Semantic Priming and Verbal Learning in Current Opiate Users, Ex-users and Controls

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To my mum and dad

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Overview

This thesis concerns how memory processes and biases may be implicated in substance dependence. The literature review begins by outlining different models of drug dependence and research into cognitive function in addiction. It then outlines the structure of long-term memory, before reviewing and discussing the implications of the limited evidence available for cognitive biases operating in semantic and episodic memory of individuals who are addicted. The review ends by discussing implications for future research and by suggesting additional paradigms that could be used to further investigate the role of memory in addiction. The empirical paper describes a study which investigated semantic priming and verbal learning in current opiate users on a methadone maintenance programme, ex opiate-users in rehabilitation and healthy non-using controls. It is one part of a joint project, the other part having been carried out by a fellow clinical psychology trainee who investigated response inhibition in the same sample population. Both current and ex-users showed preserved semantic priming. Ex-users showed a verbal learning impairment compared with controls, whilst both current and ex-users showed impairment in recalling semantically unrelated words, but intact recall of semantically related words. This may suggest a relative impairment in the ability of opiate users and ex-users to impose structure to unstructured information (e.g. use of mnemonic strategies) and a greater reliance on semantic memory when encoding new information. Providing opiate using clients with highly structured information may be beneficial to intervention. The critical appraisal gives a reflective account of the research process, the study and the treatment implications of the findings.

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Part 1: Literature Review

Episodic and Semantic Memory Biases in Substance Dependence

Abstract

This review aims to outline the importance of memory biases in substance dependence. Models of drug dependence have highlighted memory as being an important component in compulsive drug taking. Despite this, research has focused less on memory than it has on other areas of cognition. Studies looking at semantic memory biases have used methods that tap implicit semantic memory (e.g. semantic priming and other memory association paradigms) and the few studies that looked at episodic memory biases (only in alcohol misuse) have tended to use incidental learning tasks and free recall. The findings of these studies indicate that both semantic and episodic memory in addicts may be biased towards activation of drug concepts by drug cues. Methodological limitations are considered and implications for future research outlined.

Relevant articles included in the present literature review were identified by cross-searching a number of databases generated using MetaLib, a service available to members of UCL, and by hand searching the reference section of journal articles. Databases searched included EMBASE, MEDLINE, Journals@OVID, PsycINFO and PubMed. Terms searched were memory, memory biases, cognitive biases, addiction, drugs, drug dependency, substance abuse.

1. Introduction

Drug and alcohol problems are influenced by a wide range of social, psychological and biological factors. The term 'dependence' was introduced as an alternative to 'addiction' by the WHO in 1964. It attempted to distinguish between the physical and psychological components of dependence, although these tend to be linked in such a way that it is difficult to differentiate between them (Lindsay & Powell, 1987).

People may initially decide to use drugs or alcohol to enhance their mood or because of peer group pressures. However, after repeated use, many substances lead to dependence and addiction. The DSM-IV (American Psychiatric Association, 1994) describes substance dependence as being characterised by continuous use despite the awareness of the long-term negative consequences, repeated attempts to cut back or quit substance use, and a gradual increase in substance intake over time.

The present review outlines some of the models of drug dependence that have been proposed to date. It will then focus more closely on how memory processes may be directly implicated in substance dependence and, after outlining the structure of long-

term memory, it will present the available evidence for cognitive biases operating in semantic and episodic memory of individuals who are addicted.

2. Models of Drug Dependence

Different models of drug dependence have been proposed by different theorists, and below is an outline of some of the most influential cognitive and behavioural perspectives. These models tend to highlight and emphasize different mechanisms as being important in the aetiology and maintenance of substance addiction.

2.1 Conditioning Models

Conditioning theories involve both classical and operant conditioning as mechanisms leading to drug dependence.

In classical conditioning theory, drug 'cues' (people, places, drug paraphernalia) become conditioned stimuli, i.e. have become associated with the direct unconditioned effects of the drug, and come to evoke conditioned responses similar to the unconditioned effect of the drug (e.g. physiological arousal, drug craving, drug seeking) (Drummond, 2000).

In operant conditioning theory, an individual learns through repeated experience that a particular behavioural response has predictable effects on a specific goal (e.g. obtaining a drug), and therefore is more likely to repeat the response again. Responses followed by a reward are strengthened whereas those followed by no reward or punishment are weakened. 'Reinforcement' is an operant conditioning process that involves the consistent presentation of a stimulus (positive reinforcer) or the consistent removal of a

stimulus (negative reinforcer) contingent upon a particular response, which then tends to increase the probability that the response/behaviour will be repeated. Using a drug to experience its pleasurable reward or to alleviate negative symptoms of craving and withdrawal are examples of positive and negative reinforcement, and are the basis of the Opponent Process theory of addiction proposed by Solomon and Corbit (1973).

According to conditioning models of addiction, substance misuse is, therefore, seen as originating from learned or 'conditioned' behaviours, and craving and other withdrawal symptoms are seen as central to relapse. Conditioning models are helpful in explaining how the strong rewarding properties of a drug and the repeated pairing of drug use with particular objects, places and people may lead to drug taking and relapse. The models have, however, been criticised for adopting a reductionist stance to the development of drug addiction, by focusing on individuals acquiring behavioural habits purely through conditioning and reinforcement and without considering how cognitions (thoughts and beliefs) may also contribute to shaping a person's behaviour.

In response to these limitations, cognitive theories of addiction emphasize how thoughts and beliefs about the self and one's ability to resist drug use are activated by internal (e.g. feelings and body symptoms) and/or external cues (stimuli associated with the drug), leading to cravings for the drug. They maintain that although conditioning contributes to compulsive drug taking, it is not the only process involved in addiction.

2.2 *Tiffany's Cognitive Model*

Tiffany's cognitive model of drug and alcohol urges (Tiffany, 1990; Tiffany & Conklin, 2000) suggests that there is weak support for the assumption that craving is directly responsible for drug use (drug craving and consumption are only weakly associated). According to the model, addictive drug use is regulated by automatic processes, whereas craving is regulated by non-automatic processes. These non-automatic processes are activated and lead to craving when automatic drug-seeking and drug-using behaviours are obstructed (i.e. when the drug is desired but it is not available). According to the model, craving refers to the activation of non-automatic processes to resolve the problem, thus these processes are more likely to represent cognitive and behavioural demands of the problem solving situation than they are to represent classically or operant conditioned responses.

2.3 *Robinson and Berridge's Incentive-Sensitization Model*

In their incentive-sensitization theory of addiction, Robinson and Berridge (2003, 2004) also suggest that craving is independent of reinforcement. Their model however explains cravings in terms of motivation. The model focuses on how drug cues trigger excessive incentive motivation for drugs, leading to compulsive drug seeking and drug taking, and to relapse. Robinson and Berridge argue that drug seeking can, and often does, occur in the absence of craving. The central idea of the theory is that addictive drugs share the ability to sensitize (render hypersensitive) brain systems involved in the process of incentive motivation and reward. Conditioning processes lead to excessive attribution of incentive salience (prominence) to drug effects and drug-related stimuli, causing pathological "wanting" to take drugs. Incentive salience (drug "wanting") is however

distinguished from the conscious experience of reward (drug "liking"/craving). The model suggests that the increase in sensitized drug "wanting" occurs outside of conscious awareness and independently of any conscious "liking" of the drug, thus predicting that drug taking may occur without verbally expressed or consciously experienced drug "liking" or craving. Activation of this system may constitute an implicit rather than an explicit psychological process, and reflect an unconscious motivational process. According to the model, a person becomes aware of this activation only by engaging in interpretive cognitive processes, which are needed to translate implicit activation into explicit subjective feelings of drug craving and drug "liking".

Compared to behavioural models, cognitive theories of addiction offer a more sophisticated understanding of compulsive drug use, as they integrate additional perspectives by incorporating craving within a network of cognitive processes that, as they inter-relate, influence drug use and relapse.

3. Addiction and Memory

Building on these ideas, models of drug addiction which more explicitly attempt to highlight the interrelationship of different cognitive processes and their corresponding neural circuits have been recently proposed. For example, the behavioural and cognitive models of drug addiction described above do not explicitly allocate an important role to attention and memory processing of drug-related stimuli in actual drug use, although they all indirectly implicate their influence in compulsive substance use.

Neurobiological accounts of addiction have been proposed, however, which place a significant emphasis on how frequent drug use may change neural circuits involved in memory, therefore suggesting that memory processes are essential to explaining changes in behaviour produced by addictive drugs (e.g. Berke & Hyman, 2000; Nestler, 2001, 2002; White, 1996).

3.1 Volkow, Fowler and Wang's Model

Volkow, Fowler and Wang (2003) propose a model which explicitly incorporates a memory component to explain compulsive drug intake seen in dependence, and which integrates evidence from their own imaging studies. The model comprises four neural networks, all of them modulated by drugs of abuse. These include brain circuits of reward (including the nucleus accumbens and ventral pallidum), motivation and drive (including the orbitofrontal cortex and subcallosal cortex), memory and learning (including the amygdala and hippocampus) and control (including the prefrontal cortex and anterior cingulate gyrus). In drug dependence, the value of drug and drug-related stimuli is enhanced at the expense of other reinforcers. This is a consequence of both conditioned learning and of the resetting of reward thresholds as an adaptation to the high levels of brain-reward pathway stimulation induced by drugs of abuse. During exposure to the drug or drug-related cues, the memory of the expected reward results in over-activation of the reward and motivation circuits while decreasing the activity in the cognitive control circuit.

The model proposes that the pattern of activity in the four-circuit network influences how an individual makes choices among behavioural alternatives (see Figure 1). These choices are influenced systematically by the reward, memory, motivation and control circuits:

- The response to a stimulus is affected by its momentary salience i.e. expected reward.
- If the individual has been previously exposed to the stimulus, its saliency value is affected by memory. Memories are stored as associations between the stimulus and the positive/pleasant or negative/aversive experience it previously elicited.
- The value of the stimulus is weighted against that of other alternative stimuli and changes as a function of the internal needs of the individual (motivation/drive). The stronger the saliency value of the stimulus (which is in part conveyed by the prediction of reward from previously memorised experiences), the greater the activation of the motivational circuit and the stronger the drive to procure it.
- The decision to act or not to act to procure the stimulus is processed in part by the prefrontal cortex and the cingulate gyrus (control).

Non-dependent brain *Drug-dependent brain*

Figure 1: Model of the four circuits supposedly involved with addiction and how their pattern of activity changes from non-dependency to dependency (adapted from Volkow et al., 2003).

Patterns of activity in this four-circuit network may be at the core of behavioural choice. During addiction, it is suggested that greater activity in the dopamine-regulated reward circuit and the motivational/drive and memory circuits overcomes the inhibitory control normally exerted by the prefrontal cortex, resulting in compulsive drug taking. This is depicted in Figure 1 showing strength of connectivity between the four factors in a non-dependent and a drug-dependent brain. Volkow et al. (2003) propose that the decision to take a drug will depend on the expected positive feelings (the reward) to be had from taking it, which in turn will be affected by previous knowledge and memories, as well as a person's internal needs or motivation.

3.2 Addiction Research

Despite the potential significance of memory processes in addictive behaviours, research into the cognitive, as opposed to physiological, components of addiction has focused primarily in the areas of decision making and reward, reinforcement and impulsivity, attentional bias and impairments in cognitive functions in addiction (mostly in executive functions but including some research on impairments in memory).

Neuroeconomics research (which brings together the disciplines of neuroscience, economics and psychology to examine brain function in decision making) has distinguished between two competing neural systems that are stipulated to play an important part in the development and maintenance of substance dependence: 1) the "reflective/executive system" which is directly implicated in choices for delayed outcomes and rewards. It involves the prefrontal cortex, and is implicated in executive functions such as prediction of outcomes, planning toward a goal, determining future consequences of current activities and social control; 2) the "impulsive system" which is implicated in choices for immediate outcomes and rewards. It involves the limbic brain regions, and is implicated in reacting to stimuli and in initiating physiological responses (Bechara & Damasio, 2005). Research on decision making and reward has found that substance-dependent individuals are less tolerant of delays in reinforcement and are more influenced by the salience of the drug reward, i.e. they are more impulsive than non-substance-dependent individuals (see Bechara, 2005 and Bickel et al. 2006 for a review). This can be explained in terms of a hyperactive impulsive system that overwhelms the reflective/executive system, thus placing more emphasis on immediate,

as opposed to delayed, rewards and consequences (Bechara, 2005). Results of fMRI studies lend support to this hypothesis (see Bickel et al., 2006).

Attentional bias is another cognitive process that has received considerable interest in addiction research, especially in the areas of alcohol and tobacco dependence. Several studies have shown that substance-dependent individuals with high levels of craving or motivation to use the substance selectively attend to substance-related stimuli (see Duka, Sahakian & Turner, 2003 and Weinstein & Cox, 2006 for reviews). Weinstein and Cox (2006) propose that the desire or motivation to use drugs or drink alcohol increases attention for drug or alcohol-related stimuli. This in turn leads to substance use, thus contributing to the development and maintenance of drug or alcohol dependence. Attentional processes may not therefore only co-vary with substance use, but they may also play a causal role in its development (Weinstein & Cox, 2006).

Research on brain deficits and impairments following chronic drug use indicates that drugs of abuse have detrimental effects on memory and cognition, and that the impairment of memory and cognition with chronic regular use of some drugs may not be reversed by prolonged abstinence (see Ghoneim, 2004 for a review). Neuropsychological studies have also shown the existence of significant impairments in executive functioning of users of a number of substances. This increases with the severity of use, and the impairments appear to be relatively lasting over time (see Lundqvist, 2005 for a review).

In the last decade researchers have started to investigate in more detail how memory processes may also contribute to compulsive drug use, and the remaining of this literature review will focus on reviewing the available evidence for memory biases in addiction.

4. Long Term Memory

Memory can be characterised as the mental function of retaining data (learning), or the storage system which holds the data and the data that is retained. A distinction can also be made between availability (the presence of information in memory storage, which is necessary but not sufficient for information to be remembered or used at a given time), and accessibility (for remembering to occur, information must also be accessible from storage). Accessibility is highly cue and process dependent (Eysenck & Keane, 1995).

Theoretical accounts of memory follow two main branches: processing and structure approaches. Processing theories focus on implicit (automatic) and explicit (controlled) memory processes, which appear to operate in fundamentally different ways. Structure theories focus on the memory systems underlying brain structures (Ray, Bates & Bly, 2004).

4.1 Declarative and Procedural Memory

Within the structural theories of memory, Cohen and Squire (1980) distinguish between *declarative* and *procedural* knowledge. Declarative knowledge corresponds to 'knowing that' and involves conscious recollection (explicit memory). Procedural knowledge corresponds to 'knowing how' and refers to the ability to perform skilled actions (e.g.

how to play the piano or ride a bicycle) without the involvement of conscious recollection (implicit memory).

4.2 Episodic and Semantic Memory

Tulving (1985, 1989) argued that long-term memory best be conceived of as three systems: episodic, semantic and procedural. The episodic memory component is seen as providing a record of the learning event, i.e. it allows us to be aware of having experienced something before. Episodic memory refers to memory for personal episodes. It is an autobiographical memory which stores memories of specific events or episodes with the context in which they occurred (e.g. a particular place at a particular time). It is a 'where, what, when' memory system. According to recent theoretical formulations, episodic memory allows the individual to not only travel back in time in his/her own autobiography, but also allows time travel into his/her future, to anticipate and envisage future events (Tulving, 2002).

Over time such a distinctive record may no longer be of value. For example, after we have used a new word for some time the meaning of the word may be represented without its episodic contextual component. It may then be included into a more general and abstract semantic memory system where cognitive representations of the world can be represented without, as it were, the colour of the experience as it was first learnt. Semantic memory contains information about our stock of knowledge about the world, including language and concepts. Knowledge is encoded in relation to other knowledge rather than in relation to oneself, and there is no accompanying stored coding of time and place. This allows a huge saving in the storage of information in the system since

episodic memories can be replaced once semantic memories have included the information. Tulving (1985) draws a distinction between the semantic experience of knowing something (noetic), and contrasts this with the episodic experience where recollection is involved and he call this 'self-knowing' or 'autonoetic' memory.

Tulving (1989) provided some evidence to support the distinction between the two kinds of long-term memory. He was interested in discovering whether different parts of the brain are active in episodic and semantic memory. He measured and recorded blood flow in different areas of the cortex, using a radioactive substance injected into the bloodstream. He found that the amount of blood flow within the cortex differed for the two memory tasks: episodic memory was associated with a high level of activation of the frontal cortex, whereas semantic memory was associated with high activity in the posterior regions of the cortex. The fact that different parts of the brain were especially active during retrieval of episodic and semantic memories is consistent with the view that there are at least partially separate episodic and semantic memory systems. Evidence for the dissociation of episodic and semantic memory has also been obtained pharmacologically (for a review see Curran & Weingartner, 2002).

5. Memory Biases in Addiction

Cognitive processing of drug-relevant stimuli has become an area of increasing interest in trying to better understand the nature of addiction and relapse. For example, there is growing evidence that drug-users pay more attention to drug-related information than to neutral information (for reviews, see Duka, Sahakian & Turner, 2003 and Weinstein & Cox, 2006). Much less however is known about possible memory biases in addiction.

The present review will focus on presenting the available evidence for biases in semantic and episodic memory in substance dependence, most of which comes from studies of alcohol misuse. Memory processes however are extremely complex, and although different memory tasks are used to tap different memory systems, no one task can claim to tap one cognitive or memory system or process exclusively (for example, in order to remember information, an individual has to pay attention to the stimuli first).

Semantic memory can be tapped explicitly (e.g. verbal fluency tasks), or implicitly (e.g. semantic priming). Studies looking at semantic memory biases in substance dependence have used methods that tap implicit rather than explicit semantic memory. Implicit memory is revealed when "previous experiences facilitate performance on a task that does not require conscious or intentional recollection of previous experiences" (Schacter, 1987, p.501). Episodic memory is by definition a type of explicit memory, and it is therefore tested by employing methods that tap explicit memory (e.g. recall and recognition). Explicit memory is revealed when "performance on a task requires conscious recollection of previous experiences" (Schacter, 1987, p.501).

5.1 Semantic Memory Biases in Addiction

The associations between a drug and events surrounding its use are represented in semantic (i.e. verbal, conceptual) memory networks (Baker, Morse & Sherman, 1987; Rather, Goldman, Roehrich & Brannick, 1992). Semantic memory structures are thought to support the operation of substance outcome expectancies and other cognitive processes that have been linked to individual differences in the risk of developing

alcohol and other drug use disorders (Kramer & Goldman, 2003), and in risk of relapse following treatment (Connors, Tarbox & Faillace, 1993).

Semantic priming tasks are procedures widely used in cognitive science to measure representations of interrelations between words and are especially useful for understanding the structure of semantic memory (Collins & Loftus, 1975). In the semantic priming paradigm, faster responses to a target word following exposure to a prime word reveal associations between the prime and target concepts in memory (Neely, 1977). Semantic priming therefore refers to the facilitation of responding to a word (e.g. night), when it is preceded by a semantically related word (e.g. day), as compared with a semantically unrelated word (e.g. river). The stronger the association between the prime and target words, the greater the reduction in response time (RT) (Collins & Quillian, 1969). The semantic priming effect has been explained in terms of associative network theories of semantic memory (Collins & Loftus, 1975; Quillian, 1967). Presentation of the prime is thought to activate a node within the semantic memory network, and this activation is assumed to spread to associated nodes, which facilitates processing of these words if they appear as targets. This process is thought to be automatic (Neely, 1991).

Other paradigms from the cognitive and social cognition literatures have been adapted to evaluate implicit semantic processes in drug and alcohol use. Many of these methods assess associative strength of related concepts in memory. The underlying assumption is that through repeated substance use, various cues and outcomes associated with use come to automatically evoke a conceptually related response based on associations in

memory. Easy activation of substance-related concepts during testing is deemed to be determined by the strength of associations in semantic memory (Ames, Franken & Coronges, 2006).

5.1.1 Semantic Memory Biases in Alcohol Users

Semantic priming procedures have been adapted to assess associative (semantic) memory networks related to addiction. In one of the first such studies, Hill and Paynter (1992) used a word-to-word lexical priming paradigm (e.g. drink-beer) and found that alcohol-dependent participants showed a facilitatory effect (i.e. faster RT) when they responded to alcohol-related stimuli whereas non-dependent drinkers showed no such facilitation. Zack, Toneatto and MacLeod (1999) assessed the ability of mood-related words to prime alcohol words in problem drinkers, and found that negative mood words (e.g. worry) significantly reduced RT to alcohol targets (e.g. beer) in problem drinkers with high levels of psychiatric distress. They also included a word-to-word (alcohol-alcohol) condition to verify within category activation of alcohol concepts and, as in Hill and Paynter's study (1992), they found activation of alcohol concepts by alcohol cues. In a more recent study, Zack, Poulos, Fragopoulos and MacLeod (2003) used priming sentences denoting negative and positive mood states and used time to read alcohol target words as the dependent variable. They found that negative mood phrases consistently primed alcohol targets in a sample of university students, whilst positive mood phrases did not.

In one of the first studies to show priming of alcohol expectancies, Roehrich and Goldman (1995) used a Stroop colour-word paradigm and found that participants primed with alcohol expectancy words (e.g. happy, mellow) consumed significantly more beer after a time delay than did participants exposed to neutral primes. Similarly, Stein, Goldman and Del Boca (2000) found that participants exposed to positive alcohol expectancy words drank significantly more alcohol. In a study by Weingardt, Stacy and Leigh (1996), phrases describing the expected effects of alcohol were found to prime RT to alcohol targets in university students, and the degree of priming correlated with the extent of alcohol use.

To examine memory processes involved in alcohol use, Stacy, Leigh and Weingardt (1994) investigated the accessibility of behavioural outcomes (e.g. relaxation) and their associated behaviours (i.e. alcohol use) under different conditions among individuals with different levels of drinking experience. This included asking participants to take part in a word association questionnaire which required them to write down the first behaviour they could think of when they read phrases that described potential results or consequences of various behaviours, including drinking alcohol. They found that participants' previous drinking behaviour strongly predicted accessibility of alcohol-related responses, suggesting that drinking behaviour influences the strength of memory association between alcohol use and culturally available outcomes from drinking. Similarly, Stacy and Newcomb (1998) investigated memory associations in a community sample by assessing outcome-behaviour (measured as in the above study) and cue-behaviour (asking participants to respond to ambiguous words with the first

word they can think of) and found that memory association measures directly and independently predicted alcohol use frequency.

5.1.2 Semantic Memory Biases in Marijuana Users

Stacy (1995) assessed memory associations in alcohol and marijuana use in a college sample by looking at cue-behaviour associations to ambiguous alcohol and marijuana-related words and drawings. The results indicated that the memory associations were again significantly related to alcohol and marijuana use independently of other possible correlates such as family history of alcohol use, friends' drug use and acculturation (defined as the cultural learning experienced by immigrants, which may predict changes in behaviour patterns and memory associations). In a prospective study of alcohol and marijuana use, Stacy (1997) investigated the predictive effects of memory associations (cue-behaviour associations to ambiguous alcohol and marijuana-related words and pictures, and outcome-behaviour associations), as well as looking at the predictive effects of explicit outcome expectancies cognitions measured by a self-generated expectancy scale for alcohol and marijuana use. After controlling for prior drug and alcohol use and other potential confounding predictors, Stacy found memory associations to be better predictors of subsequent substance use than explicit outcome expectancies, sensation-seeking, acculturation and gender. Outcome expectancies and sensation-seeking predicted alcohol use but not marijuana use. These findings suggest that different aspects of cognition may be involved in drug-use motivation, an implicit component that is represented by the spontaneous activation of memory associations, and a more explicit cognitive process represented by outcome expectancies. Using the

same procedures as in Stacy and Newcomb (1998), Stacy, Ames, Sussman & Dent (1996) and Ames and Stacy (1998) assessed outcome-behaviour and cue-behaviour associations in alcohol and marijuana use in a sample of high-risk adolescents and drug offenders respectively. Both studies found that memory associations were the best predictors of alcohol and marijuana use while controlling for gender, ethnicity and acculturation.

5.1.3 Semantic Memory Biases in Opiate Users

In a study which investigated the processing of sentences describing craving and withdrawal in opiate-dependent individuals, Weinstein, Feldtkeller, Myles, Law & Nutt (2000) tested: 1) abstinent opiate-dependent individuals who were maintained on methadone and who were awaiting methadone after a weekend of abstinence, 2) a group of opiate-dependent individuals not maintained on methadone, and 3) a control group of family members. They used a priming task which involved reading sentences describing withdrawal, craving or neutral contexts followed by either drug-related, neutral or non-words. Weinstein et al. (2000) hypothesized that participants should react faster when processing words compatible with their salient state, i.e. that the influence of withdrawal after abstinence from methadone over the weekend would increase attentional biases toward craving and withdrawal-related sentences. The results of the experiment showed that the methadone-maintained participants were faster in recognising drug-related words that followed sentences describing withdrawal compared with neutral words that followed neutral sentences. Although the findings did not extend to faster recognition of drug-related words following craving sentences, Weinstein et al. (2000) provide some

evidence of biases elicited by "contextual" priming of information that reflect the salient state of withdrawal.

Weinstein, Myles, Wilson, Bailey and Nutt (1996, cited in Weinstein et al., 1998) investigated the processing of sentences describing automatic thoughts and beliefs associated with drug craving in opiate-dependent participants who attended a methadone-maintenance clinic after a weekend of abstinence and in a control group of clinical and administrative staff at the clinic. The participants were tested on a contextual priming task which required responding to craving (positive expectancies and avoidance of withdrawal) and neutral sentences which were followed by either drug-related words, neutral words or non-words. Participants had to decide whether the targets were proper words or non-words. Overall, opiate addicts were found to show a significant bias towards drug-related words when primed by addiction-related sentences. In the same study, Weinstein et al. (1996) investigated the role of outcome expectancies in the evaluation of drug-use and 'drug-high' situations. They presented the same participants with three types of sentence pairs: drug use, 'drug high' and positive which were followed by negative or positive target words. Participants were instructed to indicate by pressing one of two keys whether they thought the words described an appropriate or inappropriate outcome for the situation. The findings showed that compared with control participants, dependent participants endorsed more positive outcomes to 'drug high' and drug-use situations. Weinstein et al. (1996) conclude that the findings from the two studies imply that thoughts and beliefs about drug use may play an active role in drug craving in opiate-dependent individuals.

5.1.4 Implications of Findings on Semantic Memory Biases in Addiction

Semantic priming and memory association paradigms used in studies on substance dependence have found a substance-consistent pattern of memory in dependent participants. Hill and Paynter (1992) explain these findings in terms of semantic memory functioning revealing aspects of cognitive structure and functioning unique to the individual. The semantic priming effect is sensitive to idiosyncratic conceptual structures which can change through experience and learning (in terms of the relationships among concepts). For an individual addicted to a particular substance, it is likely that the meaning of the substance and the concepts associated with it (environmental cues, drug stimuli and perceived affective outcomes associated with drug use) will have changed and intensified during the change from non-dependent to dependent status. As a result of such changes, concepts associated with the drug are likely to have become more strongly interrelated and modelled as memory templates that are activated in drug-relevant contexts. Thus through repeated drug use, cues and outcomes associated with drug use come to automatically activate thoughts about drug experiences. Stacy (1995, 1997) suggests that behaviour is controlled and directed by the current pattern of activation in memory, and that memory activation is often an implicit or relatively spontaneous process. Implicit memory processes may facilitate drinking or drug taking through associations that cause alcohol or drug-related concepts to come to mind automatically whenever cues related to the addiction are considered. The activation of alcohol or drug-related concepts may then influence behaviour by activating automatic action plans containing the procedural information necessary to initiate drinking or drug taking (Tiffany, 1990). This would explain how memory

systems function to anticipate future circumstances, even over time periods (Stein et al., 2000), and would help explain relapse in people who are trying to remain abstinent.

5.2 Episodic Memory Biases in Addiction

In comparison to how semantic memory processes may implicitly facilitate drug taking, explicit memory processes may theoretically affect drug use by informing conscious, controlled decision making. In Tulving's (2002) terms, an individual's episodic memory for past pleasure/lack of pain when intoxicated will influence his/her decisions about future personal experiences. It has in fact been hypothesised that change in drinking depends primarily on explicit memory (Rather et al., 1992), and that conscious, non-automatic cognitive processes must be activated in order to counteract automatic drug use action plans once they have been activated (Tiffany, 1990). If explicit memory is biased toward recalling drug-related information, an individual who is trying to remain abstinent may be either 1) impaired in the ability to recall information that is related to coping strategies and concepts designed to maintain abstinence, or 2) distracted by explicit memories of rewarding drug experiences. Despite this, very little research has been carried out on biases in explicit memory in addiction, and only three studies which look at biases in episodic memory were identified, all of which relate to alcohol misuse.

In a study by Franken, Rosso & van Honk (2003), alcoholics and light drinkers were compared on an incidental learning task of alcohol, general incentive (food) and neutral pictures. The pictures were placed in front of a coloured circle, and the participants were required to name the colour of the circle as quickly as possible. Following this, participants were then asked to name as many pictures they had seen as possible (free

recall). Alcoholics showed enhanced memory for alcohol cues compared to the light drinkers, and compared to neutral or general incentive cues. The findings also indicated that stronger memory bias was associated with an increase in craving. Franken et al. (2003) suggest that alcohol cues may be more easily encoded by alcoholics because of stronger associative links between alcohol-related memories and alcohol-related cues.

Kahler (2001) reviewed some evidence for the involvement of a process of conscious appraisal of drinking behaviour before change in excessive alcohol use may take place. He examined generation (implicit semantic memory) and recall (explicit episodic memory) of information supporting and opposing reduction in alcohol use in a sample of excessive drinkers. He developed two measures, a 'decisional balance fluency test' to measure participants' ability to generate reasons to change and reasons not to change their drinking, and a 'memory for alcohol consequences task' (based on the incidental recall principle) to assess biases in explicit memory for alcohol-related information. Kahler (2001) found that generation of reasons to change drinking was positively associated with negative alcohol expectancies and stage of change. Correspondingly, generation of reasons not to change drinking was positively associated with positive alcohol expectancies. He also found indications of a potential bias in explicit memory, in which information that was more consistent with current beliefs and behavioural intentions was more easily recalled, although this effect was found only for recall of information opposing change in drinking. The results suggested that drinkers concerned about the negative outcomes of reducing drinking and who are not considering changing their drinking in the near future may place higher processing priority on information opposing change.

Zack, Toneatto and MacLeod (2002) looked at anxiety and explicit alcohol-related cognitions in problem drinkers. More specifically, they used a cued recall task (incidental learning) to measure conscious recall of alcohol-related target stimuli in response to negative affective cues, and recall of negative affective targets in response to alcohol-related cues. They found that higher anxiety at test was associated with increased recall of alcohol targets paired with negative affective cues, thus showing an association between anxiety and alcohol-related memory.

6. Implications for Further Research

A number of theoretical models of drug addiction only indirectly implicate the influence of memory processes of drug-related stimuli in actual drug use. Some neurobiological accounts of addiction have, however, highlighted changes in the neural circuits involved in memory, therefore suggesting that memory processes may play an important role in addiction. There are early examples of theorists who tried to account for the shift to substance addiction in terms of complex memory schemata based on past experiences of substance use (e.g. Leventhal & Cleary, 1980; Niaura, Goldstein & Abrams, 1991; White, 1996. Cited in Orford, 2001), and more recently Volkow et al. (2003) proposed a theoretical model of drug addiction which explicitly incorporates a memory component to explain compulsive drug taking.

Despite the potential significance of memory processes in addictive behaviours, research in this area has received less emphasis than research in other cognitive components supposedly implicated in addiction. Empirical investigations of implicit cognitive biases in addiction have used methods and paradigms drawn from cognitive science and

cognitive neuropsychology. These methods make inferences about cognitive processes and structures based on behavioural responses. Most paradigms used to evaluate implicit memory biases in drug addiction have focused on associative strength of information processing, and have relied on associative tasks including semantic priming paradigms. As Ames et al. (2006), however, point out, it is possible that these methods may not only reflect implicit or spontaneous cognitions, but may also include more conscious, post-access processes. For example, when considering attentional bias, one single Stroop task has been shown to reflect the influence of the emotional salience of drug-related words on attentional processes within a short time frame (i.e. within a second), as well as reflecting a difficulty in disengaging attention from emotionally salient stimuli (i.e. carryover effect) which occurs more than a second after the word is removed from the screen (see Ames et al. 2006).

It can similarly be argued that some of the semantic priming studies outlined in this review do not provide a clear-cut separation of demands on non-controlled versus controlled processes in memory. As Morgan et al. (2006) explain, semantic priming tasks involve interactive processes which are both automatic and controlled: activation of a node within the semantic memory network, which in turn spreads to associated nodes thus facilitating processing of semantically related words, occurs early in the processing of a word stimulus. Other controlled processes which require conscious effort have however also been hypothesised to be involved later in the processing of a word, these being expectancy effects and semantic matching (Neely & Keefe, 1989). It may then be possible to use more complex semantic priming tasks which manipulate the length of time between the presentation of a prime and a target (very short, e.g. 250

msec and longer e.g. 750 msec) to investigate automatic and controlled processes in semantic memory respectively.

Within the literature on memory biases in addiction, most empirical investigations have focused on implicit memory, with very little research carried out on biases in explicit memory. The few studies looking at episodic memory biases and alcohol misuse have tended to use incidental learning tasks and free recall. Nonetheless, verbal learning tasks which look at susceptibility to interference may also prove useful in assessing whether such bias is present in drug-addicted individuals. Volkow et al. (2003) maintain that in drug addiction the value of drug and drug-related stimuli is enhanced at the expense of other reinforcers. Additionally, Hill and Paynter (1992) hypothesise that change from non-dependent to dependent status leads to concepts associated with the drug of abuse becoming more strongly interrelated and modelled as memory templates that are activated in drug-relevant contexts. It may then be possible that the memory templates which are activated when drug-relevant cues are presented, and which would lead to enhanced memory for drug-related cues in a learning task, may also cause interference in the recall of previously learnt neutral information which is less 'reinforcing' for the drug-dependent individual.

The last decade has seen a growing interest in the study of memory processes in addiction, but research in this area remains in its infancy. Although fewer studies have looked at memory compared to studies looking at other cognitive processes in addiction, findings to date appear to support the idea that memory processes may indeed play a significant part in the aetiology and maintenance of compulsive drug taking. Future

research which employs other paradigms developed in cognitive science and cognitive neuropsychology may help further understand the role of memory in addiction.

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Part 2: Empirical Paper

Semantic Priming and Verbal Learning in Current Opiate Users, Ex-users and Controls

Abstract

Research on semantic and episodic memory deficits in opiate abusers is limited and findings of studies have been inconsistent. In the present study, semantic priming and verbal learning were assessed in 16 current opiate users on a methadone maintenance programme, 16 ex opiate users in rehabilitation programmes who had been abstinent for an average of 19 months and 16 healthy controls. The groups were matched on IQ, age and employment status. Current and ex-users showed intact automatic and controlled semantic priming. Ex-users showed a verbal learning impairment compared with controls. Both current and ex-users were impaired in recalling semantically unrelated words, but unimpaired in recalling semantically related words. The findings may suggest a relative lack of spontaneous use of mnemonic strategies and imply that highly structured information would help opiate-using clients in treatment.

Introduction

Research in addiction has seen a growing interest in the study of cognitive processes and biases implicated in chronic drug use and interest in memory biases has gained momentum in the last decade (e.g. Ames, Franken & Coronges, 2006; Battistella, 2007). There is also an increasing body of literature on impairments in cognitive functions in addiction, suggesting that the chronic use of illicit drugs may be associated with generalised neuropsychological deficits. In addition to these general deficits, there may also be subtle differences associated with the abuse of different classes of drugs, including impairments in implicit and explicit memory (see Lundqvist, 2005 and Rogers & Robbins, 2001 for reviews). Research on cognitive biases and deficits in drug abuse, including abuse of opiates, suggests that both may contribute to the persistence and high relapse rates of drug abusers, and that further understanding in these areas may help in improving treatment of substance abuse.

The cognitive science literature has distinguished between two kinds of memory processes that appear to operate in fundamentally different ways: implicit (automatic) and explicit (controlled) processes. Automatic processing tends to be rapid and is stimulus driven (e.g. retrieval of highly learned information from long-term memory). In contrast, controlled processing is slower and more deliberate and is critical for integrating information, planning and allocating cognitive resources (e.g. inhibition of inappropriate responses) (Ray, Bates & Bly, 2004). Tulving (1985, 1989) further proposed that long-term memory should be understood in terms of separate episodic and semantic systems. Episodic memory provides a record of the learning event with the context in which it occurred. Tulving terms this 'self-knowing' or 'autonoetic' memory.

It involves recollection or recognition, and it is by definition a type of explicit memory. Semantic memory refers to a more general and abstract system, where cognitive representations of knowledge of the world can be represented without the specific learning event and context. In this system, knowledge is encoded in relation to other knowledge rather than in relation to oneself, and there is no accompanying stored coding of time and place. Tulving terms this 'knowing something' or 'noetic' memory. Semantic memory can be tapped explicitly (e.g. verbal fluency tasks), or implicitly (e.g. semantic priming tasks).

Research on brain deficits and impairments following chronic drug use indicates that drugs of abuse may have detrimental effects on memory, and that some of these impairments may not be reversed by prolonged abstinence (see Ghoneim, 2004 for a review). The impairments often identified relate to short-term or working memory, with few studies looking at long-term semantic and episodic memory. There has also been substantially less research into neuropsychological deficits in chronic abusers of opiates as compared to abusers of stimulants and cannabis. Studies which have investigated deficits in episodic and semantic memory in opiate users have yielded contradictory findings. Some have found deficits in semantic memory (Darke, Sims, McDonald & Wickes, 2000; Davis, Liddiard & McMillan, 2002) and in episodic memory (Darke et al., 2000; Block, Erwin & Ghoneim, 2002; Ersche, Clark, London, Robbins & Sahakian, 2006). Others have found no deficits in either semantic memory (Rounsaville, Jones, Novelly & Kleber, 1982; Heishman, Weingartner & Henningfield, 1999; Ornstein et al., 2000; Verdejo, Toribio, Orozco, Puente and Perez-Garcia, 2005; Prosser et al., 2006) or

episodic memory (Heishman et al., 1999; Davis et al., 2002; Mintzer & Stitzer, 2002; Mintzer, Copersino & Stitzer, 2005).

These conflicting findings may be due to a number of methodological problems, including lack of control for polydrug use, lack of healthy controls or use of pain management participants as controls, differences in the duration of abstinence of ex-users and use of different tasks to tap episodic and semantic memory. The interpretation of neuropsychological deficits in opiate abusers is also complicated by the high incidence of methadone treatment, which may exaggerate cognitive deficits through its own pharmacological actions. For example, in a study looking at the acute effects of methadone in patients admitted to an opiate detoxification programme, Curran, Kleckham, Bearn, Strang and Wanigaratne (2001) found that a single dose of methadone could induce episodic memory impairments on a task of delayed prose recall.

Assessment of semantic memory deficits is important as it may reveal impaired processing of semantic relationships between stimuli (words or concepts) and an inability to process contextual relationships between stimuli. Semantic memory contains our knowledge about the world, concepts and language. Altered semantic memory may impact on drug-users' ability to apply their knowledge in daily life to making decisions and planning, including with regard to their drug use.

All previous studies of opiate users investigating semantic memory have used verbal fluency tasks which do tap controlled or explicit functions of semantic memory but also rely on the use of executive functions such as working memory and attention (Morgan &

Curran, 2006). Automatic or implicit aspects of semantic memory can be tapped using more sensitive measures such as semantic priming paradigms. Semantic priming refers to the facilitation of responding to a word (e.g. night), when it is preceded by a semantically related word (e.g. day), as compared with a semantically unrelated word (e.g. river). The stronger the association between the prime and target concepts, the greater the reduction in response time (RT) (Collins & Quillian, 1969). Implicit semantic memory has been found to be relatively intact in the face of severe deficits in explicit cognitive functioning. For example, patterns of preserved implicit but impaired explicit cognitive functions have been found in neurological syndromes like Korsakoff's syndrome and Alzheimer's disease (see Jasiukaitis & Fein, 1999). To our knowledge, only one study has employed a semantic priming task to implicitly evaluate semantic memory in addicts. Jasiukaitis and Fein (1999) assessed chronic cocaine abusers who had cognitive impairments at both 4-5 weeks and 6 months abstinence and non-drug-using controls. They found normal semantic and repetition priming effects in the cognitively impaired cocaine abusers, who nonetheless showed pronounced deficits on other explicit cognitive tests.

It is also possible to dissociate automatic from controlled processes involved in semantic priming. The semantic priming effect has been explained in terms of associative network theories of semantic memory (Quillian, 1967; Collins & Loftus, 1975). Presentation of the prime is thought to activate a node within the semantic memory network, and the activation is assumed to spread to associated nodes, which facilitates processing of these words if they appear as targets. This process is thought to be automatic (Neely, 1991), but other mechanisms have also been hypothesised to contribute later in the processing

of a word. These are expectancy effects and semantic matching (Neely & Keefe, 1989). Expectancy refers to the pre-lexical mechanism whereby a set of potential targets is generated from the prime, and it is believed that the processing of words outside the expectancy-generated set is inhibited, leading to increased RTs for unrelated words. Semantic matching refers to the matching post-lexically of the primes and targets for semantic similarity. Both expectancy and semantic matching are thought to be controlled processes, requiring conscious effort. In a semantic priming paradigm, it is possible to investigate automatic and controlled processes by manipulating the length of time between the presentation of a prime and a target (stimulus onset asynchrony - SOA). Automatic processing occurs early in the processing of a stimulus, therefore using a very short SOA (250 msec) allows investigation of automatic processes. At longer SOA (700 msec) the action of more controlled processes can be explored. In a study looking at semantic priming after acute and chronic ketamine use (Morgan et al., 2006), a difference in priming effects at the long and short SOA was found, demonstrating a differentiation between automatic and controlled processing.

Explicit memory processes have theoretically been implicated in drug use and abuse by informing conscious, controlled decision making. In Tulving's (2002) terms, an individual's episodic memory for past pleasure/lack of pain when intoxicated will influence his/her decisions about future personal experiences. It has in fact been hypothesised that change in drinking depends primarily on explicit memory (Rather, Goldman, Roehrich & Brannick, 1992), and that conscious, non-automatic cognitive processes must be activated in order to counteract automatic drug use action plans once they have been activated (Tiffany, 1990). Consistent activation of drug concepts by drug

cues has been shown in studies on semantic memory biases in addiction (e.g. Ames & Stacy, 1998; Hill & Paynter,1992; Stein, Goldman & Del Boca, 2000; Zack, Poulos, Fragopoulos & MacLeod, 2003). Less research has been conducted on biases in episodic memory in addiction, with the few studies available to date (all of which relate to alcohol misuse) indicating that processing of drug cues in episodic memory may also show a bias towards encoding and remembering drug-related cues and concepts (Kahler, 2001; Zack, Toneatto & MacLeod, 2002; Franken, Rosso & van Honk, 2003). Semantic and episodic memory biases in addiction have been explained in terms of the meaning of the substance and its associated concepts having changed and intensified and being stored as memory templates which are then activated in drug-relevant contexts (Hill & Paynter, 1992).

As well as biases, deficits in controlled processes in episodic memory may further contribute to addiction problems. Heishman et al. (1999) tested 15 polydrug abusers who were not physically dependent on any drug at the time of testing (67% had used heroin in the previous 30 days) and 15 non-drug-using controls on measures assessing automatic and controlled processes. They included a verbal learning task to assess recognition and recall memory and they recorded the number of intrusion words generated during the task as a measure of controlled processing (ability to inhibit inappropriate responses). They found that participants in the 2 groups did not differ in tasks assessing working memory, explicit learning and memory (recall and recognition), access to semantic memory and metacognition. They however found that drug abusers made more intrusion errors during recall of categorically related words, as well as taking longer to solve sets of pictures composed of fragmented drawings of common objects (a

measure of perception of unstructured information). Heishman et al. (1999) argue that their findings are consistent with a selective impairment in controlled reflective functioning in addiction.

The present study aimed to investigate memory function and bias in opiate users who were on a methadone maintenance programme (current users), compared with ex-users who were opiate-abstinent in rehabilitation programmes (ex-users) and healthy controls (non-users). More specifically:

- To assess automatic and controlled processes in semantic memory, a semantic priming task was used in which SOA was manipulated. This part of the study was exploratory, because no study to date has assessed semantic memory in opiate users using a semantic priming paradigm.
- To assess episodic memory and bias, a verbal learning task was used which manipulated classes of category words (neutral versus drug). In line with the findings from Heishman et al. (1999), we hypothesised that compared to non-users, current users would make more intrusion errors during recall of categorically related words. We anticipated that ex-users would show the same impairment if this is due to pre-existing factors predisposing to chronic drug use and not due to current drug use.
- An exploratory aspect of this part of the study concerned how this may be influenced by the presentation of drug-related category words. If explicit memory in drug users is biased towards recalling drug-related information, current users may remember more drug-related words than controls, and show

increased interference effects of drug-related words when recalling neutral words.

- Similarly, individuals in the early stages of abstinence should continue to show facilitation in processing drug-related cues. We would therefore expect them to show a similar pattern of performance to current users, with more drug-related words remembered than controls and with increased interference of drug words when recalling neutral information.

Method

Design and Participants

An independent group design was used to compare current opiate users who were receiving daily methadone as part of a methadone maintenance programme (users), ex-opiate users who were opiate-abstinent and in rehabilitation programmes (ex-users) and healthy controls (non-users).

Current users were recruited from a London drug treatment clinic via referrals by their key workers. Ex-users were recruited from four London drug rehabilitation programmes. At the time of testing, all ex-users reported being abstinent of all drugs. All ex-users, except one, also reported being abstinent from alcohol. The one person consuming alcohol reported drinking it responsibly. Both current users and ex-users had a self- and key-worker reported history of primary opiate addiction. Snowball sampling (Coolican, 1999) was employed to obtain participants for the control group. Non-users had either never used opiates or had tried the drug once and had no self-reported history of drug or alcohol addiction. All participants were paid £7 for taking part in the research, either in

cash or in vouchers. The research was approved by Camden and Islington NHS Ethics Committee (see Appendix 1).

Procedure

Potential participants in the users and ex-users groups were identified and initially approached by their clinic/rehab key-workers. At this time they were given an information sheet to read in order to consider the study (see Appendices 2 and 3). If interested, they were then taken individually to a quiet room where more information about the study was given and where they had the opportunity to ask questions. If willing to participate, they were then asked for written consent (see Appendix 4), after which they completed the tasks outlined below. Participants were excluded if they breathalysed positive for alcohol. They were further asked to provide a urine sample at the end of testing which was tested for methadone and illicit drugs (opiates, cocaine, benzodiazepines, amphetamines and cannabinoids). Testing was conducted on site (i.e. at the drug treatment clinic for current users and at the different rehabilitation centres for ex-users).

Participants in the control group were mainly tested in laboratory rooms at University College London (UCL) but 2 were tested in their own home. They also provided informed written consent if willing to participate (see Appendices 4 & 5). Urine samples were not collected but control participants were screened for both current and past problematic substance use using the Cut-down, Annoyed, Guilty, Eye-opener Scale (CAGE; Ewing, 1984) to detect problematic alcohol use, and the CAGE-aid (Midanik, Zahnd & Klein, 1998) to detect problematic drug use. Using a cutoff value of two or

more positive responses, the CAGE's sensitivity in various populations ranges from 61% to 100% and its specificity ranges from 77% to 96%. Using the same cutoff value, the CAGE-aid's sensitivity is 70% and its specificity 85%. Control participants were excluded if they scored two or more affirmative responses on either measure. Participants with a current diagnosis of schizophrenia were excluded from the study in all three groups.

Tasks for both parts of the study (one part was by another trainee clinical psychologist, see Appendix 6) were combined so that each participant took part in one session which lasted for approximately one hour and fifteen minutes. Participants completed the tasks in the order outlined below (tasks in grey are not relevant to this part of the study and will therefore not be discussed in the present report).

	ORDER OF TESTING	
1	**CAGE and CAGE-AID**	
2	VAS 1	
3	**Spot the Word**	
4	**Verbal Learning Task**	
5	**Semantic Priming Task**	
6	**Verbal Learning Task – Delayed Recall**	
7	**BDI**	
	Participants will then do the following tasks in two different orders (half the participants in each group will complete condition 1 first and half will complete condition 2 first).	
8	Condition **1** MAT	Condition **2** MAT
9	VAS 2	VAS 2
10	Go-no-go	Go-no-go
11	Dot Probe	Dot Probe
12	**BAI**	**BAI**
13	Condition **2** MAT	Condition **1** MAT
14	VAS 3	VAS 3
15	Go-no-go	Go-no-go
16	Dot probe	Dot probe
17	VAS 4	VAS 4
18	Dot probe picture ratings	Dot probe picture ratings
19	**Obtain urine sample**	**Obtain urine sample**

Measures and Materials

Demographics: age, level of education and employment status were assessed via self-report. The 'Spot the Word' test (STW; Baddeley, Emslie & Nimmo-Smith, 1993) was used to estimate pre-morbid IQ. It is a lexical decision task which involves presenting the participant with 60 pairs of words, each comprising one real word and one pronounceable pseudo word with a plausible orthographic structure. The participant is required to identify the real word in the pair, and performance is assessed by adding the number of correct responses. Reliability and validity, as measured using the Alpha coefficient, are 0.776 and 0.692 respectively. Performance on this test correlates highly with performance on the National Adult Reading Test (NART; Nelson, 1982).

Mood: current mood state was assessed using the Beck Depression Inventory (BDI; Beck & Steer, 1987) and Beck Anxiety Inventory (BAI; Beck & Steer, 1990). The BDI and BAI are 21-item self-report questionnaires measuring depression and anxiety symptoms respectively. Using the Alpha coefficient, both have been found to have good internal consistency (BDI= 0.86; BAI= ranges from 0.85 to 0.94).

Verbal Learning task: this task measures verbal recall and susceptibility to interference. It was designed specifically for the present study, although procedure and instructions followed those used in the Rey Auditory Verbal Learning Task (RAVL; Rey, 1964). The task was specifically designed for the present study because of unavailability of existing verbal learning tasks which include a list of opiate-related words. Stimuli were a list of 16 neutral words (list A) and an interference list of 8 neutral and 8 drug-related words (list B) (see Appendix 7). List A consisted of 8 semantically unrelated and 8

semantically related words (names of types of birds). List B also consisted of 8 semantically unrelated and 8 semantically related words (drug-related). Because of the ambiguous nature of some of the opiate-related words included, the list was piloted on staff working at the drug treatment clinic who confirmed activation of drug-related concepts when presented with the stimuli. Presentation of semantically related and unrelated words in both lists was counterbalanced. The following instructions were read to participants: *"I will now read a list of words to you. When I get to the end of the list, please repeat back to me as many words as you can remember in any order".* Participants were then read out the words in list A at the rate of one word per second. This was repeated three times (i.e. three learning trials for list A were given). Participants were then presented with list B after the following instructions: *"You will now be read a different list of words. When I get to the end of the list, please repeat back to me as many words as you can remember from this list in any order".* Only one learning trial of list B was given, after which participants were again requested to recall as many words as possible from list A (trial 4). Delayed recall of list A was also assessed at a later stage during testing (i.e. after the semantic priming task outlined below). Number of words recalled was recorded for each trial of list A and list B, as well as number of repetitions, intrusions and other errors.

Semantic Priming task: the stimuli were 360 concrete nouns and 120 pseudo-words. These were arranged in three conditions: related (e.g. bed-wardrobe: 60 word pairs), unrelated (bed-parsnip: 60 word pairs) and pseudo (e.g. bed-fip: 120 word pairs). Participants were presented with a prime word for 200 msec, then, following an interval, were presented with the target word for 200 msec. Participants could respond for 2000

msec after the target was presented and between each trial (i.e. prime-target word pair) there was a blank screen for 2500 msec. The task was run with two different stimulus onset asynchrony (SOA; time between the onset of a prime and a target): short SOA (250 msec) and long SOA (750 msec). The order of the trials was randomised, with the constraint that any given trial type could not occur more than three times consecutively. All stimuli were presented in the centre of a computer screen using DMDX software (http://www.u.arizona.edu/ ~jforster/ dmdx/official/htm). Participants were asked to indicate whether the target was a real or a pseudo-word by pressing one of two buttons. Participants were told to respond as quickly and as accurately as they could. Reaction times (RTs) and accuracy were recorded automatically.

Statistical Analyses

Variable distributions were checked for normality and square-root transformations were used where appropriate. Post-hoc comparisons (simple effects) were Bonferroni corrected.

Demographics: One-way analyses of variance (ANOVA) were used to compare the groups demographic and questionnaire data. Categorical variables (e.g. level of academic qualifications) were analysed using Chi-Squared tests.

Verbal learning: A 3 x 3 repeated measures ANOVA (RMANOVA) was used to analyse overall recall of list A words over trials 1 to 3, with group as a between-participants factor (current users, ex-users and controls) and trial number (1, 2 and 3) as a within-participants factor. One-way ANOVAs were used to separately analyse total recall of

words in list A trial 4, list A delayed recall and list B. Recall of category and non-category words was analysed with a 3 x 2 x 2 RMANOVA, with group as a between-participants factor and list (list A, trial 1 and list B) and category (category words (bird and drug) and non-category words) as within-participants factors. Bivariate correlations (Pearsons) were performed within groups to analyse relationships between demographic information, questionnaire data (total scores only), length of abstinence (for ex-users only) and measures of verbal learning.

Semantic priming: Two 3 x 2 x 2 RMANOVAs were used to separately analyse RT and error data, with group as a between-participants factor and word relatedness (related and unrelated) and SOA (short and long) as within-participants factors. A one-way ANOVA was used to analyse RT pseudo words data.

Greenhouse-Geisser corrections were used where appropriate. All data were analysed using SPSS for Windows version 11.5.

Results

Demographics, Estimated Premorbid IQ and Mood Data (Table 1)

There were 16 participants in each of the 3 groups (48 participants in total). Of the total number of participants, 56 % were male. The percentage of unemployed participants in the 3 groups ranged from 69% (non-users) to 88% (ex-users). There were no significant group differences in age. The groups differed in level of academic qualifications (X^2=9.21, df=2, p=0.01) (information on level of academic qualifications was missing for 3 current users), with ex-users having significantly fewer qualifications at A level

standard or above than both the other groups. Non-users tended to score marginally higher than the other two groups in the STW test ($F_{2,45}$=2.56, p=0.089). There were significant differences between the groups in mean scores on the BDI ($F_{2,45}$=30.07, p<0.001) and BAI ($F_{2,45}$=15.80, p<0.001). Post-hoc comparisons (Bonferroni adjusted) showed current users scoring significantly higher in depression and anxiety than ex-users (BDI and BAI, p<0.001) and non-users (BDI and BAI, p<0.001).

Table 1: **Group mean scores (and standard deviations, SDs), percentages and ranges for demographic, estimated premorbid IQ and mood information.**

	Group		
	Methadone Maintained (current users)	**Rehabilitation (ex-users)**	**Control (non-users)**
N	16	16	16
Ratio males:females	8 : 8	12 : 4	7 : 9
Percentage Unemployed	81%	88%	69%
Age	37.56 (6.98) Range: 25 to 51	35.38 (6.45) Range: 26 to 49	32.69 (8.37) Range: 24 to 56
Academic Qualifications			
GCSEs or below	6	14	6
A Levels or above	7	2[a]	10
Spot-the-Word score	45.81 (7.55)	44.31 (5.02)	49.06 (5.59)
BDI score	32.19 (10.52)[b]	13.25 (7.94)	8.75 (8.57)
BAI score	27.44 (17.80)[b]	8.50 (6.88)	6.13 (6.22)

[a] indicates a significant difference of ex-users compared to current users and non-users (p= 0.01).

[b] indicates significant differences of current users compared to ex-users and non-users (p < 0.001).

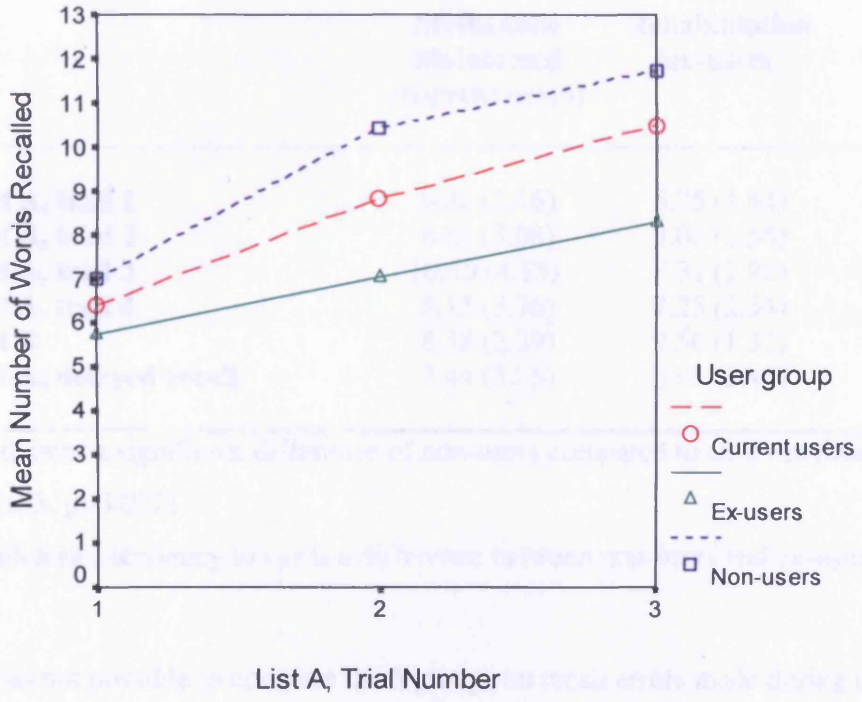
Urine screens were carried out for the current users and ex-users groups. Fifteen current users provided a urine sample (1 refused), and of these, 3 were not returned from the laboratory. Of the 12 urine samples screened, 11 tested positive for methadone, 9 tested positive for opiates, 6 tested positive for cocaine and 2 tested positive for benzodiazepines. Only 5 samples were screened for cannabis use, and none were positive. Of the 12 ex-users tested (4 refused to provide a urine sample), 10 samples were returned by the laboratory (2 were missing). All samples returned screened negative for all substances. Length of drug abstinence in the ex-users group ranged from 1.5 months to 38 months (mean 19.2 ± 13.1 months). None of the control participants reported a significant history of opiate use. Some non-users reported recreational use of other substances (e.g. cannabis) which did not meet the threshold for problematic substance use, as assessed by the CAGE-aid (Midanik, Zahnd & Klein, 1998).

Verbal Learning Task

Overall Word Recall (Figure 1, Table 2)

A repeated measures ANOVA on the total number of list A words remembered over trials 1 to 3 showed a tendency towards a Group x Trial interaction ($F_{3.41, 90}$=2.32, p=0.075) and a significant main effect of both Group ($F_{2,45}$=4.58, p=0.015) and Trial ($F_{1.7, 90}$=63.01, p<0.001). As seen in Figure 1, all 3 groups showed an increase in number of words recalled in list A from trial 1 to trial 3. The ex-users group recalled the least number of words over the 3 trials, followed by current users and by non-users, who recalled more words overall. Post-hoc comparisons (Bonferroni adjusted) revealed group differences in trials 2 and 3, with non-users recalling more words than ex-users in both trials (trial 2, p=0.006; trial 3, p=0.022).

Figure 1: **Mean number of words in list A recalled by participants in the 3 groups over learning trials 1 to 3.**



There were no group differences in the total number of list B words recalled and in the total number of list A words remembered in trial 4. There was a tendency towards a group difference in total number of words remembered in delayed recall of list A ($F_{2,45}$=2.53, p=0.09). Post-hoc comparisons (Bonferroni adjusted) showed non-users scoring marginally higher than ex-users (p=0.099) (Table 2).

Table 2: **Mean (SDs) number of words remembered in list A, trials 1 to 4, list B and list A delayed recall, by participants in the 3 groups.**

	Group		
	Methadone Maintained (current users)	**Rehabilitation (ex-users)**	**Control (non-users)**
List A, trial 1	6.38 (2.16)	5.75 (1.44)	7.00 (2.45)
List A, trial 2	8.81 (3.08)	7.06 (2.54)	10.44 (3.10)[c]
List A, trial 3	10.50 (4.15)	8.31 (2.82)	11.75 (3.26)[c]
List A, trial 4	8.13 (3.76)	7.25 (2.54)	9.38 (3.34)
List B	8.38 (2.39)	7.56 (1.32)	8.63 (2.06)
List A, delayed recall	7.44 (3.05)	6.63 (3.40)	9.19 (3.41)[t]

[c] indicates a significant difference of non-users compared to ex-users (trial 2, p=0.006; trial 3, p=0.022).

[t] indicates a tendency towards a difference between non-users and ex-users (p=0.099).

It was not possible to compare the 3 groups on recall errors made during trial 4 or delayed recall of list A (total number of errors and number of drug-related versus non-drug-related intrusions) because of floor effects.

Recall of Category and Non-Category Words (Figure 2, Table 3)

When comparing the number of category words (bird-related and drug-related) and non-category words (non-bird-related and non-drug-related) remembered in list A, trial 1, and list B (Table 3), analysis showed a significant interaction of Group x Category ($F_{2,45}$=5.26, p=0.009) and of List x Category ($F_{1,45}$=17.97, p<0.001). Main effects of both List ($F_{1,45}$=44.30, p<0.001) and Category ($F_{1,45}$=130.87, p<0.001) were also found, indicating that overall more words were recalled in list B compared to list A, and that

more category words (bird and drug) were recalled compared to non-category words (Figure 2). Post-hoc comparisons (Bonferroni corrected) showed that in list A, non-users tended to recall more non-category words than current users (p=0.061) and that they recalled significantly more non-category words than ex-users (p=0.045). A group difference in recall of drug words in list B almost achieved significance, with current users recalling more than ex-users (p=0.054).

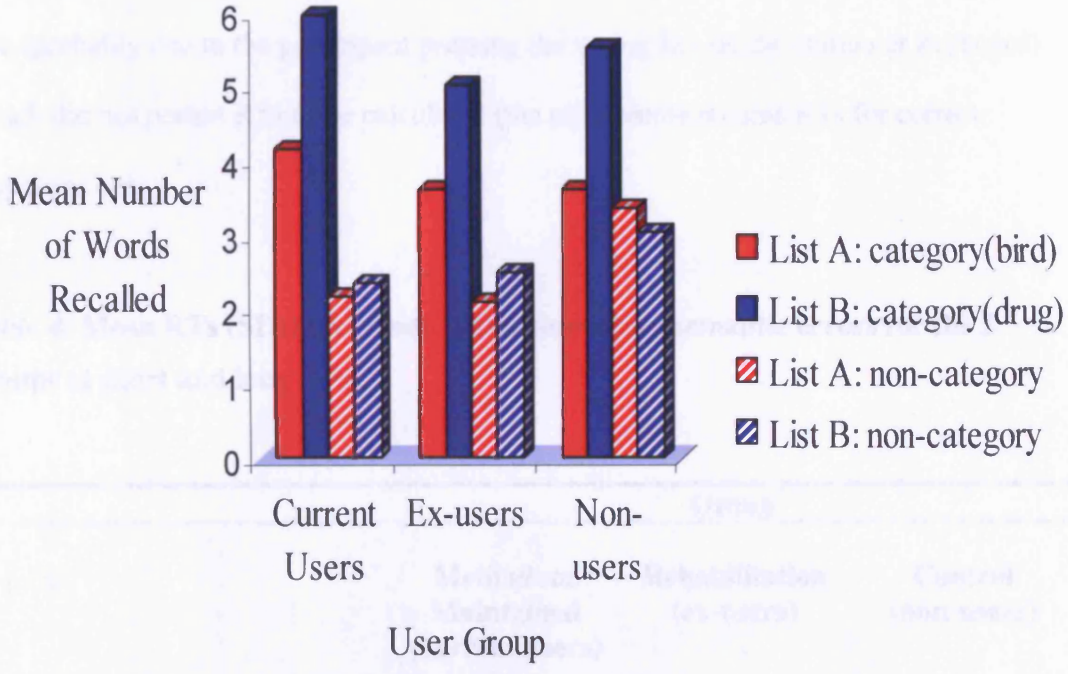
Table 3: **Mean number (SDs) of category (bird and drug-related) and non-category (non-bird and non-drug-related) words in list A, trial 1, and list B recalled by participants in the 3 groups.**

		Group		
		Methadone Maintained (current users)	**Rehabilitation (ex-users)**	**Control (non-users)**
List A, trial 1	**Bird-related**	4.19 (1.33)	3.63 (1.26)	3.63 (1.54)
	Non-bird-related	2.19 (1.33)	2.13 (1.15)	3.38 (1.69)[d]
List B	**Drug-related**	6.00 (1.46)	5.06 (0.93)[t]	5.56 (1.55)
	Non-drug-related	2.38 (1.50)	2.50 (0.89)	3.06 (1.53)

[d] indicates a significant difference of non-users compared to current users (p=0.02) and ex-users (p=0.015).

[t] indicates a tendency towards a difference of ex-users with non-users (p=0.054).

Figure 2: **Mean number of category and non-category words in list A (trial 1) and list B recalled by participants in the 3 groups.**



Correlations

There were no significant correlations between BDI and BAI scores and any measure of verbal learning within the current user and non-user groups. Within the ex-user group, there was a negative correlation between BAI score and delayed recall of list A ($r=-0.62$, $p=0.01$). Length of abstinence did not correlate with any measures of verbal learning.

Semantic Priming Task

Reaction Time Data (Table 4, Figure 3)

Mean reaction times (RTs) for the 3 groups in each condition are shown in Table 4. RT data were unavailable for one participant in the control group because of a 100% error rate (probably due to the participant pressing the wrong key on the computer keyboard) which did not permit RTs to be calculated (the programme records RTs for correct responses only).

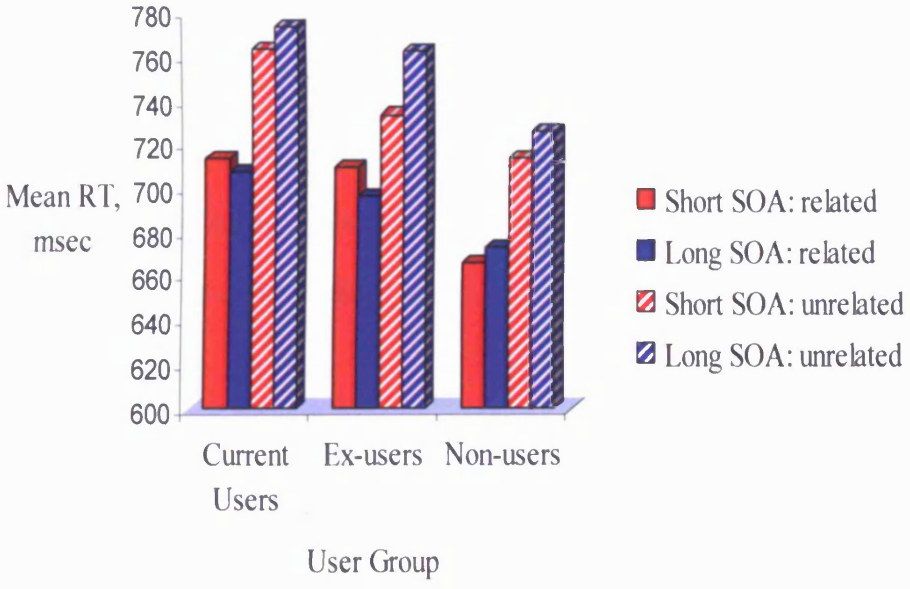
Table 4: **Mean RTs (SDs) and mean (SDs) percentage semantic errors for the 3 groups at short and long SOA.**

			Group		
			Methadone Maintained (current users)	**Rehabilitation (ex-users)**	**Control (non-users)**
RT	**Short SOA**	**Related**	713.77 (146.11)	709.72 (143.71)	666.11 (177.96)
		Unrelated	763.52 (134.18)	733.64 (145.35)	713.83 (169.28)
	Long SOA	**Related**	708.03 (130.86)	696.93 (135.32)	673.27 (178.49)
		Unrelated	773.93 (130.84)	763.07 (137.72)	726.17 (167.90)
% errors	**Short SOA**	**Related**	5.76 (9.09)	4.74 (5.26)	0.48 (1.32)
		Unrelated	12.15 (8.77)	13.69 (5.34)	14.16 (20.69)
	Long SOA	**Related**	5.10 (11.36)	2.13 (3.31)	1.90 (3.67)
		Unrelated	9.84 (13.67)	10.03 (8.08)	11.98 (24.59)

There were no group differences in RT. There was a significant interaction of Word Relatedness x SOA ($F_{1,44}$= 5.46, p= 0.024). Post-hoc comparisons (Bonferroni adjusted) show significant differences in mean RTs at both short and long SOA between related

and unrelated word pairs (short SOA, $p<0.001$; long SOA, $p<0.001$). There was also a main effect of Word Relatedness ($F_{1,44}= 85.74$, $p< 0.001$), with RTs being faster for semantically related word pairs compared to semantically unrelated pairs (Figure 3). This confirms significant semantic priming occurred in all 3 groups. There was no main effect of Group or group wise interactions in RTs for pseudo words, indicating that groups did not differ overall in simple speed of responding.

Figure 3: **Mean RTs at short and long SOA for the 3 groups.**



Error Data (Table 4)

There was no main effect of Group or group-wise interactions, indicating that accuracy was well matched across the groups. There was a trend towards a significant interaction of Word Relatedness x SOA ($F_{1,45}=3.24$, $p=0.079$). Post-hoc comparisons (Bonferroni

adjusted) showed differences in mean percentage errors at both short and long SOA between related and unrelated word pairs (short SOA, $p<0.001$; long SOA, $p=0.001$). There was a significant main effect of Word Relatedness ($F_{1,45}=20.95$, $p<0.001$), with more errors being made with semantically unrelated word pairs, and a main effect of SOA ($F_{1,45}=7.62$, $p=0.008$), with more errors at the short SOA.

Discussion

This study compared 16 opiate users on a methadone maintenance programme (current users), 16 ex-users in rehabilitation programmes who had been abstinent for an average of 19 months (ex-users) and 16 healthy controls (non-users) on tasks assessing semantic and episodic memory. The 3 groups were similar in age, unemployment status and estimated premorbid IQ, although ex-users had fewer qualifications at A level standard or above than the other 2 groups. Current users had higher levels of depression and anxiety compared to both other groups.

The results of this study suggest that current users and ex-users do not have impairments in semantic memory, with both groups performing as well as controls in the semantic priming task. Our findings of intact semantic memory in current users and ex-users are consistent with those of a number of studies which used category fluency tasks (e.g. Rounsaville et al., 1982; Heishman et al., 1999; Ornstein et al., 2000; Verdejo et al., 2005; Prosser et al., 2006). Our findings are however in contrast with those of Darke et al. (2000) who found opiate users on a methadone maintenance programme to be significantly worse than controls, and of Davis et al. (2002), who found opiate users receiving methadone to be significantly worse than ex-users. All these previous studies

assessing semantic memory in opiate users used verbal fluency tasks which, as well as tapping explicit (controlled) semantic memory, also tap executive functions such as working memory and attention. We could find only one study which looked at implicit (automatic) semantic memory using a simple semantic priming task, but this was on a sample of cognitively impaired cocaine users and ex-users (Jasiukaitis & Fein, 1999). The present study is the first with opiate users to employ a sensitive measure of semantic memory which is less dependent than fluency on executive functions, and which allowed for both automatic and controlled processes to be investigated. In current users receiving methadone treatment and abstinent ex-users, both automatic and controlled processes were unimpaired.

Our findings of largely unimpaired episodic memory in current users are in line with those of studies which compared polydrug abusers to healthy controls (Heishman et al., 1999), opiate users on a methadone maintenance programme with healthy controls (Mintzer & Stitzer, 2002) and opiate users on a methadone maintenance programme with abstinent ex-users and controls (Davis et al., 2002; Mintzer et al., 2005). In contrast, other studies have reported impairments (Block et al., 2002; Ersche et al., 2006). The differing findings may be explained by marked methodological differences between studies, as a wide range of different tests have been employed and differing types of polydrug using populations with different abstinence periods tested. In our sample of current users, we found no correlation of anxiety and depression with measures of episodic or semantic memory. These findings are consistent with those of Ersche et al. (2006) who also found cognitive impairments to be independent of depression. Depression has however been associated with reductions in cognitive

functioning including memory (Ghoneim, 2004). More specifically, depression has been associated with deficits in episodic memory and learning whilst performance on implicit memory tasks tends to be spared (Evans, 2004). The latter would explain the present findings of semantic memory being unaffected by high depression scores in the current users group. The finding of unaffected performance on the verbal learning task may be explained by the hypothesis that the cognitive impairments seen in depression could be secondary to an underlying motivational deficit, as depression has also been associated with difficulty on 'effortful' as compared to 'automatic' tasks (Evans, 2004). Curran et al. (2001) found a slight but significant improvement in simple reaction times following administration of methadone in their sample of opiate users admitted to an opiate detoxification programme. They explain this finding as reflecting a motivational effect on performance, possibly mediated by a decrease in withdrawal symptoms following methadone. The participants in the present study were also tested after administration of methadone, and it is possible that this may have affected their motivation and contributed to their unaffected performance. In our sample of ex-users, anxiety correlated negatively with delayed recall, but this did not lead to a significant difference in their performance compared to the other 2 groups.

In the present study, the only significant overall group difference in word recall was between controls and ex-users, with the latter performing significantly worse in trials 2 and 3 of list A. The findings therefore suggest that abstinent ex-users exhibit verbal learning impairments compared to healthy controls but not current users. No differences emerged on the level of recall in the first trial of list A or the first trial of list B. However, the learning curve of ex-users was shallower, and significant differences

emerged in trials 2 and 3. The finding of current and ex-users not differing significantly is consistent with other studies (e.g. Davis et al., 2002; Mintzer, et al., 2005; Ersche et al., 2006).

Our finding of ex-users performing significantly worse than controls is, however, unexpected. Interestingly, in the present study both current and ex-users were found to be worse than controls at remembering non-category words. The groups did not differ in recalling category words. Memory for non-category words requires processing of unstructured information, whilst memory for category words requires processing of structured information. Thus, when structure was provided, current opiate users and ex-users performed well. Memory for unrelated words is enhanced if a participant uses strategies to impose a structure on the stimuli (e.g. imagery). It is therefore possible that healthy controls were using such strategies to enhance their recall and that participants in the two opiate groups made less use of them. Our findings support those of Heishman et al. (1999) who found that their polydrug abusing sample did not differ from controls in recalling a list of categorically related words. Their drug-abusing sample, however, showed significant deficits on tasks involving processing of unstructured information, measured by identifying fragmented pictures and by the number of intrusion errors in remembering. Floor effects meant that it was not possible to analyse intrusion errors in the present study. Nonetheless, as current and ex-users displayed intact semantic memory and intact memory for category words, but impaired memory for non-category words, it could be argued that both display a selective deficit in processing of unstructured information, and that both may rely on their (unimpaired) semantic memory in order to overcome this deficit.

In the present study, ex-users tended to recall fewer drug-related words than current users, and this difference almost achieved significance (p=0.054). These findings do not support our hypotheses of current and ex-users remembering more drug-related words than controls, and of current and ex-users showing the same biases towards recalling drug-related information. All groups remembered more drug-related words, indicating that these captured participants' attention more than neutral category words (e.g. heroin versus magpie). Current users however showed a subtle bias towards recalling more drug-related words than ex-users, suggesting greater memory of drug words in this group. The literature on anxiety disorders introduces the possibility that cognitive biases may inhibit, as opposed to facilitate, responding to drug-related cues in abstinent individuals. Studies on panic disorder and social phobia have in fact shown that anxious patients are slower in processing threat-related words (Weinstein & Nutt, 1995; Weinstein, Neal, Lillywhite, Potokar & Nutt, 1996). Fedtkeller, Weinstein, Cox and Nutt (2001) used a semantic priming paradigm to test alcohol-dependent participants with various lengths of abstinence (3 to 14 days; 15 days to 6 months; more than 6 months), and found that those who had abstained for up to 14 days reacted more slowly to alcohol-related words that followed sentences describing avoidance of withdrawal than did control participants, and that the first two groups also reacted more slowly to alcohol-related words that followed craving sentences, compared with neutral words following neutral sentences. This is in contrast with what would have been predicted from previous research. They explain this in terms of individuals who have committed themselves to abstinence requiring elaborate attentional resources to process these stimuli, leading to task interference and longer RTs. They argue that in line with evidence for interference in anxious patients in their processing of threat-related

information, it is possible that alcoholics with shorter lengths of sobriety may find withdrawal-related information threatening, thus increasing their latency of response (Fedtkeller et al, 2001). It is plausible that inhibition of drug-related words may have occurred in ex-users because the abstinent individuals were consciously trying to inhibit cues that were incongruent with their abstinent status.

Limitations to our study include a relatively small sample size, large variability in lengths of abstinence among ex-users and higher anxiety and depression scores in the current user group compared to ex-users and controls. Performance of current users was, however, unrelated to anxiety and depression, as well as performance of ex-users being independent of length of abstinence. We could not control for polysubstance use, which is typical of this client group, and therefore tight conclusions about effects of opiates on memory cannot be drawn from the present study. This is because other drugs of addiction are known to affect memory, including benzodiazepines, cocaine and cannabis (Curran & Weingartner, 2002; Ghoneim, 2004; Lundqvist, 2005). The interpretation of neuropsychological deficits in opiate abusers is also complicated by methadone treatment, which may exaggerate cognitive deficits through its own pharmacological actions. Curran et al. (2001), for example, found that a single dose of methadone could induce episodic memory impairments on a task of delayed prose recall, although attention and comprehension were not affected (immediate recall was unimpaired). Methadone can also magnify the effects of sedatives and tranquilizers (Ghoneim, 2004) and therefore cause drowsiness. In the present study we did not record dosage and timing of administration of methadone. The effect of methadone, however, peaks about three hours after administration, and as participants in the present study were tested soon

after administration of their daily methadone dose, and therefore outside the peak time of its effect, it is unlikely that performance was affected by its sedative effects. This also appears to be confirmed by our findings of no group differences in overall simple speed of responding in our semantic priming task. To avoid differential effects of methadone on performance, future research should, however, aim to measure the size of the dose of methadone administered and ensure that all participants are tested after the same length of time.

A further limitation of the present study relates to the unavailability of information on duration and intensity of opiate and other drug use in our current and ex-user samples. A number of studies found no correlation of duration or intensity of opiate use with degree of deficits on measures of memory (e.g. Darke et al., 2000; Verdejo et al., 2005; Prosser et al., 2006). Some studies, however, suggest that heavier use of opiates and/or cocaine in long-term users is associated with greater likelihood of neuropsychological impairment (see Rogers & Robbins 2001; Ghoneim, 2004; Lunqvist, 2005), and that concomitant use of more than one drug over protracted periods of time may have additive negative effects (Ghoneim, 2004; Lunqvist, 2005). Future research could aim to control for the effects of polysubstance use and history of drug use upon performance by taking a careful drug history and by setting maximal limits on the frequency and quantity of use of other drugs. This would allow for tighter conclusions about the effects of opiates to be made, although it would inevitably decrease the ecological validity of the study.

No drug currently exists that only affects memory. Many affect arousal and many alter aspects of attentional and executive functions (Curran & Weingartner, 2002; Ghoneim, 2004). Performance changes on a memory task therefore may reflect alterations in memory, arousal or attentional processes or a combination of effects. Heroin dependent individuals have also shown an attentional bias for heroin cues which was significantly predicted by heroin craving-levels, thus indicating that selective processing may be related to motivational-induced states in general (see Rogers & Robbins, 2001 and Lundqvist, 2005). It is possible that participants in the current users group in this study may have been experiencing high levels of craving at testing and that attention and motivation may have affected their performance on the memory tasks. These are all variables that were not measured in the present study but that could have affected the results.

Despite these limitations, our study is unique as it is the first to employ a sophisticated semantic priming paradigm to investigate semantic memory in opiate users. Other strengths include providing a direct comparison of current opiate users on a methadone maintenance programme, abstinent ex-opiate-users and healthy non-drug-using controls who were similar in age, premorbid IQ and unemployment status and who were screened for drug use thus offering objective confirmation of current drug status.

In summary, this study showed preserved automatic and controlled semantic priming in current and ex opiate users compared with healthy controls. Ex-users had a verbal learning impairment compared with controls and both current and ex-users were impaired in recalling unrelated (non-category) words, but unimpaired in recalling

semantically related words compared with controls. As semantic processing was intact, this may suggest a relative lack of use of mnemonic strategies with unstructured information. This suggests that in order to aid clients in remembering and accessing strategies to obtain and maintain abstinence, services may benefit from providing them with meaningful contextual information regarding treatment and strategies.

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Part 3: Critical Appraisal

The intentions of this research were to compare 3 groups (current opiate users on a methadone maintenance programme, ex-opiate users abstinent from using heroin or methadone and controls who had never used opiates) on measures of semantic and episodic memory. Data collection was to be shared with a fellow trainee, with each of us running each other's tasks in the same testing session which was estimated to take about one hour. We developed our protocol early on in the research process, and power calculations indicated we should have aimed to recruit a total of 60 participants, 20 in each of the three groups.

We knew from discussions with our supervisors and from my past personal experience of working in a dual diagnosis unit that recruiting participants in the current user group would be likely to take longer than recruiting participants in the other two groups. This is because current users tend to lead a chaotic life style and are known to have a high did-not-attend (DNA) rate for all types of appointments. We also knew from discussions with our supervisors that inclusion/exclusion criteria would need to be realistic, meaning that in order to recruit enough participants in the current user group, we would need to be prepared to test individuals who may be using other substances on top of their prescribed methadone (this having its limitations but also improving the ecological validity of the study). This decision was taken in the knowledge that this client population are polysubstance users who are likely to supplement their methadone use with other substances including heroin, crack, benzodiazepines (BDZ) and alcohol.

We introduced ourselves and our research to key-workers in the chosen drug treatment service (a large centre in London with over 300 methadone-maintained clients in its

database) before starting recruitment, in the belief that this would give us the best possible start in order to recruit the number of participants needed. From the experiences of past trainees who carried out research with the same three groups of participants, we estimated that recruitment in the other two groups would not be as difficult and as time consuming (participants in these two groups do not lead such transient and chaotic lives and are much more likely to attend appointments). We therefore decided to concentrate our initial efforts in recruiting the current user group and we decided that we would start recruiting for the other two groups after we had recruited most of our current user sample. Together with my fellow trainee I felt aware of the possible difficulties in the recruitment process, and I felt confident that we would achieve our aim by being 'non-naïve', flexible and by coordinating testing between the two of us.

Despite working hard to anticipate possible difficulties in recruitment and despite feeling that I had 'prepared' myself for any eventuality, we were faced by problems that we had not initially considered. We started recruitment at the London drug treatment centre in October 2006 and despite inclusion and exclusion criteria being relatively broad (we only excluded participants whose primary drug of choice was not heroin, participants who breathalysed positive for alcohol and participants who had a current diagnosis of schizophrenia and were taking antipsychotic medication) and receiving more referrals than the number of participants we required, recruitment was slow. This was primarily because of a high rate of DNAs, despite the fact that we tried to arrange appointments at convenient times for the participants and were proactive in reminding them of their forthcoming appointment. Considering that the DNA rate within the clinic is approximately 50%, even though appointments at the clinic importantly involve clients

receiving their prescription for methadone, it is unsurprising that many participants DNAd their appointments to take part in our research project. In addition, although payment in the form of a £7 supermarket voucher did act as an incentive to many, it did not to others. One participant pointed out that in the past he had been paid around £80 for two hours spent doing a medical trial, whilst another agreed to take part "to do me a favour", as he clearly explained that taking part for £7 was "not worth my while".

It also proved quite difficult to be as flexible as we had wanted. We realised that despite there being two of us recruiting, we still only had between one and two days each week to test participants because of our university and placement commitments which were often inflexible. At the same time, another researcher was recruiting participants from the same centre for a different study. This meant that we had to ensure that we would not be seeing people on the same days, as the availability of testing rooms was limited. It is also possible that we may not have received as many referrals from the key-workers as we could have, had we been the only people doing research at that time. By spending time at the centre, it became obvious that the staff are very busy and I feel that requests to think about suitable clients to be referred for two different research projects may have felt like an extra burden on their already stretched time. Strict opening and closing times at the drug centre, including the centre closing for lunch every day and the fact that no clients were allowed to be inside the building when it was closed, meant that on a good day we would manage to test only two participants (one in the morning and one in the afternoon). On a bad day we would test none, despite spending the whole day at the centre. As well as many instances of DNAs, additional use of alcohol also proved a problem, as some participants breathalysed positive and had to be asked to return when

sober. Altogether we managed to recruit 16 participants instead of the 20 we had hoped for and this took us between October 2006 and January 2007.

Taking part in research gave some of the participants the opportunity to talk about their drug use and their difficulties to someone who was not directly involved in their treatment. The testing process gave me the opportunity to reflect on how difficult some of these people's lives are because of their enslavement to drug use. I came across participants whom, because of their drug use, had lost their children, their families, their jobs and status and their homes. Testing participants during the month of December highlighted even more poignantly how drug addiction affects people's lives: I was aware from working in a dual diagnosis clinic that the period approaching Christmas and the new year is a particularly difficult time, as it brings forth strong feelings of loneliness, isolation, powerlessness and lost opportunities. Two women explained that they were grateful to be able to take part in the research, as it meant that they could use the voucher to buy their children a little present for Christmas. Comments like these felt powerful to me and at times roused feelings of guilt for having such an 'easy and privileged life' and of powerlessness for being unable to offer them more than a mere small financial incentive. As a researcher whose primary role is nonetheless that of a clinician, coming face to face with such hardship can feel disempowering.

The use of mood state questionnaires gave me the opportunity to talk about how the participants were feeling and about some of the difficulties they were going through. Compared to the other two groups, scores on the depression inventory were higher for the methadone maintained participants, who often described feeling sad, worthless,

guilty and disappointed in themselves. As with any vulnerable client group, signs of significant distress or suicidal thoughts needed to be carefully considered. One of the participants I tested indicated in her questionnaire that she had suicidal thoughts and wishes and after discussing this with her I felt it necessary for the doctor and the lead clinician at the centre to see her. Such an occurrence highlighted to me how important it is not to lose sight of the *person* who is taking part in the research.

Sadly, when drug abuse becomes part of a person's life, sometimes one does not need to have death wishes for things to take a tragic turn. One of the last participants I tested just before Christmas died of a heroin overdose a few days later. I was the last person to see her alive at the centre. The information relating to her mood state helped us ascertain that she had no suicidal thoughts or wishes and that her death was an accident. Ironically, she was one of the least chaotic participants I tested: she worked and looked after her teenage son. My first reaction to the news was one of shock and sadness. This was then followed by anxiety relating to the fact that the data I collected would be scrutinised to look for any signs of suicidal intentions. I had already seen many other participants by the time I tested this person and I could not recall her testing session at first. This caused me to question whether I had been thorough in checking the depression and anxiety questionnaires and whether I missed signs of suicidal intentions. It also made me consider whether I could have done something more to anticipate what had happened and whether I may be held responsible for not realising that she was distressed. Support from my supervisors and from my fellow trainee was important at this time.

Spending time in the clinic gave me an insight into what it is like to work in a drug treatment centre and what it may feel like to be a user of such a service. Staff are friendly but very busy and at times have to deal with unpleasant instances of clients attending appointments under the effect of drugs and alcohol and becoming abusive towards them. The clinic is a large building with access through a very prominent and heavy iron gate. It has barred windows and a large bare and impersonal waiting area. It also has surveillance and security guards and swipe-entry doors have to be used to move from the waiting area to the interview rooms. It can be a demoralising environment for both staff and clients and one that does not inspire hope and recovery.

We finished testing the methadone maintained group in January 2007 and at around the same time we started approaching rehabilitation centres and job centres to recruit our ex-user and control groups. We believed that recruitment for these two groups would be quicker and easier, but were soon proved wrong. We found that many rehabilitation and job centres were unable to help. Some of the rehabilitation centres that we approached were going through a number of managerial and structural changes and the timing of our request was inconvenient to them. Other centres were willing to help but did not have any service users whose primary drug of choice used to be heroin, whilst others mentioned our study to their residents, who were nonetheless unwilling to take part. None of the job centres we approached allowed us to use their service to recruit the control participants, and for this reason we decided to ask friends, family and other fellow trainees for 'suitable referrals'. This setback initially affected our confidence and morale, since after taking so long to recruit our user group, we thought we would have an easier time with the remaining of our sample. Fortunately, sharing data collection

with a fellow trainee meant that we were able to support each other and help maintain each other's motivation through these difficult times. I found this to be a very valuable and positive experience and I was fortunate to work alongside another trainee whose resilience, support and good humour helped me considerably. We decided to continue sharing recruitment of both ex-user and control participants, which meant that both of us had the experience of testing all three groups in our sample (although not in equal numbers). Our perseverance paid off and we were eventually able to obtain a sample of 16 ex-user and 16 control participants in May 2007.

Testing the rehabilitation and control participants was a very different experience to testing the methadone maintained group. Obtaining consent from the rehabilitation centres took longer than expected, but once this was agreed, testing participants was a lot more straightforward. Although testing had to be carefully scheduled around therapy groups, community meetings and voluntary work commitments of some of the people in rehabilitation, all appointments were kept, and the fact that at times myself and my fellow trainee were able to test participants in parallel meant that sometimes we were able to test as many as 6 participants in one day. This gave us a much needed sense of progress. Furthermore, contact with individuals who had moved on from the difficult days of drug taking and whose future looked more positive gave me a sense of relief and hope. The rehabilitation centres we recruited from (3 residential and 1 day centre) varied from one another in their length of treatment and in their therapeutic styles. All nonetheless offered intense therapeutic experiences in pleasant and empathetic settings. At the time of testing, two of the residential centres were being redecorated. Paradoxically, and despite the centres looking like building sites, this added to the sense

of progress, with residents commenting on it as a positive development and looking forward to the buildings being finished. Generally, I sensed feelings of belonging and of caring for the environments that surrounded the rehabilitation participants, this being a possible reflection of their more positive sense of self now that they were no longer living such chaotic lives.

I also found that, differently from the methadone maintained clients, more rehabilitation participants showed interest in the research and asked questions about it. They were also more willing to talk about their experiences of having being caught in the cycle of drug abuse and dependence and to talk about their progress to abstinence. Some talked about this with pride but also with realism, commenting on how they realised that they were still vulnerable and needed to continue working on their recovery. One of the participants told me about another resident who tested positive for drugs a couple of weeks earlier and who was discharged from the programme as a consequence (most programmes advocate total abstinence from drugs and alcohol, with some permitting responsible use of alcohol). It was sad to hear that this person had very quickly gone back to regular use of heroin and to hear the concerns that the research participant had about her. People in residential programmes often become friends and knowing that a friend is sliding back to a life of addiction must be emotional and difficult. It was a positive experience for me to hear about the impact that therapy was having on some of the residents. One commented on how he had been helped to identify triggers and vulnerabilities to drug taking and how best to avoid them. This made me feel positive about the clinical side of my training, knowing that it can be helpful and valued by people.

As already mentioned, we were unable to recruit our control group from job centres as we had initially planned. This meant that we had to resort to employing a snowball approach to the recruitment. Although not ideal as it is a non-random sample (Coolican, 1999), we were careful to test individuals who matched our user and ex-user groups on variables such as education history and employment. As recruiting from job centres would also have not provided us with a truly random sample (Coolican, 1999), snowball sampling provided us with the best chance of obtaining the participants needed in the time scale available to us. I tested 4 out of the 16 participants we recruited for our control group. The biggest dilemma about testing them revolved around the fact that they were either directly or indirectly known to me. This raised the issue of reliability and validity of self-report drug use, as they may have felt more compelled to give socially desirable answers. In order to minimise this, I was transparent in acknowledging the potential difficulties of having to share such personal information with me and I further emphasised confidentiality and anonymity to them.

The main findings of the study were that current users and ex-users showed preserved semantic priming and that both current and ex-users were impaired in recalling unrelated words, suggesting a possible lack of use of mnemonic strategies with unstructured information and a greater reliance on semantic memory when trying to remember newly learnt information. These findings have implications for treatment. As already mentioned, explicit memory processes have been implicated in conscious, controlled decision making (Tulving, 2002) which is important in changing drug using behaviour and in maintaining abstinence (Rather et al., 1992). Therefore, as well as affecting people in their day-to-day functioning, deficits in episodic memory may also have an

impact in treatment success, since approaches such as cognitive behavioural therapy involve explicit memory and learning. The findings of unimpaired semantic memory and memory for structured information, but impaired ability to remember unstructured information in current and ex opiate users, suggest that in order to aid clients in remembering and accessing strategies to obtain and maintain abstinence, services may benefit from providing them with meaningful contextual information regarding treatment and strategies. It may also be helpful to offer clients some training in using mnemonics in order to enhance their memory for coping and relapse prevention strategies.

The fact that the participants in this study were not homogenous in their drug use or used other substances in conjunction to opiates means that tight conclusions about the effects of opiates on memory cannot be drawn from the present findings. Nonetheless, the present sample realistically reflects the client group that uses drug services, therefore offering a high degree of ecological validity to the study. The comparability of the groups also adds to the validity of this study. Current users displayed higher levels of anxiety and depression compared to ex-users and non-users, but this difference is likely to enhance ecological validity, as high anxiety and depression are typical of comorbidity in this client group (Darke & Ross, 1997). Our initial power calculations indicated that we should have aimed for 20 participants in each of the 3 groups. Unfortunately, we were only able to recruit 16, which inevitably lead to some loss of power in the present study. The increased power that 20 participants in each of the 3 groups would have given us may have resulted in the difference in number of drug-related words recalled

between current and ex-users reaching significance, as well as possibly also allowing for other significant relationships among variables to be detected.

My interest in research started during my undergraduate degree and conducting research was an important part of my role as an assistant psychologist. After gaining a place on the clinical psychology training course, I felt strongly about continuing to do research alongside clinical work once I qualified. However, as clinical training progressed, research felt less of a priority. Despite the difficulties involved in carrying out a study with a chaotic client group and having to combine research with placement and university commitments, the experience of conducting this piece of research as part of my thesis has revived my interest in combining research and clinical practice post-qualification.

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Tulving, E. (2002). Episodic Memory: From Mind to Brain. *Annual Review of Psychology*, 53, 1-25.

Appendices

Appendix 1 **Ethical Approval Letter**

Camden & Islington Community Local Research Ethics Committee
Room 3/14
Third Floor, West Wing
St Pancras Hospital
4 St Pancras Way
London
NW1 0PE

Telephone:
Facsimile:
Email:

03 July 2006

Professor H Valerie Curran
Professor of Psychopharmacology
Sub-Department of Clinical Health Psychology
University College London
Gower Street
London
WC1E 6BT

Dear Professor Curran

Full title of study: **Inhibition and memory in opiate users, ex-users and non-users**

REC reference number: **06/Q0511/52**

The Research Ethics Committee reviewed the above application at the meeting held on 26 June 2006.

Ethical opinion

The Committee was generally very content with this application. The main point of discussion centred on the reasons why the healthy participants are to be recruited from local Job Seekers Centres. Although it was understood that they might be demographically similar to the other group of participants the Committee questioned why the healthy participants were sourced from the Job Seekers Centres specifically.

The members of the Committee present gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation.

Ethical review of research sites

The Committee agreed that all sites in this study should be exempt from site-specific assessment (SSA). There is no need to complete Part C of the application form or to inform Local Research Ethics Committees (LRECs) about the research. The favourable opinion for the study applies to all sites involved in the research.

Conditions of approval

The favourable opinion is given provided that you comply with the conditions set out in the attached document. You are advised to study the conditions carefully.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Application		06 June 2006
Investigator CV	C.I. - Helen Valerie Curran	
Protocol	1	05 June 2006
Peer Review	Stefania Battistella - proof of review and funding	01 February 2006
Peer Review	Natasha Constantinou - proof of review and funding	01 November 2005
Participant Information Sheet: Non-Users	1	05 June 2006
Participant Information Sheet: Ex-Users	1	05 June 2006
Participant Information Sheet: Current Users	1	05 June 2006
Participant Consent Form: Users - current and former	1	05 June 2006
Participant Consent Form: Non-Users	1	05 June 2006

Research governance approval

You should arrange for the R&D Department at all relevant NHS care organisations to be notified that the research will be taking place, and provide a copy of the REC application, the protocol and this letter.

All researchers and research collaborators who will be participating in the research at a NHS site must obtain final research governance approval before commencing any research procedures. Where a substantive contract is not held with the care organisation, it may be necessary for an honorary contract to be issued before approval for the research can be given.

Membership of the Committee

The members of the Ethics Committee who were present at the meeting are listed on the attached sheet.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

06/Q0511/52 Please quote this number on all correspondence

With the Committee's best wishes for the success of this project

Yours sincerely

Ms Stephanie Ellis
Chair

Email:

Enclosures: *List of names and professions of members who were present at the meeting and those who submitted written comments*

Standard approval conditions

Copy to:

North Central London Research Consortium
Room 3/21, Research Governance Unit
3rd Floor, West Wing
St Pancras Hospital
London
NW1 0PE

Appendix 2 Current Users Information Sheet

Camden and Islington NHS
Mental Health and Social Care Trust

Participant Information Sheet

Research Study: Inhibition and memory in opiate users, ex-users and non-users

Researchers: Natasha Constantinou and Stefania Battistella (Trainee Clinical Psychologists)

You are invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please read the following information. Please ask us if there is anything that is unclear or if you would like more information. Take time to decide whether you wish to take part.

What is the purpose of the research study?
To understand what effect opiate (heroin and methadone) use has on people's memory and the way they control their responses. Research has shown that different drugs affect these two functions. In this study we are looking at 1) people who are using methadone at the moment, 2) people who no longer use methadone or heroin, and 3) people who have never used.

Why have I been chosen?
We have asked you to take part because you are using methadone at the moment. We will also be approaching around 30 other people who also currently use methadone.

Do I have to take part?
You do not have to take part in the study if you do not wish to. Your decision to take part will not affect your care management in any way. If you decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you can withdraw at any time without having to give a reason.

What will happen if I take part?
We will arrange to meet you once for about an hour at the ******* Centre, after you have taken your methadone. First we will ask you a little about your drug use. You will then be asked to complete some computer tasks. We will also ask you to complete some questionnaires. When this is completed, we will give you a voucher worth £7. All information collected about you during the study is strictly confidential and will be coded by number. Your name will not appear on any forms.

What are the advantages and disadvantages of taking part?
We do not foresee that taking part will cause you distress. We hope that the information we collect from this study will improve our understanding of the effects of heroin and methadone, and so help to improve services to methadone clients.

What will happen to the results of the study?
The results will be written up as part of a thesis, which we hope will be published in a scientific journal. A summary of the findings will be available to all who took part.

Who is organising and funding the study?
The study is organised and funded by Camden and Islington NHS Trust and University College London.

Contact for further information:
If you would like further information or have any questions, then please leave a message for us at the ******* Centre.

Thank you for taking time to read this.

Date: 8th February 2006. All proposals for research using human participants are reviewed by an ethics committee before they can proceed. This proposal was reviewed by Camden and Islington Health Services NHS Trust Ethics Committee.

Appendix 3 Ex-users Information Sheet

Camden and Islington NHS
Mental Health and Social Care Trust

Participant Information Sheet

Research Study: Inhibition and memory in opiate users, ex-users and non-users

Researchers: Natasha Constantinou and Stefania Battistella (Trainee Clinical Psychologists)

You are invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please read the following information. Please ask us if there is anything that is unclear or if you would like more information. Take time to decide whether you wish to take part.

What is the purpose of the research study?
To understand what effect opiates (heroin/methadone) have on people's memory and the way they control their responses. Research has shown that different drugs affect these two functions. For this study we are inviting three groups of participants: 1) people who are using methadone at the moment,
2) people who no longer use methadone or heroin, and 3) people who have never used these types of drugs.

Why have I been chosen?
We have asked you to take part because you no longer use opiates. We will also be approaching around 40 other people from the Jobcentre and other clinics.

Do I have to take part?
You do not have to take part in the study if you do not wish to. Your decision to take part will not affect your care management in any way. If you decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you can withdraw at any time without having to give a reason.

What will happen if I take part?
We will arrange to meet you once for about an hour at the centre. As we are looking to hear from people who do not use opiates, you will first be asked some questions about your drug use. You will then be asked to complete some computer tasks and questionnaires. When this is completed, we will give you a voucher worth £7. All information collected about you during the study is strictly confidential and will be coded by number. Your name will not appear on any forms.

What are the advantages and disadvantages of taking part?
We do not foresee that taking part will cause you distress. We hope that the information we collect from this study will improve our understanding of the effects of drugs, and so help to improve drug treatment services.

What will happen to the results of the study?
The results will be written up as part of a thesis, which we hope will be published in a scientific journal. A summary of the findings will be available to all who take part.

Who is organising and funding the study?
The study is organised and funded by Camden and Islington NHS Trust and University College London.

Contact for further information:
If you would like further information or have any questions, then please leave a message for us at the centre.

Thank you for taking time to read this.

8th February 2006
All proposals for research using human participants are reviewed by an ethics committee before they can proceed. This proposal was reviewed by Camden and Islington Health Services NHS Trust Ethics Committee.

Appendix 4 **Consent Form**

Camden and Islington NHS
Mental Health and Social Care Trust

Participant identification code:

Consent form

Confidential

Research study: Inhibition and memory in opiate users, ex-users and non-users.

Name of researchers: Natasha Constantinou and Stefania Battistella

1. I confirm that I have read and that I understand the information sheet for the above study.
   Yes/No

2. I have had an opportunity to ask questions and discuss this study
   Yes/No

3. I understand that I am free to withdraw from this study:
   - At any time
   - Without reason
   - Without affecting my management at the clinic/hostel

   Yes/No

4. I agree to take part in the above study.
   Yes/No

Name of participant	Date	Signature of participant
Name of researcher	Date	Signature of researcher

Appendix 5 Non-users Information Sheet

Camden and Islington NHS
Mental Health and Social Care Trust

Participant Information Sheet

Research Study: Inhibition and memory in opiate users, ex-users and non-users

Researchers: Natasha Constantinou and Stefania Battistella (Trainee Clinical Psychologists)

You are invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please read the following information. Please ask us if there is anything that is unclear or if you would like more information. Take time to decide whether you wish to take part.

What is the purpose of the research study?
To understand what effect opiates (heroin/methadone) have on people's memory and the way they control their responses. Research has shown that different drugs affect these two functions. In this study we are looking at 1) people who are using methadone at the moment, 2) people who no longer use methadone or heroin, and 3) people who have never used.

Why have I been chosen?
We have asked you to take part because you do not and have never used methadone or heroin. We will also be approaching around 20 other people.

Do I have to take part?
You do not have to take part in the study if you do not wish to. Your decision to take part will not affect your care management in any way. If you decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you can withdraw at any time without having to give a reason.

What will happen if I take part?
We will arrange to meet you once for about an hour and a quarter. As we are looking to hear from people who do not use opiates, you will first be asked some questions about your drug use. You will then be asked to complete some computer tasks. We will also ask you to complete some questionnaires. When this is completed, we will give you £7 cash. All information collected about you during the study is strictly confidential and will be coded by number. Your name will not appear on any forms.

What are the advantages and disadvantages of taking part?
We do not foresee that taking part will cause you distress. We hope that the information we collect from this study will improve our understanding of the effects of drugs, and so help to improve drug treatment services.

What will happen to the results of the study?
The results will be written up as part of a thesis, which we hope will be published in a scientific journal. A summary of the findings will be available to all who took part.

Who is organising and funding the study?
The study is organised and funded by Camden and Islington NHS Trust and University College London.

Contact for further information:
If you would like further information or have any questions, then please leave a message for us at the Jobcentre.

Thank you for taking time to read this.

Date: 8th February 2006
All proposals for research using human participants are reviewed by an ethics committee before they can proceed. This proposal was reviewed by Camden and Islington Health Services NHS Trust Ethics Committee.

Appendix 6 Joint Project

The empirical paper in the present thesis describes one part of a joint project carried out by myself (Stefania Battistella) and another Clinical Psychology Trainee (Natasha Constantinou). My part of the study focused on memory in current opiate users, ex-users and controls, the other part looked at response inhibition in the same sample. Whilst participants recruitment and data collection were shared between us, data analyses and write up of the theses were done independently of each other.

Appendix 7 **Word Stimuli included in the Verbal Learning Task**

List A	List B
Swallow	School
Kingfisher	Syringe
Treat	Tennis
Freezer	Butter
Penguin	Smack
Greenhouse	Methadone
Turkey	Tumbler
Eye	Sideboard
Rebel	Clock
Swan	Dealer
Magpie	Heroin
Nutshell	Inject
Pasture	Actor
Owl	Salad
Starling	Works
Anchor	Brown