 2001. Changes in substance use, health and criminal behaviour in the five years after intake. Department of Health.

Ornstein, T.J., Iddon, J.L., Baldacchino, A.M., Sahakian, B.J., London, M., Everitt, B.J., Robbins, T.W., 2000. Profiles of cognitive dysfunction in chronic amphetamine and heroin abusers. Neuropsychopharmacology 23, 113–126.

Owen, A.M., Downes, J.J., Sahakian, B.J., Polkey, C.E., Robbins, T.W., 1990. Planning and spatial working memory following frontal lobe lesions in man. Neuropsychologia 28 (10), 1021–1034.

Owen, A.M., Sahakian, B.J., Semple, J., Polkey, C.E., Robbins, T.W., 1995. Visuo-spatial short-term recognition memory and learning after temporal lobe excisions, frontal lobe excisions or amygdalo-hippocampectomy in man. Neuropsychologia 33 (1), 1–24.

Paulus, M.P., Tapert, S.F., Schuckit, M.A., 2005. Neural activation patterns of methamphetamine-dependent subjects during decision making predict relapse. Arch. Gen. Psychiatry 62 (7), 761–768.

Pettinati, H.M., Pierce Jr., J.D., Belden, P.P., Meyers, K., 1999. The relationship of Axis II personality disorders to other known predictors of addiction treatment outcome. Am. J. Addict. 8 (2), 136–147.

Quirk, A., Lilly, R., Rhodes, T., Stimson, G., 2004. Negotiating a script: the dynamics of staff/client relationships. In: Tober, G., Strang, J. (Eds.), Methadone Matters. Martin Dunitz, London.

Rogers, R.D., Robbins, T.W., 2001. Investigating the neurocognitive deficits associated with chronic drug misuse. Curr. Opin. Neurobiol. 11 (2), 250–257.

Rogers, R.D., Everitt, B.J., Baldacchino, A.M., Blackshaw, A.J., Swainson, R., Wynne, K., Baker, N.B., Hunter, J., Carthy, T., Booker, E., London, M., Deakin, J.F.W., Sahakian, B.J., Robbins, T.W., 1999. Dissociable deficits in the decision-making cognition of chronic amphetamine abusers, opiate abusers, patients with focal damage to prefrontal cortex, and tryptophan-depleted normal volunteers: evidence for monoaminergic mechanisms. Neuropsychopharmacology 20 (4), 322–339.

Rogers, R.D., Tunbridge, E.M., Bhagwagar, Z., Drevets, W.C., Sahakian, B.J., Carter, C.S., 2003. Tryptophan depletion alters the decision-making of healthy volunteers through altered processing of reward cues. Neuropsychopharmacology 28 (1), 153–162.

Rogers, R.D., Lancaster, M., Wakeley, J., Bhagwagar, Z., 2004. Effects of beta-adrenoceptor blockade on components of human decision-making. Psychopharmacology 172, 157–164.

Rounsaville, B.J., Kosten, T.R., Weissman, M.M., Kleber, H.D., 1986. Prognostic significance of psychopathology in treated opiate addicts. A 2.5-year follow-up study. Arch. Gen. Psychiatry 43 (8), 739–745.

Saxon, A.J., Wells, E.A., Fleming, C., Jackson, T.R., Calsyn, D.A., 1996. Pretreatment characteristics, program philosophy and level of ancillary services as predictors of methadone maintenance treatment outcome. Addiction 91 (8), 1197–1209.

Sheehan, M., Oppenheimer, E., Taylor, C., 1993. Opiate users and the first years after treatment: outcome analysis of the proportion of follow-up time spent in abstinence. Addiction 88, 1679–1689.

Simpson, D.D., Joe, G.W., 1993. Motivation as a predictor of early dropout from drug abuse treatment. Psychotherapy 30, 357–368.

Teichner, G., Horner, M.D., Harvey, R.T., 2001. Neuropsychological predictors of attainment of treatment objectives in substance abuse patients. Int. J. Neurosci. 106, 253–263.

Trull, T.J., Sher, K.J., Minks-Brown, C., Durbin, J., Burr, R., 2000. Borderline personality disorder and substance use disorders: a review and integration. Clin. Psychol. Rev. 20 (2), 235–253.

Verdejo-Garcia, A.J., Perales, J.C., Perez-Garcia, M., 2007. Cognitive impulsivity in cocaine and heroin polysubstance abusers. Addict. Behav. 32 (5), 950–966.

Wechsler, D., 2001. Wechsler Test of Adult Reading (WTAR^{uk}). Adapted for UK use. The Psychological Corporation (Harcourt Assessment), London.

Woody, G., McLellan, A.T., Luborsky, L., O'Brien, C.P., 1985. Sociopathy and psychotherapy outcome. Arch. Gen. Psychiatry 42, 1081–1086.

Young, R.C., Biggs, J.T., Ziegler, V.E., et al., 1978. A rating scale for mania: reliability, validity and sensitivity. Br. J. Psych. 133, 429–435.