The acute effects of methadone on long-term users.

Submitted in partial fulfillment for the degree of Doctorate in Clinical Psychology.

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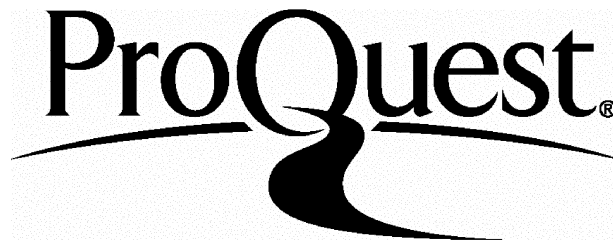
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ABSTRACT.

Methadone is the most commonly prescribed drug for the treatment of opiate

dependency. The effects of methadone on cognition have been rarely examined. This

study investigates the effects of an extra dose of methadone on long-term methadone

users. Measures included in the study assess the effects of methadone on mood,

cognition, psychomotor performance, craving, coping and suggestibility.

The project was undertaken at Camden & Islington addiction treatment service. A

double-blind, placebo controlled cross-over design was employed. Eighteen

participants were recruited and tested on two separate occasions with a week between

each testing session. All participants were given a third increase in their daily

methadone dose.

Most participants had been using opiates for between 2 and 5 years and all

participants had been taking methadone for a minimum of six months. The average

daily methadone dose was 43.5mls, however 22% of the participants were buying

illicitly additional methadone and 67% of participants reported using heroin in the last

week. The use of additional opiates was validated by urinalysis results. 28% of

participants had not reported heroin use in the last 72 hours despite a positive urine

result. Interestingly, 2-3 hours post drug administration participants were unable to

identify whether they had been given methadone or placebo.

Additional methadone did not significantly alter any aspects of psychomotor or

cognitive functioning. However, the research sample did vary from the standardised

population sample on the digit cancellation task. Although the memory task impairment did not reach statistical significance it is notable that a fifth of participants scored lower than the standardised sample.

Methadone had a significant effect on craving. An increase in methadone dose increased participants' craving for heroin and the implications of this are discussed. Suggestibility did not alter with an additional methadone dose but there was a significant difference between the research sample and the standardised sample with drug users being significantly less suggestible. The possible effects of this finding on clinical management are discussed. Methadone users were found to significantly differ from the general population on the coping strategies that they adopt. These results are discussed with reference to the current literature and targets for further research are identified. Clinical implications for drug services and for clients are drawn out.

ACKNOWLEDGEMENTS.

1.0   <u>INTRODUCTION.</u>

Methadone maintenance is the main treatment of opiate dependency offered by the
NHS in the UK. In conjunction with allied psychosocial approaches, it is the first line
of treatment aimed at harm reduction if not eventual abstinence. Research on the
effects of methadone in patients on maintenance therapy is fraught with
methodological problems and has been very limited to date. This thesis aims to
examine the effects of methadone on cognition, mood and drug craving within a
treatment population. It also assesses its effects on coping and suggestibility.

In this chapter I will firstly review methadone treatment and outline its advantages and
disadvantages. I then proceed to look at the research on its effects on cognition,
mood, craving and coping.

1.1 The history of methadone treatment.

After the discovery of the opiate pethidine in 1939, scientists in Germany continued to
work on compounds of similar structures and discovered methadone. Its discovery
was credited to Bockmuhl and Ehrhart in 1941 and it was called 'Hoechst 10820' and
later "polamidon". There is no evidence that it was made as part of a German attempt
directed by Hitler to replace opium supplies cut off by the war. This myth is thought to
have emerged because one of methadone's first trade names was 'Dolophine', a
derivative of adolf. In fact, Dolophine was created as a drug trade name after the war,
in America, and was thought to derive from the Latin 'dolor' (pain) and French 'fin'

(end). At the end of the war, all German drugs and related research was requisitioned by the allies as spoils of war and placed under American management. The US department of Commerce in 1945 published The Kleiderer report stating that despite having a different structure, the drug closely mimicked the pharmacological action of morphine. Because the formula for methadone was distributed around the world it came to have many different trade names. Isbell (1947) initiated the first full investigations with methadone and reported its euphoric effects as well as the rapid development of tolerance to its effects.

The earliest report of methadone in the U.K was in the Lancet in 1947. This considered the drug to be less dependency forming than other opiates and to be a better analgesic than morphine. In 1955 the Home office was aware of 21 methadone addicts, by 1960 the number had risen to 60. Heroin overtook morphine as the most prescribed opiate in 1962. By 1970 as a result of setting up clinics the numbers had risen to 1987. In 1969 the new drug clinics began operating. The clinics were set up to provide a legal supply of drugs, attract heroin users into contact with services and prevent the illicit market in drugs and the crime associated with it. The overall aim was to help clients get off drugs altogether. By the end of 1969 supplies of injectable methadone in the form of physeptone tablets were readily available. In the early 1970s the number of opiate addicts increased. This was thought to be due to an increase in young people taking opiates for pleasure as oppose to medical treatment.

In America, Dole and Nyswander (1966) had found that they could not stabilise opiate users without continually increasing their dose of opiates. They pioneered the radical

treatment of prescribing methadone and found that once an adequate treatment dose had been achieved they could maintain people on that dose for long periods of time. They used doses between 80mg and 150mg. Although they viewed this treatment as a physical treatment for a physiological condition, they also combined it with intensive psychosocial rehabilitation.

Through the 1970's, the incidence of heroin use in the U.K. continued to rise and clinics started to doubt the efficacy of prescribing the client's drug of choice as a way of promoting change. Prescribing practice moved away from predominantly injectable heroin to oral methadone on the basis that (a) it was more therapeutic to provide a non-injectable drug and (b) because of its long half life, it could be taken once a day rather than every few hours. A large scale research study between 1971 and 1978 (Hartnoll and Mitcheson, 1980) concluded that heroin provision maintained the status quo but stopped the problems associated with the acquisition of drugs. In contrast, methadone meant that people were more likely to leave treatment but were also more likely to achieve abstinence, and this led to the questioning of maintenance heroin prescribing.

The early 1980's saw another dramatic increase in the use of heroin. The main response to this was the provision of methadone detoxification services. Further, more non-statutory drug services were introduced in addition to Community Drug Teams in most areas, most of which also prescribed methadone.

The spread of HIV infection among injecting drug users became a major public health issue in the 1980's and 1990's (Moss, 1978). There was mounting evidence that retention in methadone maintenance treatments reduced the likelihood of infection of the virus (Ball et al, 1988) and this led once more to an expansion of methadone maintenance services. It also led to a reversal of abstinence orientated programmes, harm reduction became the central aim in Britain and all over the world.

1.2 Epidemiology of methadone and its current use.

Methadone is currently used primarily in the treatment of heroin dependence. The treatment involves substituting heroin with this longer acting opioid. The criteria for 'dependence' is classified by DSM IV (19xx) and outlined below:

Criteria for Substance Dependence.

A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three or more of the following, occurring at any time in the same twelve month period.

1. **Tolerance**, as defined by either of the following:

a) a need for markedly increased amounts of the substance to achieve intoxication or desired effect

b) markedly diminished effect with continued use with the same amount of the substance

2. **withdrawal** as manifested by either of the following:

a) the characteristic withdrawal syndrome for the substance (see criteria for

withdrawal)

b) the same or closely related substance is taken to relieve or avoid withdrawal

symptoms

3. the substance is often taken in larger amounts or over a longer period than was

intended

4. there is a persistent desire or unsuccessful efforts to cut down or control substance

use

5. a great deal of time is spent in activities necessary to obtain the substance (e.g.

visiting multiple doctors or travelling long distances)

6. important recreational , social or occupational activities are given up or reduced

because of substance use

7. the substance use is continued despite knowledge of having a persistent or recurrent

physical or psychological problem that is likely to have been caused or exacerbated by

the substance (e.g. current cocaine use despite recognition of substance induced

depression).

Specify if:

with physiological dependence - evidence of tolerance or withdrawal

without physiological dependence - no evidence of tolerance or withdrawal

It is important to understand the prevalence of methadone use within England. The

most recently published Department of Health statistics, (Department of Health,

1997), states that there were 25110 registered addicts in England in that year, 12229

of those were using methadone and 7507 of those 12229 were using methadone only

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(i.e. no other illicit or prescribed medication). These figures are obtained from the National Addicts Index, located at The Department Of Health. Practitioners are obliged to notify the database before prescribing any control drugs for the treatment of dependence. This ensures that clients cannot be treated at different places and also enables statistics on prescribing practices and the prevalence of addiction to be collected. The prescribing of methadone also requires an extra license that doctors must obtain from The Department Of Health.

1.3 Pharmacology of methadone.

Methadone mixture is prescribed for opiate users in 1mg/1ml format.

Methadone hydrochloride consists of: Carbon (21 atoms); Hydrogen (27 atoms); Nitrogen (1 atom); Oxygen (1 atom); Hydrochloride

Opiates appear to mimic the action of some of the body's naturally occurring chemicals called peptides, in particular: endorphins, enkephalines and dynorphins. Studies of the binding of opiates and peptides to specific parts of the brain have suggested the existence of as many as eight types of opioid receptors. Opiates directly cause a number of actions: effects on the central nervous system, effects on the peripheral nervous system, histamine release related effects and other effects for which there is no identified and/or proven causal link.

Table 1: Summary of the major effects of methadone.

central nervous system effects (CNS)	peripheral nervous system effects (PNS)	histamine release effects	no identified causal effects
euphoria	dry mouth	itching	amenorrhea
sleep	constipation	sweating	altered sexual desire
warm feeling in stomach	small pupils	blushing	hallucinations
drowsiness	difficulty passing urine	skin flushing	swelling of feet
pain relief		constriction of airways	delayed orgasm
nausea & vomiting			heart pounding
respiratory depression			anxiety
heavy feeling in arms & legs convulsions			weight gain

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In the past decade physiologists have identified different types of opiate receptors in the brain. This in turn has led to the classification of different drugs acting on those receptors. There are two major classifications of opioid agonists. Firstly morphine like agonists which act as agonists primarily at mu receptors and perhaps kappa and delta receptors. The second classification is opioids producing mixed actions. These are sub-divided into mixed agonist-antagonist and partial agonist. There is a difference between those that are morphine like agonists and those that have mixed actions. Morphine like agonists are strong analgesics but as the dose increases so does the potentially dangerous effects such as respiratory depression.

1.4 The advantages of methadone treatment.

Pharmacology.

Methadone has several advantages in the treatment of opioid dependence. Firstly, as it is available as an oral preparation, it therefore removes the need for the user to inject. Secondly it stops the user suffering from withdrawal symptoms from heroin. Thirdly, because it is very long-acting, this means that there is no rush or "hit" and the methadone effect comes on more slowly and is less intense than heroin.

The half-life of a drug is time that it takes for the blood levels of a drug to drop to 50% of the peak concentration. The half life of heroin is around three minutes. Methadone's half-life depends on whether it is the first dose or part of an ongoing programme and shows considerable individual variation. After three days of a stable

daily dose, the half life is extended to between 13 and 47 hours with a mean average of 25 hours. Once stability has been achieved, blood levels vary little. Methadone takes around 30 minutes to start being absorbed and up to four hours to reach peak blood level. The pharmacological profile of methadone means that doses (once established) do not have to be constantly altered as a tolerance does not develop in a rapid way as it does with heroin. Heroin users report that they have to keep continually increasing their dose to achieve the same effect.

Treatment philosophy.

Opinion is broadly divided between two major camps which are known as 'abstinence approaches' (such as advocated by organisations including Narcotics Anonymous) or 'harm minimisation approaches' where there is an acceptance of additional illicit drug use and safer practice is advocated. Broadly speaking harm minimisation services includes effects on three main aspects of drug using; physical health, psychological health and social effects.

The main reason for the change from abstinence orientated approaches to harm minimisation was the public health risk caused by HIV infection. The risk of HIV transmission meant that drug users had to be offered treatment provision under the NHS. Many users were unwilling to engage in abstinence treatments and therefore alternative treatments had to be introduced. Services include the provision of needle exchanges, condoms etc.

Physical health effects.

The reduced risk of HIV infection as a result of methadone maintenance is one of the most pervasive arguments for methadone treatment. The exact way that methadone reduces HIV risk has not been isolated and seems to be due to a variety of reasons. The provision of needles reduces sharing practices (Caplehorn, 1995; Baker, 1995) and oral methadone in principle eliminates the need for injecting. Some research has looked at the behaviour of injecting per-se and speculates that it is the conditioning aspect of injecting that makes it so appealing, (Corty, 1995). The reinforcing effect of injecting is removed once an oral preparation is given.

Additionally the provision of condoms means that sexual risk behaviour may be reduced, although research has shown that risk behaviour connected to drug using changes significantly more than sexual risk behaviour (Grella, 1996). The need to secure heroin also alters with the provision of methadone. For example, women working as prostitutes to finance their drug use are exposed to high risk of HIV and would not need to continue this sexual risk behaviour if provided with methadone.

Psychological health.

The reported prevalence of psychiatric comorbidity in drug users is high, (Milby, 1996). Anxiety disorders have been reported as being as high as 55% and affective disorders 36%. The debated question is whether opiate dependency produce

secondary anxiety and dysthymic syndromes on otherwise healthy persons, or whether

the opiate misuse by patients is an attempt to self-medicate pre-existing

psychopathology. Research by Musselman (1995) argues that patients are self-

medicating. Furthermore he argues that improvement occurs when patients are in

methadone programmes because methadone has mood stabilising properties in

disorders mediated or moderated by endogenous endorphins. This pharmacological

effect he sees as more important than psychotherapeutic interventions.

Capelhorn (1994) found that subjects were three times as likely to die when they were

not in methadone maintenance as they were in it. Death was due to a variety of

reasons including overdose and suicide.

Craving.

Methadone also has the ability to blunt the craving for other opioids (Caplehorn,

1993). An early double-blind, placebo controlled study showed that methadone

weakened the euphoric effect of intravenous injections of heroin and other short acting

opioids (Dole, 1966). Therefore methadone reduces the reinforcing effects of heroin

which in turn should reduce the use of non-prescribed opiates by clients in methadone

maintenance treatment. The theory of "craving" is expanded in section 1.7.

Treatment retention.

If all the above advantages are taken into consideration one of the most important aims

must be recruiting and retaining patients in treatment. The evidence from randomised

control trials indicates that it is methadone per se rather than other factors which

retains patients in treatment (Newman, 1979).

Social effects of methadone maintenance.

Heroin use leads to a lifestyle which is mainly concerned with the procurement of

drugs. Advocates of methadone treatment point to the way it allows patients to

'normalise' their lives, such as allowing them more time to secure employment which

in turn provides other interests besides drug use (Rittmannsberger, 1994).

Another main social effect is the role of methadone in preventing crime. Many heroin

users commit crimes to fund their drug use and with the free provision of methadone

treatment this need to offend is removed (Bell, 1992).

The provision of methadone services is also a way of engaging patients in

psychotherapeutic treatments aimed at looking at the negative and positive aspects of

their drug use and allowing them space to decide upon the effect of drug use on their

lives. Prochaska and DiClemente (1992) proposed this as a theory described as "stages

of change in addictive behaviour" and many methadone services have incorporated

these ideas into their treatment approaches.

1.5 The disadvantages of methadone treatment.

One of the main disadvantages of methadone treatment is the lack of clarity as to its aims and the methods of achieving them. As mentioned some services use methadone solely as a drug used to help manage the withdrawal symptoms caused by stopping using heroin. Other see methadone as a long-term treatment (making the service provision very expensive). The reality would seem to be that a variety of different services are needed, tailored to different client needs. More research is clearly needed to isolate how best to match patients to treatments (Nurco, 1994).

There is still confusion as to the appropriate dosage of methadone for use in treatment, with many services using lower doses than recommended, (Hartel, 1990). One of the main paradoxes in the available research is that much of it recommends that higher methadone doses reduce additional illicit drug use (Hartel, 1990). At the same time, one of the main criticisms of methadone treatment is the large amounts of additional illicit drugs used by clients. Such additional use includes not only heroin but other non-opiate drugs (Drake, 1993). Some of the benzodiazepines taken are prescribed, but many are used illicitly.

One reasonable criticism of maintenance programs is that the patient is just receiving yet one more drug and that even succeeding in abstinence from heroin may lead to increase and use of other types of drugs. There are many research studies about the frequent conjoint use of cocaine and heroin (Kidorf, 1993).

Another disadvantage of methadone treatment is that it has been adopted so extensively across the country that it has led to the exclusion of the use of other drugs in the treatment of problem drug use, especially in the field of opiate detoxification where other drugs such as naltrexone have therapeutic potential (Ling, 1994).

1.6 Drug effects on cognition.

The literature on the effects of centrally acting drugs on cognitive functioning has accumulated in quantity more than quality since it's beginnings in the late 1950's. It seems that a range of different drugs can effect cognitive functioning to a greater or lesser extent. In the cognitive research literature relatively little attention has been paid to opioid drugs compared with other classes of psychoactive drugs such as benzodiazepines, anticholinergics. It is possible that this stems from the belief that opioids "do not produce robust impairment of human performance". (Roache, 1991)

Many of the studies that do look at the cognitive effects of opioids including methadone are poorly designed, have not used placebos or control groups and have no statistical analysis, (for review see Zacny, 1995). Further, in many trials (including Rounsaville, 1981) the research subjects are infact poly-drug users and therefore it is difficult to ascertain the effects of individual drugs. Grant et al (1978) found that thirty-seven percent of poly-drug users had neuropsychological deficits using the Halstead-Reitan battery. In earlier pilot investigations they had found between forty five and sixty four percent of poly-drug users with neuropsychological impairments. However, these results were not found by Bruhn (1975) or by Fields (1975), both of

whom report no difference between poly-drug users and controls. Grant et al (1979) looked at a mixed group of substance abusers but relied on self-reported history only to verify drug use, as such the results are uninterpretable.

Research studies use three major groups of participants: (1) Healthy volunteers are those who have no history of drug abuse; (2) non-dependent opioid abusers i.e. those who have a history of opioid abuse but at the time of the study were not physically dependent on opioids; (3) Opioid dependent volunteers i.e. at the time of the research physically dependent on opioids.

In general research suggests that some opioids (mixed agonist-antagonists) more than others (morphine or codeine) impair psychomotor and cognitive functioning in healthy volunteers who have no history of opioid abuse. However, because of tolerance mechanisms, those who use opioids habitually are much less likely to have impairment of cognitive processes by acute doses of opioids (Zacny, 1995).

Heroin and morphine studies.

Morphine has an effect on motor performance with many studies reporting a decrease in speed at which tasks were performed (Zacny, 1995). However, the research shows that tolerance develops such that after chronic use of morphine at a fixed dose, the deleterious effect on motor performance disappears. Morphine also impairs sustained attention in both patients and healthy volunteers and is an analgesic. Information processing and intellectual functioning appears to be less affected by morphine.

Only one study with healthy volunteers has assessed the cognitive effects of heroin

(Smith et al, 1962), so it is difficult to conclude which parameters of functioning are

impaired. Studies on the effects of heroin on opiate dependent users (Fraser et al,

1963, 1964) suggest minimal psychomotor impairment with heroin although these did

not assess information processing or memory. However, because of the marked

similarity between heroin and morphine in terms of their efficacy at the mu receptor

and their ability to produce physical dependence one could speculate that the effects

would be similar to morphine.

Methadone studies.

Motor performance and reaction time

Two studies have looked at simple motor responses in methadone maintained patients,

(Gordon, 1970 and Kelley et al, 1978). Participants were tested at 1 hour and 25 hours

after drug administration. Results were compared to a matched set of non opioid

users. These studies found no differences as a function of methadone administration.

In another study (Rothenberg, 1977), methadone maintenance patients were given a

small dose of oral methadone and tested on a reaction time task. Healthy normal

participants were also given the same dose and tested with the same task. Methadone

impaired task performance by the healthy volunteers but not by the patients. This is

one of only two studies that has directly compared opioid dependent users with non

drug abusers. Lodemann et al (1995) compared thirty four patients with a matched

control group and tested them on the Weiner Act-React-Test-System. This measures visual perception, response speed, attention and sensomotor co-ordination. They concluded that there was no significant difference between the two groups and that therefore methadone should not effect driving performance.

Information processing.

In an early study Isbell et al (1948), tested the speed and accuracy of symbol copying and performance on arithmetic tasks by 15 former opioid abusers who were given increasing doses of methadone that eventually induced physical dependence. Physical dependence is poorly defined and classified by the attending doctors subjective oppinion as oppose to any quantitative measurement. As such the study is hard to replicate and "dependence" is a meaningless classification, loosely interpretted as drug withdrawal would cause the patient to sufer physical symptomatology. At doses of methadone ranging up to 400mg in some participants, the rate at which the tests were performed did not decrease but the number of errors relative to those occurring before the period of physical dependence did increase. The results have to be interpreted carefully because of the small numbers of participants and the lack of statistical analysis.

Gritz et al (1975) compared methadone maintenance clients with former heroin dependent users. No differences between the two groups was found on performance on the Digit Symbol Substitution Test (DSST). However, impairment was found in the methadone maintenance clients on a hidden word task and a nonsense syllable learning

task. It is possible that methadone results in permanent changes of ability and therefore that both groups had decreased ability. Appel and Gordon, (1976) compared the results with a matched set of non-opioid users to see if this was the case and found no differences in performance. Additionally a placebo controlled study using a wide range of doses found no differences on the DSST as a function of dose (Walsh, 1994).

Sustained attention.

Methadone appears not to affect sustained attention adversely. Kelley, (1978) found no difference in a 10 minute letter cancellation task at one hour versus 25 hours following a single 63mg dose. In another study Appel, (1982) found similar results on a 45 minute continuous performance task. Rothenberg (1977) found no difference between methadone maintained patients and normal volunteers in a 10 minute choice visual reaction time test.

Short-term memory.

The two studies that have tested short-term memory in methadone maintained patients did not find any impairment of function. (Gritz et al, 1975; Kelley et al, 1978).

Long-term memory, learning and comprehension.

In the 1948 study by Isbell in which physical dependence on methadone was induced in former opioid abusers, participants were given an IQ test before and during the period

of physical dependence. IQ did decrease but no comparison group was tested and no statistical analysis performed. In a later study with methadone maintained patients, Lombardo (1976), used the WAIS (Weschler, 1958) to test the effects of different doses of methadone. No difference was found in the effects of 40 verses 80mgs. Gritz et al (1975) used several tests of learning ability and found that methadone maintained patients had impaired ability to freely recall a story following 65mgs of oral methadone. However when cues were present (i.e. using a story recognition test) there was no impairment. Methadone patients also had impairment on learning verbal associations (Wescher, 1945). This association was only shown on the 'difficult' paired associates where words are not logically related, such as 'storm' and 'nation'and not on 'easy' associates. These findings imply that methadone impairs episodic memory but leaves semantic memory intact.

A number of studies have concentrated on the possible short-term cognitive effects of withdrawing from opioids in those who are physically dependent on them. Folli et al, (1992) found that their performance on a sustained attention task was not impaired when compared to healthy volunteers. Other studies have used naloxone to precipitate withdrawal in methadone maintained clients. Performance would be classified as impaired if administration of naloxone resulted in lower cognitive performance than before naloxone. No differences were found in the Stroop or digit span test (Kanof et al, 1992) or in an immediate recall test or the DSST (Preston et al, 1988). Results from these studies suggest that methadone detoxification has no acute effect on psychomotor and cognitive functioning.

The cognitive effects of methadone have been assessed in ten studies and findings from these appear to be inconsistent. There is a need to further examine these effects in a placebo controlled study with methadone maintenance clients.

1. 7 Effects of methadone on craving.

The construct of urge or craving has occupied an important part in the conceptualisation of addictions, mainly beginning with Jellinek's (1960) writing on the etiology of alcoholism. He argued that craving was the essential defining characteristic of alcohol addiction and could be used to explain the initiation and maintenance of compulsive alcohol consumption as well as relapse after a period of abstinence. Using these explanatory concepts became unpopular as in laboratory settings Jellinek's model did not characterise the drinking behaviour of people considered to have an alcohol addiction (Marlatt, 1973). Areas that were particularly damaging was abstinent alcoholics did not necessarily engage in out of control drinking after they had consumed small dose of alcohol. There was also a rise in behavioural approaches to the study of addictions which went against the use of mentalistic concepts such as craving as explanatory concepts.

There has again been an increase in interest in the role of craving since the rise of cognitive models (Marlatt, 1978). Research has also been undertaken looking at the role of conditioning processes in drug tolerance and dependence (Baker and Tiffany, 1985). The suggestion from this work is that conditioned drug effects form the substrate of drug urges and cravings. Cravings now form part of the diagnosis for

substance dependency and although there are theoretical disputes regarding the

conceptualisation of craving, the behavioural manifestation of the construct is an

important feature of addictive behaviour.

Across all theories, drugs are assumed to create subjective emotional-motivational

states. They are subjective because they refer to the experience of the individual ,

emotional in that the urge has a hedonic quality and motivational in the sense that the

subjective urge state activates drug seeking behaviour. There is the presumption that

urges will be associated with a change in overt behaviour, i.e. the pursuit and

consumption of drugs (Baker et al, 1987). Models of craving attribute the craving to

one of two sources, either to drug withdrawal or to the positive reinforcing effects of

drugs. This positive or negative reinforcement has often been proposed as being

fundamental to the initiation and maintenance of addictive behaviour (Wise, 1988).

Repeated practice of a cognitive or motor task under fixed-stimulus conditions

typically leads to the development of a fixed level of skilled behaviour that is

qualitatively different from the performance level observed when the task was initially

undertaken. This transformation of performance with practice has been described by

many cognitive psychologists as the development of automaticity and attempts have

been made to define the essential features and cognitive processes underlying

automatic and non-automatic functioning. Therefore the notion is that with sufficient

practice on any task, performance can become automatic. There are several properties

that are seen as the key features of automatic processing (Logan, 1985): speed:

autonomy: lack of control: effortlessness and lack of conscious awareness. Laboratory

studies have shown that with practice, task performance speeds up with a corresponding decline in performance variability (Logan, 1979). Autonomy refers to the theory that under proper stimulus conditions an automised action may be initiated involuntarily. The explanation of lack of control is that automatic actions may be enacted without intention, i.e. with the appropriate eliciting stimuli it may be difficult to inhibit the elicitation of an automatic process and once initiated the process may be difficult to impede or curtail (Posner & Snyder, 1975).

The theories speculated highlight the complexity of the nature of craving and within the clinical field of addictions this has been only minimally examined. The initial question addressed in this research is what exact effect does methadone have on craving ? It would be more likely to assume that methadone reduces subjects' craving as it is prescribed to minimise the effects of heroin withdrawal and therefore eliminate the individuals need to use heroin. However, methadone due to its different pharmacological action from heroin does not produce the euphoric effect that heroin does. It is therefore conceivable that heroin users crave heroin even after methadone administration to recapture the reported euphoric effect of heroin. Similarly, the injecting procedure is eliminated when methadone is taken orally and the procedure of injecting has itself been considered to be reinforcing and part of the drug taking ritual, so this is potentially another factor that could increase the individuals' craving for heroin. All the above are issues that have not been previously examined in formalised research.

1.8 Coping.

Drug addiction could be conceived as a maladaptive means of coping utilised by individuals unable to deal with stresses in more adaptive ways. There is no empirical support for the connection between maladaptive coping styles and drug use and so it was decided to assess the participants in this research .

Coping strategies are thought to play an important mediating role in the way in which individuals respond to stressful situations. In the past researchers have attempted to assess coping styles on the basis of coping behaviour and have developed a variety of coping measures. Unfortunately these measures have often had a variety of psychometric weaknesses. As a result of which Endler et al (1990) developed a multi-dimensional measure of coping styles: the Coping Inventory for Stressful Situations (CISS).

Coping has been primarily conceptualised as a conscious response or reaction to external stressful or negative events, Folkman and Lazarus (1980). Most of the coping research has involved the use of self-report measures of coping, Krohne (1988). There is however a consensus in the coping literature that coping is about the basic distinction between emotion-focused and problem-focused coping strategies. Problem-focused coping strategies are those that refer to task-orientation as oppose to emotion-focused coping strategies that refer to person-orientation. Task-orientation refers to strategies used to solve a problem, reconceptualise it or minimise its effects.

Person-focused refers to strategies that may include emotional responses, self-preoccupation, and fantasising reactions.

Several researchers have also identified a third basic coping dimension, avoidance (Billings and Moos, 1981). Avoidance strategies may include either task or person-orientated strategies. An individual can avoid stressful situations by seeking out other people (e.g. social diversion) or by engaging in a substitute task (distraction). The avoidance -orientated coping construct is related to several other constructs in psychological literature: These include, Byrne's (1961) 'repression sensitisation', and Krohne's (1986) 'attentional diversion'.

Further analysis as part of Endler's (1990) research on validating the measure revealed that both task and avoidance orientated coping are unrelated to general psychopathology and psychological distress; the reverse appears to be true of emotion-orientated coping which is positively related to psychopathology. Psychopathology was assessed using the Basic Personality Inventory (BPI), a 240-item self-report measure designed to assess twelve facets of personality and psychopathology both within normal populations and populations experiencing distress. Endler and Parker also found that males and females that score highly on depressive symptoms (using the Beck Depression Inventory) use more emotion-orientated coping than those scoring low on depressive symptoms.

1.9 Suggestibility

A theoretical foundation to current work on interrogative suggestibility was the work by Eysenck (1943). They found that on the basis on factor analytic work with suggestibility tests, there were two main types of suggestibility, known as 'primary' and 'secondary'. Primary was usually measured by tests that were closely associated with hypnotizabilty. Secondary suggestibility was harder to define or measure and Eysenck thought that it related to being gullible. It is this gullibility aspect that makes it relevant to police proceedings and forensic proceedings.

A type of suggestibility relevant to questioning had been identified by researchers such as Cattell, 1895 and Binet, 1900, although interest in the theoretical classification of different types of suggestibility and their measurement was not really begun until the work of Stukat in 1958. Unlike any previous work Stukat measured 'personal' and 'prestige' types of suggestibility, as well as looking at leading questions. He expanded Eysenck's category of secondary suggestibility and defined it as a concept characterised by personal influence and pressure from one individual acting upon another. The need for conformity was viewed as the primary determinant of secondary suggestibility.

Gudjonsson (1986) defined interrogative suggestibility as 'the extent to which, within a closed social interaction, people come to accept messages communicated during formal questioning, as a result of which their behavioural response is affected'. This definition incorporates five components; a social interaction; a questioning procedure;

a question containing a suggestion; acceptance of a suggestion and a behavioural response, such as a verbal reply to the question asked.

Gudjonsson argues that interrogative suggestibility differs from other types of suggestibility. It especially differs from earlier mentioned primary and hypnotisable suggestibility. Studies have found that measures of interrogative suggestibility do not correlate with measures of hypnotisabilty, (Haraldarson, 1985; Register & Kihlstrom, 1988.) Gudjonsson identifies four distinguishable features of suggestibility;

1. It involves a questioning procedure which takes place within a closed social interaction.

2. The questions asked are mainly concerned with past experiences, events and recollections, in contrast to other types of suggestibility that are often concerned with the motor and sensory experiences of the immediate situation.

3. Interrogative suggestibility contains a component of uncertainty, which is related to the ability of the person to process information cognitively.

4. Questioning in a police context commonly involves considerable stress with important consequences for the witness, victim and suspect. The theoretical aspect of Gudgonsson's model of interrogative suggestibility is construed as arising through the relationship between the person, the environment and the significant others within that environment. Interrogative suggestibility is determined by the coping strategies that the person can use when faced with uncertainty and expectations of the interrogative situation.

The model defines the situation, the participants involved and their 'cognitive set', i.e. mood, thinking and expectations. This results in the interviewee adopting a general cognitive strategy towards the situation which facilities either a suggestible or resistant repertoire of responses. The questions posed will lead the interviewee to employ one or more strategies of general coping. This mental processing involves uncertainty, interpersonal trust and expectations. These three components are described by Gudjohnsson as the essential prerequisites to the process and mechanism of interrogative suggestibility, the details of which are expanded upon below.

Uncertainty refers to the interviewee not being sure as to the correct response to the question. When asked leading questions they may accept the premises contained within the questions even if they do not know the answer. The private acceptance of the suggestion is the essence of suggestibility. Some interviewees may go along with the question even knowing that it is wrong, because they are reluctant to disagree openly or because they wish to please the interviewer. In the later case they are being compliant as oppose to suggestible.

Interpersonal trust means that the interviewee believes that the interviewers intentions are constructive and genuine. Subjects suspiciousness tends to reduce their susceptibility to suggestions.

Expectation is an important prerequisite to agreeing to questions. Interviewees may be reluctant to declare uncertainty or lack of knowledge because they believe that they are expected to know the answer.

Uncertainty and interpersonal trust are insufficient on their own to cause the interviewees to accept a suggestion, because if they are uncertain about an answer they can give 'don't know' or 'not sure' answers. This means that they are not agreeing with the questions and are prepared to declare their lack of knowledge. The model assumes that most people are susceptible to suggestions when the necessary conditions of uncertainty, interpersonal trust and heightened expectation are present.

Another important aspect of the model is the 'negative feedback' administered by interviewers during questioning. This is conceptualised by Gudjonsson as a type of instruction that distorts individuals responses. An interogator who communicates negative feedback may through interrogative pressure shift unwanted but perhaps true responses in favour of untrue or distorted ones.

The term interrogative suggestibility is more commonly used in the context of police interviewing of suspects, however, the theoretical model is equally applicable to witnesses and suspects.

Schooler and Loftus, 1986, argue that their are two main theoretical approaches to interrogative suggestibility which they call the 'individual differences approach' and the 'experimental approach'. The first approach is the one illustrated by the work of Gudjohnsson and the later approach by the work of Loftus et al, 1979. This approach is concerned with understanding the conditions under which leading questions are likely to affect the verbal account of witnesses. Individual differences do not feature

prominently and interrogative suggestibility is viewed as being mediated by the central cognitive mechanism called 'discrepancy detection'.

There are no published papers where suggestibility in drug users has been researched. Drug users often have large forensic histories, assumed to be due to the large amount of crimes they commit in the procurement of drugs. It could also be postulated that suggestibility effects individuals utilisation of therapeutic interventions, especially within the field of addictions where a large amount of time os focused on behavioural change related not only to drug using behaviours but to the knock on effects of drug use on all aspects of their lives.

1.10 Methodological issues in research on methadone.

Many studies of methadone maintenance have relied on self-reported history of drug use (Grant, 1979). This is clearly problematic as centrally acting drugs may impair memory and make self-report unreliable. Motivational factors in self-report of drug use are also relevant. Biological markers should be employed to validate or question such self-report data. Additionally many of the studies into the effectiveness of methadone are carried out in Europe and therefore it cannot be assumed that the drug using population in different areas have the same problems.

Perhaps the most prevalent problem in isolating the cognitive effects of drug use is the high frequency of poly-drug use. Therefore any results cannot be attributed to any one drug. It is also difficult to isolate any drug interactions. Additionally the client

population are difficult to work with as they are often geographically unsettled, frequently do not attend for appointments and are unwilling to consider changes in their methadone dose.

1.11 Rationale for the study and research questions.

Several study designs were considered but rejected for a variety of reasons. Potentially clients could have been asked to miss a dose of methadone and the effects of this examined compared with a normal dose. However this was not acceptable to either the clients or the treating clinicians due to concerns about precipitating withdrawal. An alternative design would be longitudinal, comparing patients on and then again when they were off methadone. This design is unwieldy due to the difficulty in recruiting participants, due to research time constraints and the limited amount of clients available who would have detoxed from methadone over the course of a year. It is also possible to measure cognitive effects in a healthy volunteer sample. However a few studies have been done within this population and these show marked deficits induced in this non-tolerant population. Additionally these studies do not inform us of methadone's effect on an actual clinical population, and if there are any effects, what the likely consequences would be.

In the light of the dearth of information regarding the effects of methadone on cognition, mood and craving the current study was designed. The study aimed to assess the effects of an acute methadone challenge in clients on methadone maintenance treatment. A double-blind, placebo controlled cross-over design was

employed. This design means that no control group is required because each subject is tested before and after both methadone and placebo, therefore each participant acts as their own control. Additionally the effects of methadone are isolated because the participant is given additional methadone thus ensuring that any results are due to the methadone and not other external factors.

The research hypothesis are that;

1. Additional methadone will have sedative effects and produce cognitive impairments compared with placebo.

2. Additional methadone will produce changes in subjective ratings of opiate side-effects compared with placebo.

3. Additional methadone will produce changes in participants' subjective mood ratings.

4. Additional methadone will reduce participants craving for heroin compared with placebo. Additionally, participants who use more methadone will crave and use heroin less.

5. Methadone will increase participants suggestibility. We know drug users are associated with frequent criminal behaviour to secure drugs. Additionally the nature of addiction means that individuals are subject to peer pressure to use drugs and are therefore likely to be more suggestible in general.

6. The neuropsychological functioning of participants will differ from standardised population norms.

7. The coping strategies employed by drug users will differ from the general population.

2.0   METHOD.

2.1 Research setting.

The project was undertaken at the Camden and Islington addiction treatment services

situated at The National Temperance Hospital, London. The service has 2280 patients

registered, the majority of whom are classified as opiate dependent and poly-drug

users with a smaller number of stimulant users only. The service serves the districts of

Camden and Islington. The addiction service is an out-patient service. It offers out-

patient maintenance methadone prescribing; methadone and other out-patient

detoxifications; a daily dispensing methadone service and liaison with Social Services

for in-patient detoxification and rehabilitation facilities. There is also a General

Practice (GP) liaison team where the overall management is taken by the drug services

but the patients' prescribing is done by their GP. Additionally there is a primary health

care facility.

The addiction team is multi-disciplinary consisting of Clinical Psychologists,

psychiatrists, nurses and an occupational therapist.

2.2 Ethical Approval.

Ethical approval was gained from the ethics committees of both University College

London and Camden & Islington Community Health Services NHS Trust in

September 1996, (for approval letters see Appendix 1 and 2). Recruitment of

participants began in October 1996 and testing participants ran through January until March 1997.

2.3 Participants.

Criteria for recruitment of participants are detailed below.

Inclusion criteria.

1. Patients must be over 18 years of age.

2. Patients must have been taking prescribed methadone for a minimum of six months.

3. Patients must have been on the same dose for the past 4 weeks.

4. Patients must be on a dose of between 20 and 100 mgs

5. Patients need to have basic literary skills and be able to give informed consent.

6. Patients need to be willing to give a urine and breath sample.

Exclusion criteria.

1. Any past history of severe head injury.

2. Any organic problem associated with cognitive dysfunction e.g. Multiple Sclerosis, Epilepsy etc.

All key-workers at the service were approached and asked if they had any suitable participants for the study. They were given an information sheet about the study, (see Appendix 3). Once they had looked through their case loads they approached their patients. They asked them if they were interested and gave them an information sheet,

(see Appendix 4). If they were interested in taking part the key-worker informed me and I arranged with them a time that they would be available. I also discussed any questions that they had about the study. Patients written consent was sought using the consent form given in Appendix 5.

Twenty eight participants were put forward by key-workers and all agreed to take part in the study. Of these twenty eight, eighteen attended (64.3%), all of whom attended both testing sessions (i.e. week one and two).

The eighteen participants (4 women and 14 men) had a mean age of 37.5 (range 21 - 52 years). All of the sample were white. In terms of socioeconomic status the sample was generally representative of the treatment population although the educational status of the research sample was higher, (see section 3.1).

2.4 Design.

A double-blind, placebo controlled cross-over design was employed. Participants were assigned randomly to treatment order. There were thus two groups, one group that received methadone on day 1 and then placebo on day 8 and one group that received placebo on day 1 and then methadone on day 8, (see table 2). The research was undertaken under double-blind conditions, i.e. neither the researcher nor the participants knew if methadone was administered on the first or second testing session.

Versions of the psychological tests were counterbalanced across subjects and design thus ensuring that the four (or two) versions of each test in random order occurred equally often at each testing, (see Appendix 6 for randomisation code).

Participants were asked to attend on two separate sessions with a one week delay between each session to ensure the 'washout' of any extra methadone. The importance of attending was stressed. In addition, participants were made aware that the research was strengthened if they had used the same drugs prior to both testing sessions. Participants were told that a urine sample and an alcohol breathiliser sample would be taken. Importantly, they were also informed that results were confidential and would not be reported to their key-workers.

Table 2: Graphic representation of research design.

	day 1	day 8
50% of participants	methadone	placebo
50% of participants	placebo	methadone

2.5   Drugs.

Methadone syrup and methadone vehicle (a syrup) was obtained from Martindale pharmaceutical company. To obscure the taste of methadone, both methadone and placebo syrup were supplemented by ten drops of peppermint essence. The taste of each treatment was therefore the same. Prescriptions by the supervising clinician were

sent to a hospital pharmacy. The pharmacist dispensed both methadone (33% increase

on daily dose) and a matched quantity of placebo syrup.

2.6 Measures.

A range of tests are used to determine the effect of methadone on cognitive and

psychomotor functioning, mood, suggestibility, coping and craving. Scales were also

included to assess subjective self-ratings of physical and symptoms. Although

cognitive and psychomotor tests are placed in major categories it must be

remembered that most tests tap several cognitive and psychomotor functions. For

example tests of reaction time can also involve information processing.

National Adult Reading Test (NART).

Vocabulary correlates best with overall ability level and tends to resist the dementing

processes better than any other intellectual attainment. The residual vocabulary of

patients with neurological conditions may be the best indicator of pre-morbid mental

ability. Patients may not be able to give definitions of words but the correct

pronunciation of words when reading has been used as evidence of pre existing word

familiarity (Nelson and O'Connell, 1978).

The NART compromises 50 phonetically irregular words which the participant is

asked to read aloud. Crawford (1992) found that NART IQ scores correlate

significantly with education $(r = .51)$ and with social class $(r = .36)$. Scoring for

errors they found a split half reliability coefficient of .90 and inter-rater reliability

coefficients between .96 and .98. When they compared the NART and the WAIS IQ

scores they found that the NART predicted 72% of the verbal IQ variance. Spreen

and Strauss (1991) recommended that the NART was not used with patients who are

aphasic, dyslexic, or who have articulatory or visual acuity defects.

The test is scored by counting the number of words read correctly and subtracting this

from 50. This error score can then be converted into a I.Q. score (Nelson and

O'Connell, 1978). This test was given only once and was used to enable comparisons

with samples in the list.

Prose recall (Rivermead behavioural memory test).

The Rivermead behavioural memory test (RBMT) was designed specifically to look at

every day memory. There are several sub-tests within the whole battery. This research

used one sub-test from the test battery: the immediate and delayed recall of a prose

passage. Pre-recorded audiotapes of each of the four versions were used. The test

involved playing the tape with the short story on and asking the participant to listen

and then repeat as much of the story as they can remember (1) immediately after the

story has finished and then again (2) twenty minutes later. There are four parallel

versions of the story available, so that practice effects with the same test can be

avoided. The stories contain 21 idea 'units' from 54 to 65 words in each story. Test

instructions were standard and scoring is based on 1 point for a correctly recalled idea

unit, 1 point for an exact synonym; half a point for partial recall or synonym.

In order to pass according to norms subjects must score at least 6 on immediate recall

and at least 4 on delayed recall.

Digit Symbol Substitution Test. (DSST)

From the Wechsler Adult Intelligence Scale (WAIS) test booklet (Wechsler,

1944,1981), four versions of this test were used, all with blank squares paired with a

randomly assigned number from one to nine. Following a practice trial on the first

nine squares, the task is to fill in the blank spaces with the symbol that is paired to the

number above the blank space as quickly as possible for 90 seconds. The score is the

number of squares correctly filled in. The test is openly timed and the importance of

speed stressed at the start.

For most adults, digit symbol is a test of psychomotor performance that is relatively

unaffected by intellectual prowess (Erber, 1981). Motor persistence, sustained

attention, response speed and visuomotor co-ordination play important roles in the

normal person's performance, but visual acuity does not (Schear and Sato, 1989).

Estes (1974) points out that skill in encoding the symbol verbally also appears to

contribute to success on this test and may account for consistently observed feminine

superiority (Snow and Weinstock, 1990). Perceptual organisation components also

show up on this test (Kaufman and Reynolds, 1991).

Test-retest reliability is high, with correlation coefficients in the .82 to .88 range,

(Weschler, 1981). In a study that tested 115 healthy adult subjects, they averaged a

5% gain with a three week test-retest delay (Youngjohn et al, 1992). A study by McCaffrey in 1993 found no practice effects when the test was given four times with intervals of one week to three months. Age effects on the test are prominent (Jarvik, 1988) with raw scores dropping sharply after the age of sixty. Storandt (1976) found no relationship between cognitive ability as measured by the WAIS Vocabulary scores and digit symbol performances.

The test is consistently more sensitive to brain damage than other parts of the Weschler battery and the score is likely to be depressed even if damage is minimal. Digit symbol tends to be depressed regardless of the location of the lesion and therefore is of little use for neurological diagnosis. Butters and Cermak (1976) said that it is not surprising that digit symbol has non-specific sensitivity as it can be affected by so many different performance components. The test is very sensitive to organic dementia and is sometimes used in a whole battery as a diagnostic tool. It is also widely used in psychopharmacological studies (Bond and Lader, 1994).

Digit cancellation.

This is a paper and pencil test that requires visual selectivity at fast speed on a repetitive motor response task. It assesses many functions including sustained attention. Visual scanning and activation and inhibition of rapid responses are also necessary for successful performance. Shum et al (1990) said that lowered scores on these tasks can reflect the general response slowing and inattentiveness of diffuse damage, acute brain conditions, specific defects of response shifting and motor

smoothness or of unilateral attention. With the addition of the motor component the test requires functions relevant to a complex test of attention.

The format consists of rows of numbers randomly interspersed with a designated target number. There are 400 numbers with 40 target numbers. The patient is instructed to cross out all the target numbers. The performance is scored for errors and for time to completion. A number of versions have been made of this test, (Bond and Lader, 1974).

Failure on the cancellation task seems to be associated with spatial neglect in patients with problems involving right hemisphere lesions and with difficulties in the temporal lobe processing of information of left hemisphere patients. Normal limits for scoring are a mean time of 51 seconds (Curran et al, 1993).

Tapper.

Tapping rate is used a measure of motor sedation (Frith, 1967). In the test the participants are required to press a computer key as quickly as possible for 60 seconds.

Simple reaction time test (skrt).

The test consists of 24 trials with a random inter-trial interval. Participants are asked to press the space bar as soon as they see the stimulus object (in this case a flower)

appear on the screen. This test is frequently used in experimental drug trials as a within-subject measure that is sensitive to any sedative effects.

Bodily symptoms scale (bss). See Appendix 7 for a copy of the scale.

The bodily symptom scale is constructed and completed in the same way as the mood rating scale. It consists of 14 visual analogue scales that cover all the main physical side-effects of methadone (Bond and Lader 1996).

Mood rating scale (mrs). See Appendix 8 for a copy of the scale.

A 17 item visual analogue mood rating scale, (Bond and Lader, 1974) was used to assess subjective feelings. For each item the participant had to mark the point along a 100 mm line that represented how he or she felt at that time.

Craving. See Appendix 9 - copy of questionnaire.

The questionnaire administered was the Tiffany Heroin Craving Questionnaire (1993). Scores on this 45 item questionnaire yield five components of craving: (1) desire to use heroin; (2) intention and plan to use heroin; (3) anticipation of positive outcome from heroin; (4) relief from withdrawal and dysphoria and lack of control over use. The participant has to rate each item on a 7 point scale from strongly disagree to strongly agree. The "Americanisms" were changed on some of the items and replaced by terms in more common use in Britain.

Coping Inventory For Stressful Situations (Endler, 1990).

The CISS is a development from the Multidimensional Coping Inventory (MCI). There are forty-eight items that isolate five types of coping styles; avoidance, distraction, social diversion, task orientated and emotion. The participant has to read 48 statements containing types of activities that they may engage in when encountering a stressful situation. The participant has to rate on a scale of 1 to 5, how much they engage in each of the activities.

Task orientated coping describes purposeful task-orientated efforts aimed at solving the problem, cognitively restructuring the problem or attempts to alter the situation. The main emphasis or focus is on the task, or planning and on attempts to solve the problem. Emotional-orientated coping describes emotional reactions that are self-orientated. The aim is to reduce stress (but this is not always successful) and the reactions include emotional responses that in some cases increase stress. The reaction is orientated towards the person. Avoidance- orientated coping describes activities and cognitive changes aimed at avoiding the stressful situation. This can occur via distracting oneself with other situations or tasks or via seeking social diversion (person orientated) as a means of alleviating stress.

The alpha reliability coefficients on each of the five sub-scales ranged between 0.72 and 0.90 in a sample of 536 adults. In a sample of 302 psychiatric patients the reliability co-efficients of the sub-scales ranged from 0.73 to 0.91 (Endler, 1990).

Suggestibility (Gudjonsson).

A new measure, the Gudjohnsson was employed. The format of the Gudjohnsson (1996) suggestibility scales is the same in version one and two. Both scales comprise a narrative paragraph containing a story of an event and twenty questions that ask about the story. Some of the questions are misleading. The scales are constructed in such a way that they can be used in any population, including people with learning difficulties.

The scales are presented as memory tests although as the real purpose is to determine whether or not someone tends to be influenced by others without being aware of it. Alerting the subjects to the fact that they are being asked misleading questions reduces the effects of the questions (Warren & Tubbs, 1991.) As in a real life situation subjects are not likely to be warned that they may be asked leading questions.

The subject listens to a tape recording of a story and is asked to freely recall all that they can remember. After this they are asked specific questions about the story. This focuses their minds without alerting them to misleading questions. The narrative passage containing each story is sufficiently long so that no participant can recall all the material in the story, but it is not so long that subjects with poor memory find the task too demanding. The questions are asked after delayed recall of the passage, so the subjects recall has had the opportunity of deteriorating. The leading questions are not immediately obvious to the subject.

The two main measurements are labeled as 'yield' 1 and 2 and 'shift'. Yield refers to the extent to which an individual 'yields' to various types of suggestive (cued) questions. For example, one of the questions is 'was the boy taken home by Anna or John?" The story presented does not mention such information and therefore the correct answer would be 'I don't know' or 'it wasn't mentioned'. This answer is labeled as yield one for example the participant would score 1 on the above question for answering 'Anna'. Yield 2 refers to the answers that the participant gives to the same questions once they have been given negative feedback at the end of the first asking of the questions telling them that they got some of the questions wrong. The score known as 'shift' can then be calculated which refers to the amount of answers that the participant has changed from time 1 to time 2 of answering the questions.

The questions used to obtain the yield and shift scores contain three types of questions: leading questions; affirmative questions and false alternative questions. The leading questions are selected in such a way as to be not too obvious that they are leading, because leading questions that embody a high degree of expectation are only applicable to subjects who are highly suggestible. Affirmative questions have no salient premises or expectations but they tend to have a certain suggestive effect in that they have an affirmative response bias (Sigelman, 1981). False alternative questions imply the presence of objects, persons and events that are not mentioned in the story. Non-suggestible questions are interspersed among the leading questions. These were 'true' questions where the correct answer was an affirmative one. They are not used in the scoring of 'Yield', but they are used to score 'shift'.

Additional information collected.

Rounsaville's (1981) study concluded that there were risk factors which suggested neuropsychological impairment would be more likely. These included the use of CNS (Central Nervous System) depressants; increased age; poor academic achievement and/or a history of accidents. All this information was therefore collected to see if these factors were associated with higher levels of impairment.

2.7 Procedure.

The study involved the collection of four sets of data on each participant at Time 1 - 4 inclusive, as shown below;

Research procedure - stepwise.

Time 1 - 'pre-drug' assessment

methadone or placebo (wait 3 hours)

Time 2 - 3 hours 'post drug' assessment

< Washout: 7 days>

Time 3 - assessment

as above methadone or placebo given (wait 3 hours)

Time 4 - post assessment

Administration order for measures used.

Time 1 and Time 3.

Rivermead behavioral memory test (RBMT) - immediate prose recall

mood rating scale

bodily symptoms scale

digit symbol test

Reaction time test

Tapping test

cancellation test

RBMT - delayed prose recall

Time 2 and Time 4.

Rivermead behavioral memory test (RBMT) - immediate prose recall

mood rating scale

bodily symptoms scale

digit symbol test

Reaction time test

Tapper

cancellation test

RBMT - delayed prose recall

suggestibility tests

craving questionnaires

'what were you given' questionnaire (see Appendix 10)

During the waiting time between test session one and two participants were asked to complete the NART, Coping Inventory for Stressful Situations (CISS) and a drug information questionnaire (see Appendix 11). During the second waiting period (between test session 3 and 4) participants watched a video.

2.8 Statistical analysis.

The data were analysed using Statistical Package for Social Sciences (SPSS). A series of analysis of variance (ANOVA'S) statistical tests were used to analyse the data, in addition to t-tests for unrelated samples (for comparisons with standardised population norms). No significant results were obtained using the series of ANOVA's. Had this not been the case and significant results were found a multivariate (MANOVA) analysis of variance would have been performed to isolate the significant main effects and the significant interactions. A stepdown analysis would have enabled the significant effects to be examined and the type 1 error rate controlled for.

3.0   RESULTS.

3.1 Demographic information about participants.

There were eighteen participants in total. Table 3 gives demographic details of the

participants. Overall the participants are broadly representative of the majority of

opiate users in treatment. They are in their late thirties, studies show that most opiate

users spend a long time in treatment, in contrast to stimulant users who present for

treatment at a younger age and who are discharged from treatment sooner, (The

Department Of Health review of drug services, 1996). Two thirds of opiate users in

treatment are also male as they are in the present research sample, (The Department

Of Health review of drug services, 1996).

Table 3 : Demographic details of participants.

age (years)	mean sd range	37.50 7.87 21 - 52
sex (%)	male female	78 22
employment (%)	unemployed unskilled professional	67 28 5
education (%)	no qualifications vocational qualifications O'Levels Graduates	50 11 17 22

67% of the sample are unemployed and 28% are in unskilled employment. This is

similar to most treatment populations. However, the research sample are more

educated than most treatment populations as a quarter of the sample have degrees,

although are not in professional employment. The high level of academic achievement

is also reflected in the NART test results which show the research sample IQ mean to

be 108.1, sd = 11.95, (the general population mean is 100 and the sd is 15) see Table

4.

Table 4:

Histogram to show NART I.Q. scores.
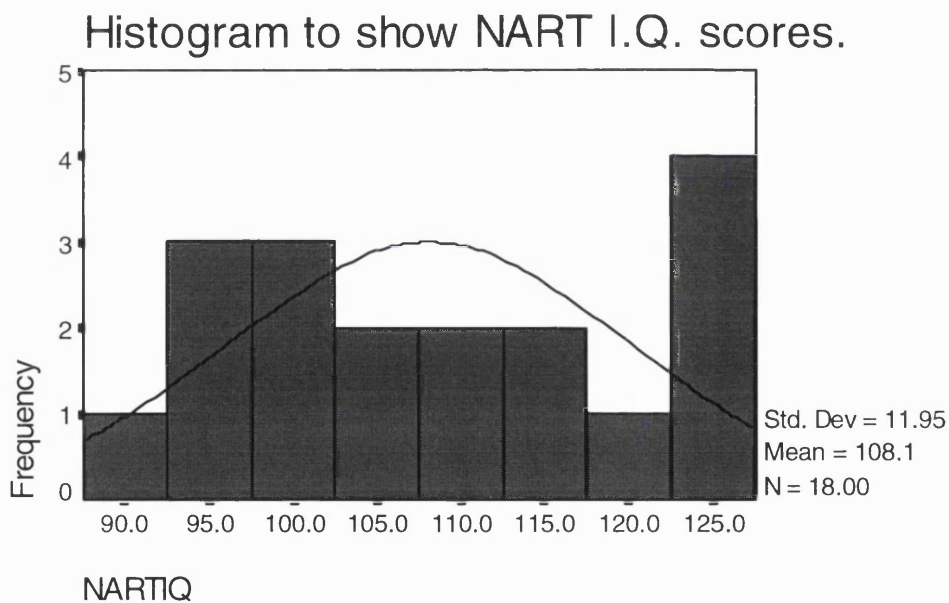
3.2 Participant's relevant medical history.

Each participant was asked specific questions concerning their medical history, the

results of which are shown in Table 5.

All the benzodiazepine users were prescribed diazepam for benzodiazepine

dependence. There were two cases with psychiatric history, both of whom had been

diagnosed by the psychiatrist at the addiction service as depressed. No participants

had a diagnosis of organic brain illness. This was one of the exclusion criteria for

participants, as organic brain illness can be associated with cognitive deficits. One

participant stated that he had two fits with a head injury as a result. These fits had not

been diagnosed as epileptic in nature and were more likely due to the effects of drug

intoxication. The head injury prevalence is low as other research studies have reported

high rates of head injuries amongst drug users, most likely associated with the high

levels of drug related criminal activity and the high prevalence of over-dose where

loss of consciousness can lead to head trauma.

Table 5: % of participants relevant medical history.

	% of participants	
participants taking any prescribed medication	None benzodiazepines	72 28
psychiatric history	no yes	89 11
diagnosis of organic brain illness (MS, epilepsy etc.)	no yes	100 0
history of head injuries with unconsciousness	no yes	94 6

3.3 Participants methadone use.

One of the sample reported that he does not always take his full prescribed methadone dose. The participant reported that he was trying to cut down and see on how low a dose he could manage. However, nearly a quarter of the sample use extra methadone on top of their prescribed dose. Of these people, three quarters of them brought additional methadone once a week when they took a single dose that was double their prescribed dose. For example, if their prescribed dose was 30mls, once a week they buy illicitly an extra 60mls.

The average daily prescribed methadone dose was 43.5 mls. This is a fairly low methadone dose as many maintenance treatment programs are based on doses of around 80mls. However it is in keeping with the policy of the service in which the study was based which is a low-threshold prescribing service where the goal is illicit opiate use abstinence and eventual total detoxification.

Table 6: % of participants - current methadone use.

Variable	% of participants	
Always take full prescribed methadone dose ?	yes no	94 6
Use extra non-prescribed methadone (A)	yes no	22 78
frequency of extra non-prescribed methadone in the sub-set who replied yes to above (A)	once a week every 2 days	75 25
Current daily prescribed methadone dose (mls)	mean sd range	43.50 16.23 20 - 80

3.4 Participants illicit drug use.

The frequency of participants illicit drug use was recorded (see Table 7). 67% of participants reported having used heroin in the last week. This is notable, especially as key-workers were asked to recruit their most stable clients for the research. The utilisation of methadone is as a substitute drug for heroin is questioned by this data. Participants reported drug use was validated by urinalysis that showed the high prevalence of opiate use (see Table 8).

Another frequently used drug was cannabis with nearly 34% of the sample using the drug 3 times a week or more often. Amphetamine use was less frequent than heroin. This accords with the notion that amphetamine users more often represent a different

sub-set of drug users who do not present for treatment with a primary opiate dependency.

The present sample, like most opiate users, are poly-drug users. In the sample, 72% of the participants had used at least one illicit drug in the last month. Only two participants reported no other drug use since starting the methadone treatment.

For most participants, history of poly-drug use was over a 2 - 5 year period (Table 8). Most subjects (89%) had also been using opiates for between two and five years. All subjects had been using methadone for a minimum of six months as stipulated in the inclusion criteria.

Table 7: % of participants reported frequency of illicit drug use in the last 5 years.

key.
2 x = twice per day
3 x wk. = three times a week
1 x mth. = one time per month
< 1 yr. = less than once in the last year.

drug type	no use	2 x day	1 x day	3 x wk.	2 x wk.	1 x wk.	1 x mth	1 x 2 mth	2 - 6 mth	7 mth - 1 yr.	< 1 yr.
cannabis	11		6	28	17	11				6	22
heroin		6			22	39	6	6		6	17
amphetamines	28					11			17		44
benzodiazepines (non-prescribed)	22				6			11	17		22
cocaine	33				6	6		6	6	6	39

Table 8: % of participants reporting different lengths of use of illicit drugs.

drug type	no use	1 year - 18 mths	18 mths - 2 yrs	2 - 5 yrs.
cannabis	11		6	83
heroin		6	6	89
amphetamines	28			67
benzodiazepines	28		11	56
cocaine	33			61

3.5 Urine screening results.

Urine results showed that 56% of the participants had taken different drugs before

testing at time one and a week later at time two. 17% of participants had taken the

same before both testing sessions and 27% had taken no illicit drugs before either

session, see Table 9.

Table 9: Urine results.

participant nos.	time 1 (methadone)	time 1 (placebo)	time 2 (methadone)	time 2 (placebo)
1	amphetamine	-	-	amphetamine
2	none	-	-	amphetamine cannabis
3	amphetamine cannabis	-	-	opiates cannabis
4	none	-	-	none
5	none	-	-	none
6	opiates cocaine	-	-	opiates
7	opiates	-	-	opiates cocaine
8	none	-	-	none
9	none	-	-	benzodiazepine
10	-	none	none	-
11	-	cannabis	cannabis	-
12	-	opiates	opiates benzodiazepine	-
13	-	none	none	-
14	-	opiates	opiates benzodiazepine	-
15	-	opiates	opiates	-
16	-	opiates	none	-
17	-	opiates	benzodiazepine	-
	-	none	opiates	-

Additionally urine results that were positive for opiate use were compared with

participants self-reported use of opiates, (see Table 10). Notably 27.8% of

participants had not reported their opiate use and their urine result was positive.

However, 11.1% reported opiate use in the last three days and their urine test result

was negative. Urine test results and participants self-reports of opiate using agreed in

61.1% of cases.

Table 10: Comparison between participants' reported opiate use and urine test results (excluding methadone).

opiates found in urine	self-reported opiate use (twice a week or more)	percentage of participants.
yes	no	27.78
yes	yes	16.67
no	yes	11.11
no	no	44.44

3.6 Alcohol screening results.

At the beginning of both testing sessions a breathiliser alcohol sample was taken. All

subjects were within normal limits with only one subject showing any alcohol reading

at all.

3.7 Participants expectations of likely cognitive effects.

Prior to beginning cognitive testing participants were asked to rate their expectations

as to what effect a third extra of their daily methadone dose would have on

concentration, memory and arousal. Their responses are recorded in Table 11.

Interestingly, an average of 83% of the participants thought that an extra third of

their daily methadone dose would have no cognitive or sedative effects whatsoever.

**Table 11: % of participants who expected cognitive and sedative effects from a
third increase in their daily methadone dose.**

Expected effects at third extra	concentration	tiredness	memory
worse	0	11	6
much worse	6	11	11
no change	88	78	83
better	6	0	0
much better	0	0	0

3.8 Cognitive and psychomotor neuropsychological tests.

Five tests were administered to each participant four times, i.e. before and after drug

and placebo at test sessions one and two: These included a simple reaction time test, a

motor speed test (finger tapping rate): digit symbol substitution test; digit

cancellation; prose recall (immediate and delayed). For list of means and standard

deviations see Tables 12.

Table 12: Means and standard deviations of tests Table administered four times.

test	pre methadone	post methadone	pre placebo	post placebo
skrt (reaction time). msec	317.17 (45.45)	311.78 (44.37)	305.67 (60.31)	315.67 (77.14)
tapper raw score (N taps)	355.89 (36.47)	344.39 (51.74)	356.06 (41.55)	351.95 (70.72)
digit symbol substitution test (N)	51.84 (10.45)	54.06 (10.44)	52.06 (11.94)	51.34 (10.64)
digit cancellation time (secs.)	73.77 (17.92)	71.29 (21.58)	68.14 (27.29)	66.93 (27.66)
prose recall immediate	10.45 (2.97)	7.00 (2.83)	7.86 (2.10)	7.20 (3.24)
prose recall delayed	6.72 (2.99)	6.28 (2.64)	6.72 (2.80)	6.34 (2.92)

A series of analyses of variance (ANOVAs) were performed to compare scores after methadone and placebo. This is summarised in Table 13. The group that had methadone as their first treatment (mean = 9.01) did significantly better on the immediate prose recall than the group that had placebo first (mean = 7.24).

Table 13: A series of ANOVA analyses of cognitive neuropsychological tests administered four times.

variable	group df (1,15)	drug/placebo df (1,15)	group by drug/placebo df (1,15)
digit symbol substitution test	F = 0.30, p= 0.59	F =1.48, p = 0.24	F = 0.07, p = 0.79
tapper reaction time test	F = 0.23, p = 0.64	F = 0.95, p = 0.34	F = 0.74, p = 0.40
digit cancellation test	F = 0.05, p = 0.83	F = 0.15, p = 0.71	F = 0.18, p = 0.68
prose recall immediate	F = 4.66, **p = 0.05**	F = 0.10, p = 0.76	F = 0.61, p = 0.45
prose recall delayed	F = 0.16, p = 0.7	F = 0.01, p = 0.93	F = 0.47, p = 0.50
skrt (reaction time test)	F =0.05, p = 0.82	F = 0.09, p = 0.77	F =1.24, p = 0.28

Test population mean comparisons.

The standardised scores on the Rivermead Behavioural memory test state that the minimum scores to pass the test are six for immediate memory recall and four for delayed memory recall. The research sample have mean scores above the minimum both before and after methadone showing that they are not generally impaired.

Despite the means of the memory test not changing as a result of methadone administration it is interesting to look at the raw data. The means of the research group are as high as the standardised norms, however when you look at the raw data you can see that there is a large amount of variation in scores. From a total of 72 test administrations (all subjects did the test four times), 22.22% of participants scored

lower than the standardised sample on immediate recall and 16.67% on delayed recall.

This amounts to nearly a quarter of participants actually having memory impairment.

The simple reaction time test (tapping rate) are frequently used in drug studies and are

not compared to standardised scores but are used as a measure sensitive to within

subject effects of drugs. In this case no significant difference was found in scores

before and after extra methadone administration.

The digit symbol test is one of the sub-tests used in The Wechsler Adult Intelligence

Scale (WAIS). The mean score for the present sample is 49.89 which gives a scaled

score of 11. The mean sub-test scaled score for the standardised population is 10 with

a standard deviation of 1 which means that the research group is within normal limits.

The digit cancellation test shows that the research group are rather slower than other

studies have found of normal subjects (e.g. Curran et al, 1993), see Table 14. This

task taps focused attention. It is possible that the sample's slow speed was in part at

least due to eye-coordination problems as methadone can affect ocular function

(Rothenberg, 1980).

Table 14: T-tests comparing study population means and standard deviations
with the research sample, on the cancellation test.

variable	research mean (sec.)	study mean (sec.)	df	t-value	p-value
cancellation test	72.07 (22.10)	51.00 (10.00)	17	3.65	**0.002**

3.9   The Bodily Symptoms Scale (BSS).

Means and standard deviations for ratings on each item of the BSS are given in Table 15, and Table 16 reports the result of the ANOVAs. There were no significant effects of drug on these ratings.

Table 15: Means and standard deviations of ratings on the bodily symptoms scale (bss).

scale variables	pre methadone	post methadone	pre placebo	post placebo
restlessness	25.67 (23.32)	21.50 (13.56)	29.39 (21.63)	26.28 (27.41)
irritability	22.45 (22.76)	15.34 (16.77)	25.61 (22.00)	19.84 (19.11)
tiredness	42.45 (28.78)	35.72 (23.30)	40.06 (31.68)	32.00 (27.89)
lack of energy	29.78 (16.36)	34.17 (15.26)	33.06 (22.68)	30.28 (23.08)
concentration	31.06 (20.60)	31.22 (18.92)	27.78 (21.93)	24.00 (21.68)
headache	10.89 (7.35)	13.28 (13.62)	8.34 (13.08)	9.06 (10.37)
short of breath	18.06 (24.52)	16.50 (21.99)	14.78 (10.17)	12.23 (9.51)
dry mouth	26.00 (33.71)	24.28 (26.65)	19.61 (23.06)	14.17 (10.73)
nausea	5.50 (5.34)	11.78 (12.06)	13.34 (15.95)	10.39 (8.24)
anxiety	30.12 (33.25)	29.39 (29.22)	20.17 (15.20)	17.50 (12.96)
sweating	28.89 (28.60)	28.34 (29.76)	25.28 (31.29)	40.56 (32.35)
blurred vision	17.67 (16.52)	19.00 (14.40)	16.34 (14.90)	18.11 (12.19)
depression	30.89 (27.86)	31.61 (28.67)	22.56 (16.36)	19.95 (17.18)
agitation	25.56 (33.43)	28.17 (33.10)	20.67 (16.56)	17.06 (16.03)

Table 16: A series of ANOVA analyses of the bodily symptom scale.

variable	groups df (1,16)	drug/placebo df (1,16)	group by drug/placebo df (1,16)
restlessness	F = 0.04, p = 0.84	F = 0.05, p = 0.83	F = 0.05, p = 0.83
irritability	F = 0.15, p = 0.71	F = 0.17 , p = 0.69	F = 0.85 , p = 0.76
tiredness	F = 2.09, p = 0.17	F = 0.65 , p = 0.43	F = 0.97 , p = 0.34
lack of energy	F = 2.81, p = 0.12	F = 0.22 , p = 0.64	F = 0.22 , p = 0.64
concentration	F = 0.25, p = 0.62	F = 2.11 , p = 0.17	F = 2.84 , p = 0.12
headache	F = 0.74, p = 0.40	F = 1.87 , p = 0.19	F = 1.20 , p = 0.29
short of breath	F = 0.14, p = 0.72	F = 1.05 , p = 0.33	F = 1.28 , p = 0.28
dry mouth	F = 1.33, p = 0.27	F = 0.09, p = 0.76	F = 0.06 , p = 0.82
nausea	F = 0.09, p = 0.77	F = 2.13, p = 0.17	F = 0.28, p = 0.60
anxiety	F = 0.45, p = 0.83	F = 1.54, p = 0.24	F = 0.95, p = 0.35
sweating	F = 0.01, p = 0.92	F = 0.68, p = 0.43	F = 1.46, p = 0.25
blurred vision	F = 0.34, p = 0.57	F = 0.34, p = 0.57	F = 0.05, p = 0.83
depression	F = 0.15, p = 0.70	F = 2.03, p = 0.18	F = 0.08, p = 0.78
agitation	F = 0.01, p = 0.94	F = 0.01 , p = 0.97	F = 0.02, p = 0.88

3.10   The mood rating scale (mrs).

The means and standard deviations for each of the 17 visual analogue scales are given

in Table 17 with ANOVA results in Table 18. There were no main effects of either

group or drug treatment. Two significant group by treatment interactions emerged.

These were on (a) troubled - tranquil and (b) incompetent - competent. The means of

both groups on these two variables are given in Table 19. Those who received

methadone as the first treatment were more tranquil and changed their "troubled"

ratings less on the second test occasion than those who received placebo first. Those

given methadone first rated themselves more competent and change less pre to post

treatment than those given placebo first.

This result has to be interpreted with caution given the number of comparisons of

scores. Findings of two significant effects may well be a Type 1 error.

Table 17: Means and standard deviations of ratings on the mood rating scale (mrs).

scale variables	pre methadone	post methadone	pre placebo	post placebo
alert	27.61 (12.52)	39.67 (18.57)	32.34 (18.03)	31.72 (17.18)
calm	29.89 (30.50)	23.22 (16.11)	28.28 (16.75)	24.50 (19.68)
strong	33.34 (23.37)	35.17 (20.43)	39.22 (18.93)	31.56 (17.13)
muzzy headed	62.50 (24.69)	55.28 (24.84)	52.00 (20.96)	58.62 (19.07)
coordinated	33.61 (21.87)	36.45 (14.03)	35.50 (20.38)	29.17 (15.46)
lethargy	45.45 (20.74)	47.78 (23.29)	48.00 (14.83)	56.39 (19.21)
contented	42.34 (25.40)	37.22 (25.18)	47.00 (24.42)	26.22 (17.75)
troubled	50.95 (21.90)	59.50 (15.81)	47.50 (28.21)	63.17 (23.14)
mentally slow	51.61 (29.21)	52.34 (27.38)	51.00 (26.20)	63.78 (16.89)
tense	57.67 (30.27)	64.28 (29.10)	53.95 (26.59)	65.23 (23.15)
attentive	42.11 (32.28)	46.95 (21.08)	42.11 (15.15)	35.17 (18.29)
incompetent	58.78 (23.74)	61.34 (21.59)	63.33 (21.08)	66.72 (13.94)
happy	40.89 (26.99)	41.45 (19.39)	39.84 (17.42)	35.28 (16.14)
antagonistic	75.73 (18.46)	73.39 (17.89)	68.94 (17.93)	73.83 (15.70)
interested	34.17 (24.74)	39.17 (17.82)	33.34 (18.65)	30.44 (13.59)
withdrawn	55.22 (27.18)	57.84 (25.06)	53.11 (15.76)	65.50 (19.13)
stoned	78.78 (16.85)	71.72 (18.27)	78.95 (19.87)	73.62 (23.80)

Table 18: A series of ANOVA analyses of the mood rating scale.

variable	groups df (1,16)	drug/placebo df (1,16)	group by drug/placebo df (1,16)
alert	F = 2.11, p = 0.17	F = 0.20, p = 0.66	F = 3.66, p = 0.08
calm	F = 0.06, p = 0.81	F = 2.33, p = 0.15	F = 0.30, p = 0.59
strong	F = 0.06, p = 0.94	F = 0.66, p = 0.43	F = 1.00 , p = 0.34
muzzy	F = 0.04, p = 0.85	F = 0.03 , p = 0.87	F = 0.42 , p = 0.53
co-ordinated	F = 0.13, p = 0.73	F = 0.12 , p = 0.73	F = 0.01 , p = 0.93
lethargy	F = 0.87, p = 0.36	F = 0.03 , p = 0.86	F = 0.01 , p = 0.98
contented	F = 0.34, p = 0.57	F = 2.15 , p = 0.17	F = 0.49 , p = 0.49
troubled	F = 0.29, p = 0.60	F = 0.95 , p = 0.35	F = 5.18 , **p = 0.04**
mentally slow	F = 0.17, p = 0.68	F = 1.95, p = 0.19	F = 1.76 , p = 0.21
tense	F = 0.06 , p = 0.81	F = 1.11 , p = 0.31	F = 0.40, p = 0.54
attentive	F = 0.35, p = 0.56	F = 0.01, p = 0.97	F = 0.02 , p = 0.88
incompetent	F = 0.56, p = 0.47	F = 0.37, p = 0.55	F = 6.05, **p = 0.03**
happy	F =0.22 , p = 0.65	F = 0.25, p = 0.63	F = 1.30, p = 0.27
antagonistic	F = 1.14, p = 0.30	F = 0.03 , p = 0.86	F = 0.12 , p = 0.74
interested	F = 2.21, p = 0.16	F = 0.22 , p = 0.64	F = 0.67, p = 0.43
withdrawn	F = 0.22, p = 0.64	F = 2.16 , p = 0.17	F = 0.90, p = 0.36
stoned	F = 0.18, p = 0.67	F = 0.85 , p = 0.37	F = 0.14, p = 0.72

Table 19: Means and standard deviations of group 1 (methadone first/placebo second) and group 2 (placebo first/methadone second) mrs variables 'troubled' and 'incompetent'.

group	variable	pre methadone	post methadone	pre placebo	post placebo
1	mrs troubled	57.22 (25.69)	62.44 (22.90)	50.00 (31.86)	61.33 (30.12)
1	mrs incompetent	58.33 (27.47)	57.78 (25.69)	60.44 (15.02)	62.33 (14.28)
2	mrs troubled	44.67 (18.11)	56.56 (8.71)	45.00 (24.56)	65.00 (16.16)
2	mrs incompetent	59.22 (20.01)	64.89 (17.48)	66.22 (27.13)	71.11 (13.60)

<u>Post tests.</u>

Suggestibility and craving questionnaires were administered twice once after the

methadone dose and once after the placebo dose.

3.11 Suggestibility.

Suggestibility scores are classified as a (1) **shift** score ; (2) **yield** scores, 1 and 2 and

(3) a **total** score. For means see table 20. ANOVA see table 21. Comparison with

population means Table 22.

Table 20: Mean scores of suggestibility tests.

suggestibility test variable	post methadone		post placebo	
yield 1	mean	3.17	mean	2.89
	sd	1.62	sd	1.53
	range	0 - 5	range	1 - 6
yield 2	mean	5.5	mean	5
	sd	2.5	sd	1.57
	range	1 - 10	range	2 - 8
shift	mean	2.89	mean	2.72
	sd	2.49	sd	2.11
	range	0 - 9	range	0 - 9
total	mean	5.94	mean	5.67
	sd	3.23	sd	2.81
	range	1 - 12	range	2 -12

Table 21: ANOVA analyses of suggestibility tests.

variable	group df (1,16)	drug/placebo df (1,16)	grp by drug/placebo df (1,16)
yield 1	F = 0.01, p = 0.94	F = 2.33, p = 0.15	F = 0.09, p = 0.76
yield 2	F = 0.17, p = 0.68	F = 1.71, p = 0.21	F = 0.19, p = 0.67
shift	F =3.51, p=.08	F = 0.31, p = 0.59	F = 0.31, p = 0.59
total	F = 1.40, p =0.25	F = 0.53, p = 0.48	F = 0.02, p = 0.89

Table 22: T test comparing standardised means and standard deviations for suggestibility test with study sample means.

variable	study sample mean	standardised mean	df	t-value	p - value
yield 1	2.89 (1.58)	4.60 (3.60)	17	4.75	**0.001**
yield 2	5.00 (2.04)	5.60 (3.80)	17	1.62	0.12
shift	2.72 (2.30)	2.90 (2.50)	17	0.36	0.73
total	5.67 (3.02)	7.50 (4.60)	17	2.77	**0.01**

Interestingly the study sample were significantly different from the general population on yield 1 and total suggestibility scores. The variance in the yield score accounts for the difference in the total score. This suggests that drug users are less likely to yield (i.e. give a false answer or change their answers to questions that are suggestible, questions with a bias toward a particular answer) after being told that they have some answers wrong and that overall they are less suggestible than the general population.

There were no significant differences in drug treatments; although there is a trend (p = 0.08) on the shift score and which treatment was given first. The group that received

methadone first had mean score of 1.89 compared to the group that had placebo first

having a mean score of 3.89.

3.12 Craving

Scores on the craving questionnaire are divided into five factors; desire to use;

intention to use; anticipation of positive outcome; relief from withdrawal or dysphoria

and lack of control. For means of each factor see Table 23 (higher scores indicate

greater craving). ANOVA see table 24. The variance in craving scores is higher post

placebo than post methadone.

Table 23: Mean scores of craving tests.

craving test factor	post methadone		post placebo	
anticipation of positive outcome	mean	39.06	mean	32.78
	sd	8.80	sd	11.96
	range	27 - 60	range	9 -52
lack of control	mean	36.89	mean	33.67
	sd	6.56	sd	8.79
	range	28 - 56	range	13 - 47
desire to use	mean	23.67	mean	18.50
	sd	6.81	sd	8.98
	range	15 - 38	range	9 - 50
intention to use	mean	30.72	mean	30.56
	sd	7.28	sd	11.40
	range	18 -50	range	9 - 43
relief from withdrawal	mean	36.56	mean	30.56
	sd	6.88	sd	11.40
	range	26 - 53	range	10 - 48
total craving score	mean	166.89	mean	142.56
	sd	22.34	sd	43.25
	range	127 - 199	range	53 - 228

Table 24: ANOVA analyses of craving tests.

variable	group df (1,16)	drug/placebo df (1,16)	grp by drug/placebo df (1,16)
anticipation of positive outcome	F = 1.60, p = 0.23	F = 5.34, **p = 0.03**	F = 2.23, p = 0.16
lack of control	F = 0.65, p = 0.43	F =1.76, p = 0.20	F =1.01, p = 0.33
desire to use	F =1.88, p = 0.19	F = 4.18, p = 0.06	F = 6.17, **p = 0.02**
intention to use	F =1.22, p = 0.29	F =2.30, p = 0.15	F = 2.44, p = 0.14
relief from withdrawal	F =1.68, p = 0.21	F = 4.98, **p = 0.04**	F =1.54, p = 0.23
total craving score	F = 2.43, p = 0.14	F = 5.56, **p = 0.03**	F = 2.11, p = 0.17

Significant differences were found between two craving variables; 'anticipation of positive outcome' and 'relief from withdrawal or dysphoria'. Both were higher after methadone administration and suggest that methadone potentially increases subjects craving for heroin.

Higher relief from withdrawal or dysphoria includes participants ratings of nausea, calmness, concentration, hot and cold flushes, tension and depression. A higher score means that participants attribute feeling better on the above measures if they were to use heroin.

Similarly, a higher anticipation of positive outcome score means that participants rated themselves as potentially feeling pleasant, happier, satisfied, contented and having more energy if they were to use heroin right now.

Desire to use heroin scores were also significant according to whether participants

had methadone or placebo first (p = 0.02). The group that had methadone first had a

mean score of 19.07, the group that had placebo first had a mean score of 23.12.

Interestingly desire to use scores were also higher post extra methadone

administration although not quite reaching significance (p = 0.06). With such a near

significance score it is likely that with a larger sample size significance would be

reached, showing that a small increase in methadone dose does increase craving for

heroin.

Table 25: Means and standard deviations of group 1 (methadone first/placebo second) and group 2 (placebo first/methadone second) Heroin Craving Questionnaire - desire to use variable.

Group	post placebo	post methadone
1	13.33 (6.06)	24.78 (7.61)
2	23.67 (11.90)	22.56 (6.00)

There was no significant difference found in either 'lack of control' or 'intention to

use' factors.

Craving scores were not correlated with either the dose of methadone that the

participant received or the amount of additional opiates they were using (measured by

positive urine results).

3.13 Participants' opinion of whether they were given methadone or placebo.

There were a total of thirty six treatment presentations, i.e. eighteen subjects attending two sessions, one session where they had methadone and one where they had placebo. Participants correctly identified that they had methadone or not in 38.9% of cases. In 36.1% of cases, participants were incorrect about whether they had received methadone or placebo. In 25% of cases participants stated that they were unsure which treatment they had received. The similarity of rates of correct and incorrect treatment guesses means that participants could not differentiate between treatments. It also provides strong evidence that the double-blind procedure had held for participants who could not tell any difference between the methadone drink and the methadone vehicle drink.

The mean score on participants' self-rating of how sure they were about whether they knew if they had been given methadone or placebo was 67.40, sd = 22.30. This was measured on a visual analogue scale. How certain they were was independent of accuracy of their prediction.

3.14 Coping Inventory results.

The CISS is divided into five main coping types: avoidance, distraction, emotion, social diversion and task orientated coping. For means of participants coping responses see Table 26. The standardised test means are separated into male and female because in the standardised sample there were significant differences between

men and women on the different types of coping styles measured by the inventory. In the present study sample, t-tests were performed comparing males and females and no difference was found between the two groups. A trend (p = 0.08) emerged toward emotional coping with females scoring higher as suggested in the literature on coping differences between genders. However, the sample had a much smaller number of females than males and so had little power to detect a difference. The research sample was therefore added together and treated as one group and compared to the standardised sample, also treated as one group. There was a highly significant (p<0.001) difference between the research and the standardised sample on task orientated and social diversion coping variables (Endler, 1990).

Methadone maintenance participants were much less task orientated in their coping. Social diversion as a coping style was also less used by the research group than the normal population.

A trend (p = 0.09) emerged whereby the methadone maintenance participants also used avoidance coping slightly less than population norms. There was no coping style the research group used significantly more than the population norms, although inspection of the means in Table 28 suggests somewhat greater use of emotion based coping.

Table 26: Coping Inventory (CISS) research sample means.

coping response	participants scores	
avoidance	mean	39.06
	sd	5.55
	range	32 - 53
distraction	mean	19.72
	sd	3.72
	range	16 - 31
emotion	mean	44.00
	sd	9.32
	range	29 - 73
social diversion	mean	12.17
	sd	2.55
	range	8 -18
task orientated	mean	45.06
	sd	8.21
	range	24 - 65

Table 27: Difference between male and female coping scale responses.

coping scale variable	research sample male mean (sd)	research sample female mean (sd)	df	t-value	p-value
avoidance	38.57 (4.45)	40.75 (9.14)	16	0.68	0.51
distraction	19.14 (2.54)	21.75 (6.60)	16	1.26	0.23
emotion	41.93 (6.55)	51.25 (14.71)	16	1.89	0.08
social diversion	12.21 (2.55)	12.00 (2.94)	16	0.14	0.89
task orientation	45.57 (9.22)	43.25 (2.87)	16	0.49	0.63

Table 28: T-test analysis comparing coping inventory standardised means and standard deviations with research sample.

variable	study sample mean (N = 18)	standardised mean (N = 537)	df	t-value	p-value
avoidance	39.06 (5.55)	41.41 (9.92)	17	1.80	0.09
distraction	19.72 (3.72)	19.01 (5.71)	17	0.81	0.43
emotion	44.00 (9.32)	40.89 (11.45)	17	1.42	0.18
social diversion	12.17 (2.55)	14.97 (4.30)	17	4.67	**0.001**
task orientated	45.06 (8.21)	58.58 (9.30)	17	6.99	**0.001**

3.15 Summary of results.

1. 11% of the participants had a co-morbid psychiatric illness.

2. 22% of participants used additional methadone to their prescribed daily dose. The average daily prescribed dose was relatively small, (mean = 43.5 mls).

3. 67% of participants had used heroin in the past week. 34% of the sample were frequently using cannabis .

4. 27.8% of particpants did not report any opiate use (excluding methadone) but had a positive urine screen (considered sensitive to opiates taken within the last 72 hours).

5. 83% of participants thought that a third increase in their daily dose would have no significant cognitive or sedative effect on them.

6. Additional methadone did not significantly alter any aspects of psychomotor or cognitive functioning.

7. Research sample participants varied from the standardised population sample on digit cancellation task only.

8. Methadone had no effect on participants physical symptoms ratings and only a very small effect on two mood symptom ratings. Methadone increased participants feeling 'troubled' and more 'incompetent'. There were also differences between groups, i.e. whether they had methadone or placebo first, with the methadone first group rating higher tranquillity and competency and changing those ratings less than the group who had placebo first.

9. Craving was effected by methadone. After methadone administration participants craved heroin more. The two significant sub-sets of the craving tests were anticipation of a positive outcome from using heroin and that using heroin would relieve withdrawal or dysphoria. Desire to use heroin almost reached significance (p=0.06) and with a larger sample size would likely reach significance. This shows that a small additional dose of methadone increases peoples desire to use heroin.

10. Participants were less suggestible than the general population although suggestibility was not effected by methadone.

11. Coping skills were significantly different from the general population. The sub-tests of the questionnaire that they differed include task orientated coping and social diversion, with the research sample employing greater use of these coping strategies.

4.0   **DISCUSSION.**

In this discussion chapter I will begin by reviewing the results on craving, coping and

suggestibility and then go on to look at methodological issues, clinical implications,

further research and conclusions.

4.1   Craving

This is the first controlled study to show that an increase in methadone can increase

craving. There are reports that doses above 80mgs reduce cravings but the data is

obtained by clinical observation and the assessment of illicit drug use. Craving has

not been previously measured and quantitatively defined and correlated with an

increase in methadone dose.

Dole (1966) stated that methadone eliminates the euphoric appeal of heroin. In fact

methadone does not give the euphoric effect that heroin does because it has a

different pharmacological action. However, this is not the same thing as reducing

people's desire for the euphoric effect that heroin does give. It is this desire that is the

essence of heroin craving.

Methadone has been described as having a two-fold effect. Firstly it is thought to

reduce the craving for heroin use per se and secondly it blocks the euphoric effects of

other drugs if they are used in conjunction with methadone. In this way additional

illicit drug use is not reinforcing if used with methadone. This is similar to the way

that antabuse (disulfiran) works in the treatment of alcohol abuse, but not so extreme. Antabuse makes the user violently ill if alcohol is used at all, whereas methadone impedes the action of heroin.

The effect described above is thought to occur at doses of between 80 and 120mgs per day. This dose ensures tolerance to the narcotic effect of opiate class drugs is held at a level high enough to block the euphoric effects of the patient using other drugs.

One potential explanation for the increase in craving found in the present study is that methadone acted as a primer for craving heroin, in the same way that one alcoholic drink can prime a craving for more alcohol or the way cigarettes can act as a primer for alcohol. Tiffany's (1990) research highlights the definitive link between cigarette smoking and relapse of alcoholics.

A more likely explanation is that the methadone dose the study participants were receiving is not high enough to control heroin craving and that any heroin use is reinforcing as it produces the craved euphoria (for fuller discussion of dose effects see below). This would also explain the participants' positive expectations for heroin use and a improvement in feelings of dysphoria. The finding that craving is not correlated in this study with daily methadone dose or extra illicit drug use seems to contradict the proposed explanation. However, on closer inspection it is possible that this is because only one subject is on the minimum dose recommended by research to stop cravings, i.e. 80mgs (Ball and Ross, 1991). The doses are therefore too small to have

any effect on craving and so many of the participants are using additional methadone and/or heroin. Therefore similarly additional drug use is not correlated with craving.

Although the above explanation seems the most likely it cannot be eliminated that the reverse is true and that craving does increase with an extra methadone dose. This would not explain previous research that extra illicit drug use reduces the higher the patient's methadone dose but it cannot be discounted as a possible conclusion from this research. The other interesting data from the craving questionnaire is that lack of control and intention to use variables were not significantly affected by methadone. The explanation could be that craving is operating at two separate levels, i.e. the participants consciously feel in control of their desire and intention to use heroin (the behavioural component), however, in their subconscious and at a more affective level they still have cravings for heroin which manifests as seeing the hypothetical experience of using as positive and as providing relief.

Unfortunately despite the author of the craving questionnaire being contacted no standardised norms are available to compare with the scores obtained in this research.

4.2 Coping.

Coping is a neglected area of psychological research with drug users. Further research into the area would be interesting to ascertain the role of drug users' coping strategies in the aetiology of drug use. For example, does a pattern of coping strategies make using drugs more likely ? Prochaska and DiClemente (1992) have incorporated

concepts of coping within their theory concerning the maintenance of drug use. They describe the maintenance of drug use as a strategy based upon a learnt behaviour, so that when under pressure the client uses drugs to deal with the situation. The treatment they advocate involves drug users recognising that when they are under pressure a relapse becomes more likely.

In the research no significant differences were found between men and women, probably due to the sample size being too small, but a trend towards females using more emotional coping styles suggests that the sample are representative of the standardised population. However, the research sample were significantly less task orientated and used less social diversion coping strategies than the normal population. This is consistent with the presentation of drug users who in treatment frequently report that they have no other strategies available to them except drug using. They report finding social or any other activity hard without using drugs. Therefore, as a reflection of their total life-style difference from the standardised sample, the coping strategies they adopt also differ. This has been recognised within drug treatment services where relapse prevention groups are run with the remit of discussing and suggesting alternative coping strategies to using drugs.

4.3 Suggestibility.

The significant difference between methadone patients and population norms in sub-test yield 1 suggests that drug users are less likely to yield (i.e. give a false affirmative answer to a variety of questions in an interview situation) than the general population.

It could therefore be proposed that any inaccuracies of drug users' reports are more likely to be deliberate than influenced by the questioner. Additionally this result could imply that high criminal figures amongst drug users are more likely to be as a result of actual criminal activity and not false confessions.

The extra methadone did not alter clients' suggestibilty. This could be due to one of two reasons. Either the methadone dose is inadequate to cause change as with the cognitive tests. A more likely explanation is that suggestibilty is a trait rather than state characteristic, i.e. it is a relatively enduring feature that will not alter or vary in different situations.

4.4 Methodological issues.

With this client population, research can be very difficult for a variety of reasons, including both unreliability and uncooperativeness. The double-blind research design used here worked well and this is a very sensitive design to elicit acute on chronic drug effects. Further, unlike many studies in this field, urinalysis was used to check self-report measures. One methodological problem was that 56% of participants had taken different drugs before test session one and two. Therefore, despite the fact that baseline measures were recorded, there could conceivably be an effect of the other drugs used in terms of an interaction with additional methadone. This is an unavoidable problem when patients are using other drugs in addition to methadone and one which reflects the real life clinical issues of this polydrug abusing population. Even in-patient studies cannot guarantee one avoids this problem.

The non-significance of an increased dose on any of the psychomotor cognitive tests warrants discussion. This could be due to the lack of cognitive effects of methadone but is more likely due to the very small extra dose of methadone given. The dose was calculated at a third of participants usual prescribed dose but this does not take into account that 22% of participants use extra methadone and 67% of participants had used heroin in the last week. Given clients' actual opiate intake, a 33% increase in their daily dose of prescribed methadone would be a much smaller increase in terms of total opiate intake. Clearly the lack of significant effect reflects both this dosage issue and the tolerance these clients had built up over years of opiate use. With this information, it is clear that a third increase in prescribed dose is insufficient to see any effects. Interestingly, the participants themselves reported their tolerance to methadone or any opiates is high and felt that the increase would not affect their level of arousal, concentration or memory.

The study design is very sensitive to any effects of drugs and has been used in other drug research studies (e.g. with patients on long-term benzodiazepine treatment for anxiety) where significant effects were found (Bond and Lader, 1991; Curran, 1992). It is likely therefore that the design and measures used are appropriate but that the dose given was not. A clinical pharmacologist was consulted about the dose and suggested a minimum of fifty and maximum of hundred percent increase in dose. However ethics committee applications produced disparate dosage recommendations about a 50% increase (one committee approving, the other feeling it was too high).

The risk of respiratory depression and patient overdose in these ambulant participants was a clear concern and a third increase was agreed upon.

In general the sample used was a good representation of drug users in treatment in the service used to recruit participants. However, the sample were biased in terms of having higher than usual educational achievements and consequent higher than expected I.Q. scores. However, this bias should not have effected the study design because of the baseline scores that are obtained before the drug is administered in the within subjects design.

4.5 Clinical implications.

Methadone maintenance as a treatment for heroin addiction.

There is an apparent paradox in the treatment of heroin users whereby many NHS treatment services offer compulsory abstinence based programmes. This paradox arises because of splitting in the medical and allied social science professions as to the whether heroin addiction is a chronic relapsing condition that addicts will battle with for the rest of their lives or an "illness" that can be treated and eradicated. What makes people come forward for treatment is the subsequent consequences that arise because of the drug use. These disadvantages may, at the beginning of drug use, seem to be advantages. For example, time is employed by most heroin users in a continual search for money and drug supply, this leads to associated criminal activity,

loss of relationships and breakdown of physical health. Initially the activity provides a structure to the day and an escape from day to day activities.

Some users may be in treatment as they have no other choice as the courts have made an instruction for compulsory treatment. One of the main obstacles facing drug services is the high relapse rates in drug users once treatment has ended. It may be that services are providing something more than just methadone, a structure or focus for drug users.

An American study found that it is not the patient characteristics that vary with regard to treatment effectiveness but the service provision (Kreek 1983). More effective treatments have high patient attendance rates and a close, consistent and enduring relationship between staff and patient. Conversely the less effective treatment programs are characterised by poor patient attendance, inadequate methadone medication and high rates of staff turnover.

It must be remembered when talking about service provision that patient characteristics and presenting problems continually change. For example, disease entities have altered with the problems due to hepatitis and HIV and their associated psychosocial sequalae. Additionally there have been changes in drug availability and fluctuations in type of drug popularity. The 1990's have seen an increase in the popularity of stimulant drugs such as MDMA (ecstasy). Social structures also change as employment and housing availability varies. The problem with treatment approaches based solely on abstinence from heroin use and the physiological

component of addiction alone is that the approach ignores the social network surrounding drug use, in addition to the potential aetiology of drug use.

Treatment centres seem to be divided by high and low dose criteria for methadone prescribing. This is conceptualised as being analogous to overindulgent parents supplying too much vs. the careful, overprotective parent not giving enough. There is a need for the philosophy of methadone prescribing to take on board the concept of an adequate methadone dose and this point will be expanded upon below. Overall the aim should be for methadone maintenance to be available for as long as is desired by the patient and as long as continuing benefit is derived from treatment.

There is a large amount of literature on the philosophy of treatment approaches relating to abstinence or maintenance prescribing practices. One of the main questions is the extent that this philosophy effects patients retention in treatment. If methadone is considered to be the treatment of choice for heroin addiction then it is essential that treatment is maintained. For example, the reported health benefits from methadone treatment include reduced injecting and the subsequent reduction in HIV and Hepatitis risk. Caplehorn (1996) reported that physicians' commitment to abstinence-orientated policies was highly correlated with patients' premature discharge. In another study, Caplehorn (1994) also found that abstinence orientated treatment centres are also less able to attract heroin users into treatment.

The efficacy of methadone maintenance treatment can only be established by thorough outcome studies. A recent American report is asking for more outcome studies to be

performed on all aspects of methadone maintenance. The nature of the American health care system means that it is more market driven than the British NHS and therefore insurance companies that have to pay large sums for methadone treatments and are questioning the evidence as to its value. They are looking in the future toward more integrated physical health care at methadone treatment units and vocational training and job placements are seen as critical treatment components and outcome measures to monitor treatment success. Further work is also needed that looks at the intergenerational drug use by implementing parenting skill groups and family therapy throughout treatment settings.

The question of how to measure treatment success is a complex one. Is success defined as: decreased illicit drug use; improved physical and emotional health; decreased anti-social activities or improved social functioning ? Most people would say that it is a combination of all of the above, but that there needs to be a change in the practice of outcome measurement from performance measures to process orientated reviews. Process orientated reviews focus on the method that outcome variables are achieved. The main problem is that there is no agreement as to what constitutes successful outcome and before outcome can be measured treatment objectives need to be clarified.

Despite poly-drug use the aim of methadone treatment is to achieve a sufficient methadone dose to stabilise the patient and retain the patient in treatment as longer treatment episodes are correlated with increased success (Hubbard et al, 1989). It

must be remembered that there are few compelling reasons to discharge a patient from treatment in the light of the risk of HIV and other health related complications.

Methadone maintenance doses.

There still seems to be confusion and inadequate knowledge about methadone dosage. As early as 1966, Dole stated that; "At present, the most that can be said is that there seems to be a specific neurological basis for the compulsive use of heroin by addicts and that methadone taken in optimal doses can correct the disorder. The proper methadone dose is one that prevents ongoing heroin use. Many methadone treatment units persist in using sub-therapeutic maintenance doses". Research studies have shown that the higher the methadone dose the lower the elicit heroin use (Ball and Ross, 1991). An additional facet of methadone dose is its effect on treatment retention. Capelhorn and Bell (1991) found that the level of dose was the single most important factor in retention in treatment programmes.

Wolff et al (1991) found a linear relationship between methadone dose and methadone concentrations in the plasma, i.e. a optimum blood level and optimum dose effect. The mean plasma levels of methadone at the 80mg dose are very close to the 400ng/ml suggested as ideal for treatment effectiveness. Their study recommends a dose calculated on an individual basis following the stage approach in Table 29.

Table 29: Recommended dose ranges over the course of treatment (determined on an individual basis).

phase	purpose	range
initial dose	relieve abstinence symptoms	20 - 40 mg
early induction	reach tolerance threshold	+/- 5-10 mg (3-24 hours)
late induction	establish adequate dose (desired effects)	+/- 5-10 mg (5-10 days)
maintenance	maintain desired effects	usually 80 +/- 20 mg (may be more than 100 mg or less than 50 mg)

One of the main obstacles to clinicians adequately prescribing methadone is their fear of overdose if patients continue to use other drugs. Another fear is that there will be an increase in the selling of methadone to secure heroin. There is also a risk to children of methadone users as it is potentially lethal to children if taken by mistake.

This research validates other research projects in that one of the potential explanations for the high amount of other drug use is the insufficient methadone dose that participants were being supplied. This may also account for their increased craving for heroin once given an additional dose.

Poly-drug abuse.

One of the main problems is that there is a high frequency of opioid dependence and conjoint other drug use. One of the main causes of death amongst drug users is the combination of alcohol, prescribed methadone and other illicit drug use. Stimulant use is high amongst heroin users and can be expected to persist independently of methadone prescribing as methadone does not treat stimulant dependence and stimulants have a different pharmacological action. Research has found that cocaine use and methadone use together is especially high (Kosten et al, 1990) and that when a reduction or abstinence from heroin use occurs the risk of increased cocaine use is high. Patients turn to cocaine use as heroin stops giving a euphoric effect if methadone is taken in a large enough dose. Another possibility is that cocaine is a CNS stimulant and that methadone users are self-medicating to counter-balance the sedative effects of methadone. One further explanation that is less supported by research is the proposal that heroin users as with all drug users have "addictive personality" profiles and the absence of the use of one drug such as heroin results in the increase use of an alternative drug or the beginnings of use of a new drug.

It must be remembered that it is possible that drug using patterns vary according to where the research is conducted. It is possible that different cities and populations favour different types of drugs. This is one of the potential explanations why research studies vary greatly on the reporting of additional drug use. Dupont and Saylor (1989) found 51% of their sample had urine samples that contained evidence of cannabis.

Another possibility is that methadone users will engage in an activity known as "boosting". This is when other drugs such as antihistamines or barbiturates are taken to enhance the methadone's opioid effect. However, the most substantial effect is to achieve a stronger than usual primary effect from the second drug, for example antihistamine or barbiturate sedation. The greatest risk in this practice is accidental overdose. It is also thought that opiate users use benzodiazepines to reduce the anxiety that often occurs as a result of the opiate levels in their blood dropping when withdrawing.

In an inner city area such as where this research was conducted it could be speculated that additional drug use is for none of the above reasons. It is possible that the sample are poorly motivated and that their enrolment in methadone treatment is as a way of ensuring a supply of methadone should money or drug supply problems occur. Additionally the associated high forensic activity means that some users are forced into treatment to avoid custodial sentencing or that they need to be seen to be addressing their drug use to receive social security benefits and to keep custody of their children. In clinical terms such feelings are attributed to the pre-contemplation or contemplation stage of motivation (Prochaska and DiClemente, 1992). This means that the participant actually wants to continue heroin use but methadone is the legal alternative and the user has not yet decided on whether the adverse consequences of their heroin use means that they want to give up. It must also be remembered that drug use is difficult to give up without awareness of the role that it fulfils in the individuals life. For some it is an escape from trauma and/or the reality of everyday existence or just a normalised part of daily life.

Urinalysis

One of the main methods of monitoring the drug use of patients enrolled in methadone maintenance treatments is by urine testing. In the USA, urine screening has been a required procedure in methadone maintenance treatment before insurance companies will pay for treatment. However, in Britain there is little guidance to the use of the monitoring procedure. In general the policy seems to be that it should not be used solely as a determinant of treatment i.e. to force a patient out of treatment, but rather as a guide to modify treatment approaches.

There are variations on ensuring that the procedure involved is maximised to ensure an accurate result. One way is to ensure that the patient does not take a sample in with them or that they don't get someone else to do their sample for them. In many services the toilets have cameras in to monitor patients. It must however be considered within the context of the human rights of the patient to dignity and respect. It must also be noted that the there are incidences when the urine screening test procedures have produced false positive and negative results (Morgan, 1984).

It has been suggested that the most efficient procedure for the collection of urine samples is random samples and that patients should be informed at the initial stages of treatment of the clinics policy. Minimising the falsification of urine results and client-staff relationships are best fostered if the patient does not see the procedure as a way

of punishing them or detrimentally affecting their treatment. The ideal use of the results is within clinical counselling situations as a basis for discussion.

Urine testing also needs to be analysed with the knowledge that different drugs are metabolised in different ways and therefore show in the urine for different amounts of time. For example, cannabis can stay in the urine for up to 28 days, a long time after there would be any likely clinical effects.

The disparity in clients reporting of illicit drug use compared to urine toxicology is likely to be as a result of fear of detection and punishment, (for example, take-out prescription privileges being withdrawn). The implications for the staff-client relationship due to other illicit drug use determined by urine results is discussed below.

The implications for psychological therapies.

The boundaries between counselling and other psychological approaches in the treatment of drug users appears to be particularly vague. In general counselling is considered the approach that generic mental health workers use to manage the overall case, i.e. to identify and address specific problems in the area of drug use, physical health, interpersonal relationships, family interactions, vocational or educational goals. Additionally they act as a liaison role between psychiatrists, medical institutions, courts and social services. Their aim is broadly as case manager as described above, to help the patient develop coping strategies for current problems and to attend to the

running of the treatment programs, its rules, privileges and policies. Treatment should therefore be geared toward both short and long term goals.

There is a boundary between this generic drug counselling and psychotherapy that is often ambiguous. In general psychotherapeutic approaches can be used in the same way as general psychotherapy although there is often the opinion voiced that lengthy psychotherapy cannot be performed whilst the mind altering drugs are being taken. More specific psychotherapeutic methods used to treat drug users include relapse prevention and motivational interviewing techniques. These treatments embody general cognitive behavioural principles, i.e. focusing on uncovering and understanding the relationship between automatic thoughts and underlying assumptions on problematic feelings and behaviours. These approaches tend to relate the above to the specifics of the drug using behaviour of the individual.

The research finding in this study that drug users are less suggestible than the general population may have implications for the efficacy of these psychological treatments. Cognitive restructuring techniques may be difficult to apply although treatments validated with drug users may have included this concept in their design. It is also possible that less suggestible clients may require longer in psychotherapeutic treatments than clients that are more suggestible. Additionally less suggestible people may be resistant to change and their lack of response to negative feedback could also contribute to their resistance to change their drug using behaviour. This lack of suggestibility could be analogous to the psychoanalytical concept of 'resistance'.

The policy regarding urine testing in relation to the overall treatment philosophy is also an important facet of the client-therapist relationship. For example the treatment overall philosophy may be one of abstinence and therefore urine screening is used to monitor other drug use and as a tool for changing treatment if other illicit drug use is detected. Such policies can foster an atmosphere of non-disclosure to other drug use and craving which makes therapeutic interventions limited in their usefulness to deal with the clients current issues and situation. In this research 27.78% of participants had positive urine tests to heroin when they had reported no use. This is within a research setting where disclosure has no treatment implications. Although participants were told this before the research began, they may have doubted it as the researcher was also clinical staff at the service. It is also interesting that key-workers are obviously not aware of the extent of their clients additional drug use as they chose clients whom they thought were more stable and therefore that illicit use would be minimised.

Especially within psychoanalytic literature, there is a lot of references to the honesty of the client within a therapeutic relationship. Part of the therapeutic process that appears not to be present in the key-working role is the negotiation of goals that the client also agrees to. Current practices regarding treatment goals seem to be dictated by treatment philosophy and it is therefore unsurprising that relapse is high and the unreported use of illicit drugs is common. Research supports the view of the importance of the relationship between staff and patients in treatment outcome, although none has been done that isolates the specifics of the relationship and their effects (Kreek 1983). However, it is unlikely that a good therapeutic relationship can

be fostered if the patient cannot be honest about their drug use as it is against the services treatment philosophy.

Craving is an important part of cognitive-behavioural interventions such as relapse prevention (Marlatt and Gordon, 1978). It is assumed that craving heroin leads to heroin use and relapse. It is not possible to attribute craving to a purely biological or psychological effect, it is likely that it is an interaction between the two. Craving is the same as many aspects of addiction treatment in that there is often a separation between the behavioural and medical consequences and therefore the subsequent treatment adopted varies according to what the craving is attributed to originating from.

For example, a dealer may move in next door to a patient and they find that their cravings increase. Therapeutic efforts would need to focus on resolving the situation rather than relying on more methadone. It is possible that in addition to the situational context and the clients' cognitive attributions as to the origin of their craving and their ability to deal with it, this research suggests the need to look at the dose of methadone the client is receiving and their subjective reports of opiate craving.

4.6 Further research.

This study has shown that placebo-controlled studies with this client group are feasible. Future research could build on this approach to study this under-researched population.

The Suggestibility measure produced some interesting results and it would be important to assess a larger sample. The implications of suggestibility on psychological therapies has not yet been explored. Furthermore, results would suggest that the criminal activity in drug users is a result of attempts to secure money to purchase drugs and unlikely to be as a result of false confessions. The impact of suggestibility also could be examined in research concerning the aetiology of drug use as it would refute the claim that drug users are highly responsive to peer pressure. The effects of suggestibility upon cognition would need to be isolated from social pressures in such studies.

Craving is very interesting and a fertile ground for further research. Further research could concentrate on the link between dose and craving. If baseline methadone doses were increased would heroin craving diminish ? This research also questions the efficacy of prescribing methadone when it is potentially increasing patients' cravings. This may therefore lead to patients additional illicit drug use and potentially increase their risk to the consequences of injecting and drug using behaviour.

The cognitive and psychomotor effects of additional methadone in this population are minimal and the dose given produced no decrements in this study. Alternatively, interesting results could be attained from an in-patient sample where additional illicit drug use can be more carefully controlled and a larger additional dose of methadone given. It is possible that more standardised neuropsychological tests should be used that compare participants in the research with standardised samples. The within-

subject tests used only isolate within subject changes that the methadone was too low a dose to detect. However, the large individual variations in participants' scores mean that a within subject design is more likely to be sensitive to any effects. As shown in the Rivermead Behavioural Memory test, the means of test results may fall within normal limits but individual participants may be functioning at low levels. Further research is needed to define the exact nature of any memory impairment. Future studies could concentrate on the specific components of memory impairment such as confabulation. It is also possible that drug users are impaired in executive, frontal lobe functions which need to be tested using specific tests. The variety of scores can be explained to some degree by the large amount of individual variation between participants that is also effected by the large range of I.Q. scores.

Once any cognitive effects have been identified, research could look at the effects of them on treatment and look toward the development of a clinical assessment tool. Currently little attention is paid to cognitive effects due to the lack of acknowledgement of any. However, as shown by the memory test there are cognitive difficulties experienced by patients that may be overlooked despite them having an effect on the patient's functioning.

Lastly an ideal research methodology for confirming cognitive impairment in drug users would be to monitor them in three separate phases; firstly prior to drug use, secondly during drug use and lastly after a long period of abstinence to determine if any change in function is restored to previous levels. The practical issues involved,

such as clients frequent geographical location changes and subsequent non-attendance would make these types of research designs fraught with difficulties.

4.7   Conclusions.

Methadone is the most commonly prescribed drug for heroin addiction, yet relatively little is known about its specific effects within a clinical population. Interesting findings from this study were especially in the areas of craving, suggestibility and coping. The craving information has important clinical implications and further contributes to the on-going debate on the dose of methadone that should be prescribed for heroin dependence. Suggestibility findings may have some implications for the efficacy of therapeutic interventions and this warrants further investigation. The effects of methadone on cognition requires further clarification and this study has led to suggestions on how this research may be carried out. The lack of cognitive effect of an increase in prescribed methadone dose reflects not only tolerance mechanisms but also the widespread use of illicit opiates by these poly drug users.

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APPENDIX 1

Ethics letter from University College London.

The University College London Hospitals

The Joint UCL/UCLH Committees on the Ethics of Human Research

Committee A Chairman: Dr F D Thompson

Please address all correspondence to:
Mrs Iwona Nowicka
Secretary to Ethics Committees
9th Floor, St Martin's House
140 Tottenham Court Road, LONDON W1P 9LN
Tel. 0171- 380 9579   Fax 0171-380 9536

Dr Valerie Curran
Senior Lecturer
Sub-Department of Clinical Health Psychology
UCL
Gower Street
London WC1E 6BT

27 September 1996

Dear Dr Curran

Study No:	**96/84**(*Please quote in all correspondence*)
Title:	**The effects of a single dose of methadone on mood and concentration. A study in long-term methadone users**

Thank you for your letter of the 10th September 1996 supplying detailed information at the request of the Committee. I am writing to let you know that this application is now approved and you may go ahead with your study.

Please note that it is important that you notify the Committee of any adverse events or changes (name of investigator etc) relating to this project. You should also notify the Committee on completion of the project or indeed if the project is abandoned. Please remember to quote the above number in any correspondence.

Yours sincerely

pp. *[signature]*

Dr F D Thompson
Chairman

APPENDIX 2

Ethics letter from Camden & Islington Health Authority.

CAMDEN & ISLINGTON
Community Health Services NHS Trust
Your Partner for Health

LOCAL RESEARCH ETHICS COMMITTEE
Medical Directorate, Vezey Strong Building, 112 Hampstead Road, London NW1 2LT
Tel: 0171 530 3055   Fax: 0171 530 3018
E-mail: sue.rodmell@dial.pipex.com

27 September, 1996

Dr H Valerie Curran
Senior Lecturer
Sub-Department of Clinical Health Psychology
University College London
LONDON
WC1E 6BT

Dear Dr Curran

Application No: 96/71
Title: The effects of a single dose of methadone on mood and concentration. A study in long-term methadone users

Thank you for your letter of 6 September in response to the Local Research Ethics Committee's letter of 2 August which was considered at the Committee's meeting on 23 September. The Committee is reassured that the methadone test dosage will only be increased by 33% rather than the original 50%. You have also clearly explained the reasoning for the sample size and the randomisation procedures. Therefore, I am pleased to say the Local Research Ethics Committee has agreed to approve this project. Also, I would like to thank you for making yourself available on the 23rd to answer any further queries the Committee may have had.

Please note that the following conditions of approval apply:

* It is the responsibility of the investigators to ensure that all associated staff including nursing staff are informed of research projects and are told that they have the approval of the Ethics Committee.
* If data are to be stored on a computer in such a way as to make it possible to identify individuals then the project must be registered under the Data Protection Act 1984. Please consult your department data protection officer for advice.

.../Page 2

Rabbi JULIA NEUBERGER: Chairman
LOUIS SMIDT: Chief Executive
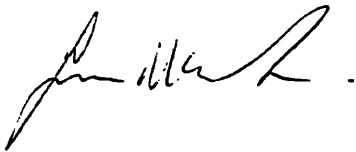
- The Committee <u>must</u> receive immediate notification of any adverse or unforeseen circumstances arising out of the trial.
- The Committee <u>must</u> receive notification: a) when the study is complete; b) if it fails to start or is abandoned; c) if the investigator/s change and d) if any amendments to the study are made.
- The Committee will require details of the progress of the research project periodically (e.g. annually).

With best wishes.

Yours sincerely

p.p. **Stephanie Ellis**
<u>Chairperson</u>

APPENDIX 3

Key-worker information sheet

Keyworker information sheet.

The effects of a single dose of methadone on mood and concentration. A study in long-term methadone users.

I am doing this research project for my Doctorate in Clinical Psychology course (based at UCL) in conjunction with Dr. Ciaron Smyth and supervised by Shamil Wanigaratne.

Inclusion criteria.

1. Patients must be over 18 years of age.
2. Patients must have been taking prescribed methadone for a minimum of six months.
3. Patients must have been on the same dose for the past 4 weeks.
4. Patients must be on a dose of between 20- 100 mgs
5. Patients need to have basic literary skills and be able to give informed consent.
6. Patients need to be willing to give a urine and breath sample.

Exclusion criteria.

1. Any past history of severe head injury.
2. Any organic problem associated with cognitive dysfunction e.g. Multiple Sclerosis, Epilepsy etc.

Procedure.

20 patients are needed.

Patients will be seen for approximately two and a half hours, preferably on the same day they have an appointment with their key-workers. They will be given either 33% extra of their normal prescribed dose of methadone or a placebo and the reverse on week 2. Each participant will complete some psychometric tests both before they take the drug and two hours afterwards. In the interim two hours patients will be asked to fill in some mood questionnaires and could then have their appointment with their key-worker. However, it is important that the patient does not leave the clinic or is unsupervised so as to ensure that they don't take any other drugs. The same procedure will be repeated on the following week. At the end of week 2 patients will be given a twenty pound payment towards expenses.

The aim of the project is to look at the cognitive effects of methadone using a double-blind placebo control design. In this way neither the researcher or the patient knows on which day the patient receives the placebo and each subject acts as his own control, thereby ensuring that no control group is needed. Routine urinanalysis results will be collected to record the presence of other drugs. **It is important to stress to the patient that the results can only be effected if the subject has taken different drugs before coming to the clinic each time, so it is hoped that this can be discouraged !**

Key-workers and the patient will be given feedback at the end of the project as to the results of the test.

If you have any patients that fit the above criteria and you would be willing to help in the study, or you require further information, please contact :
Judi Bolton.
Shamil Wanigaratne
Ciaron Smyth

APPENDIX 4

Clients information sheet

<u>CONFIDENTIAL</u>.   **<u>INFORMATION SHEET.</u>**

<u>The effects of a single dose of methadone on mood and concentration. A study in long-term methadone users.</u>

<u>Investigators:</u>

Ms. Judi Bolton.
Dr. Valerie Curran
Dr. Cairan Smyth (Senior Registrar)

It is often unclear what effects methadone is having on the people who are taking it for long periods of time. We are doing a study to find out what effects a dose of methadone has on people. The study will look at people's concentration and mood.

By taking part in this study you will be helping our research into this important issue.

By taking part you and your doctor will also be given an indication of what effect methadone is having on your mood and concentration.

<u>What the study involves.</u>

You will need to be seen on two separate days, one week apart. As far as is possible we will coincide these visits with visits to your key-worker. Each time you will be asked to fill in some forms about how you are feeling and any physical symptoms that you have. You will also be given a few straightforward tests of concentration and memory. You will do this two hours after you have taken a syrup. On one day the syrup will contain no medication and on the other day it will contain an extra amount of methadone calculated at a third of you usual dose. Neither you nor Ms Bolton or Dr. Smythe will know on which of the two days you have received the extra methadone.
On both days you will receive your normal methadone prescription and have your normal treatment at the clinic which will include giving a sample of urine.

If you have any queries you can contact **Judi Bolton** on **0171-530-3230.**

You do not have to take part in this study if you do not want to. If you decide to take part you may withdraw at any time without having to give a reason. Your decision whether to take part or not will not affect your care and management in any way.

All proposals for research using human subjects are reviewed by an ethics committee before they can proceed. This proposal was reviewed by UCL Ethics Committee and by Camden & Islington Ethics Committee.

APPENDIX 5

Consent form

CONSENT FORM.

The effects of a single dose of methadone on mood and concentration. A study in long-term methadone users.

Investigators:

Dr. Valerie Curran.
Ms Judi Bolton.
Dr. Cairon Smyth.

To be completed by the patient.
1. Have you read the information sheet about this study?
YES/NO

2. Have you had the opportunity to ask questions and discuss the study?
YES/NO

3. Have you received satisfactory answers to all your questions?
YES/NO

4. Have you received enough information about the study?
YES/NO

5. Which doctor have you spoken to about the study?
Dr................................

6. Do you understand that you are free to withdraw from this study

   *at any time
   *without giving a reason for withdrawing
   *without affecting your future medical care?
YES/NO

7. Do you agree to take part in the study?
YES/NO

Signed .... Date ....

Name in BLOCK LETTERS ....

Name of doctor ....

Signed .... Date ....

APPENDIX 6

Randomisation codes

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RANDOMISATION CODE: all tests with four versions.

subject number	Drug order	time 1 (pre)	time 2 (post)	time 3 (pre)	time 4 (post)
1	1	1	2	3	4
2	1	3	2	1	4
3	1	2	3	4	1
4	0	3	4	1	2
5	0	2	1	4	3
6	0	1	4	3	2
7	1	4	3	2	1
8	0	4	1	2	3
9	1	1	2	3	4
10	0	3	2	1	4
11	1	2	3	4	1
12	0	2	1	4	3
13	0	3	4	1	2
14	1	4	1	2	3
15	0	1	4	3	2
16	0	4	3	2	1
17	1	1	2	3	4
18	1	2	3	4	1

Drug order Key:

1 - methadone time 1 / placebo time 2
0 - placebo time 1 / methadone time 2

RANDOMISATION CODE: all tests with 2 versions.

subject number	Drug order	time 2 (post)	time 4 (post)
1	1	1	2
2	1	1	2
3	1	2	1
4	0	2	1
5	0	2	1
6	0	2	1
7	1	1	2
8	0	1	2
9	1	1	2
10	0	1	2
11	1	2	1
12	0	2	1
13	0	1	2
14	1	2	1
15	0	1	2
16	0	2	1
17	1	1	2
18	1	1	2

Drug order Key:

1 - methadone time 1 / placebo time 2
0 - placebo time 1   / methadone time 2

APPENDIX 7

BSS Questionnaire

BODILY SYMPTOMS SCALE 9

NAME :..

DATE :..........................   TIME :...........................

    a. Please rate the way you feel in terms of the dimensions given below.

    b. Regard the line as representing the full range of each dimension.

    c. Rate your feelings as they are AT THE MOMENT.

    d. Mark clearly and perpendicularly across each line, ie ———|———

No restlessness	Severe restlessness
No irritability	Severe irritability
No physical tiredness	Severe physical tiredness
No lack of energy	Severe lack of energy
No impaired concentration	Severly impaired concentration
No headache	Severe headache
No difficulty in breathing normally	Severe difficulty in breathing
No dryness of the mouth	Severe dryness of the mouth
No nausea or sickness	Severe nausea or sickness
No anxiety	Severe anxiety
No sweating	Severe sweating
No blurred vision	Severe blurred vision
No feeling of depression	Severe feelings of depression
No agitation	Severe agitation

APPENDIX 8

MRS questionnaire

MOOD RATING SCALE

NAME ....

DATE.................................

1. Please rate the way you feel in terms of the dimensions given below

2. Regard the line as representing the full range of each dimension

3. Rate your feelings as they are AT THE MOMENT

4. Mark clearly and perpendicularly across each line

ALERT	_____	DROWSY
CALM	_____	EXCITED
STRONG	_____	FEEBLE
MUZZY	_____	CLEAR-HEADED
WELL-COORDINATED	_____	CLUMSY
LETHARGIC	_____	ENERGETIC
CONTENTED	_____	DISCONTENTED
TROUBLED	_____	TRANQUIL
MENTALLY SLOW	_____	QUICK WITTED
TENSE	_____	RELAXED
ATTENTIVE	_____	DREAMY
INCOMPETENT	_____	PROFICIENT
HAPPY	_____	SAD
ANTAGONISTIC	_____	AMICABLE
INTERESTED	_____	BORED
WITHDRAWN	_____	GREGARIOUS

APPENDIX 9

Craving questionnaire

Indicate how much you agree or disagree with each of the following statements by placing a single checkmark (like this: __✓__) along each line between STRONGLY DISAGREE and STRONGLY AGREE. The closer you place your checkmark to one end or the other indicates the strength of your disagreement or agreement. Please complete every item. We are interested in how you are thinking or feeling <u>right now</u> as you are filling out the questionnaire.

RIGHT NOW

1. If there was heroin right here in front of me, it would be hard not to use it.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

2. Using heroin would not be pleasant.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

3. I would feel less sick now if I used heroin.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

4. If I had the chance to use heroin right now, I don't think I would use it.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

5. Using heroin would not sharpen my concentration.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

6. Even if it were possible, I probably wouldn't use heroin now.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

7. I am not missing using heroin now.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

8. I am going to use heroin as soon as possible.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

9. My aches and stiffness would not go away if I used heroin right now.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

GO TO NEXT PAGE

RIGHT NOW

1. Using heroin now would make things seem just perfect.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

2. My desire to use heroin seems overpowering.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

3. Right now, I am not making plans to use heroin.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

4. I could control things better right now if I could use heroin.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

4. Using heroin right now would make me feel less tired.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

5. I could not stop myself from using heroin if I had some here now.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

6. If I tried a little heroin now, I would not be able to stop using more of it.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

7. I want heroin so bad I can almost taste it.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

8. Nothing would be better than using heroin right now.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

9. I would do almost anything for heroin now.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

10. I would feel so good and happy if I used heroin now.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

GO TO NEXT PAGE

RIGHT NOW

21. I don't want to use heroin now.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

22. I would be less irritable now if I could use heroin.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

23. All I want to use now is heroin.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

24. It would be difficult to turn down heroin this minute.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

25. Starting now, I could go without using heroin for a long time.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

26. Using heroin would not be very satisfying now.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

27. If I used heroin right now, it would not help me calm down.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

28. I would not enjoy using heroin right now.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

29. I would not be able to control how much heroin I used if I had
     some here.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

30. I would feel energetic if I used heroin.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

31. If I had some heroin with me right now, I probably wouldn't
     use it.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

GO TO NEXT PAGE

RIGHT NOW

2. My hot and cold flushes would not get better if I used heroin now.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

3. I do not need to use heroin now.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

4. I will use heroin as soon as I get the chance.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

5. I have no desire for heroin right now.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

6. If I were using heroin, I would not feel less tense.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

7. Using heroin now would make me content.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

8. It would be easy to pass up the chance to use heroin.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

9. I crave heroin right now.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

0. If I were offered some heroin, I would use it immediately.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

1. Using heroin would make me feel less depressed.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

2. I have an urge for heroin.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

GO TO NEXT PAGE

RIGHT NOW

3.   I am thinking of ways to get heroin.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

4.   I could easily control how much heroin I used right now.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

5.   I think that I could resist using heroin now.

STRONGLY DISAGREE ____:____:____:____:____:____:____:STRONGLY AGREE

APPENDIX 10

"What were you given questionnaire'.

Did you receive methadone/placebo or unsure ?   ----------------------

Please mark along the line how sure you are of your answer to the above question.

       not sure   very sure

APPENDIX 11

'Drug information questionnaire'.

Subject number: ....
Date ....am/pm.

Education ....
Employment
....
....

Do you normally take your full prescribed methadone dose? ....

Do you use extra methadone on top of your prescribed dose ? ....
If YES: amount ....   frequency ....

What do you think that a extra 33% of your normal dose of methadone will do ?
Will it affect the following:

	Worse	much worse	no change	better	much better
Memory					
Concentration					
Make you tired					

Any others:
....
....

Will it make you feel good ? - If YES, in what way ?
....
....
....

Medical History:

(From patient)__:Psychiatric
               Accidents (head injuries)
               Organic brain dysfunction (e.g. epilepsy)
INCLUDE CURRENT MEDICATION
....
....
....
....
....
....

(From notes/key worker (K/W))

....
....
....
....

M - methadone
L - LSD
Can - cannabis

Subject number ....
Date ....am/pm
Time ....

All the drugs ever used (including alcohol).

LENGTH OF TIME YOU HAVE BEEN USING THE DRUG

type of drug	1 week	1-4 weeks	1 - 2 month	2 - 4 month	4 - 6	6 - 1 year	1 year - 18 month	18 month - 2 year	2 - 5 years	more 5 years

....
....

Subject number ....
Date ....am/pm
Time ....

All the drugs ever used (including alcohol).

FREQUENCY OF USE

Type of drug and route.	4 x day or more	1-2 day	every other day	twice week	once week	once month	every two month	every 2 -6 month	7 month - one year	less than once year

I = illicit   P = prescribed
In = Injection   S = snorted   Sm = smoked   T = tablet   L = liquid

Drug key.

H - heroin   T - temazepam
C - cocaine   O - OTHER
CC - crack cocaine   (specify)
E - Ecstacy
A - amphetamines
D - diazapam