Are the Driving-Related Skills of Clients in a Methadone Maintenance Programme Affected by Methadone?

G. Chesher, J. Lemon, M. Gomel, G. Murphy

National Drug and Alcohol Research Centre, University of New South Wales, 30 Goodhope Street,Paddington NSW 2021, Australia

This work was commissioned and funded by the National Drug and Alcohol Research Centre and has been reported in the Technical Report Series, No 3 of this Centre.

ABSTRACT

A study was undertaken to examine the effects of methadone, as used in the methadone maintenance program, on human performance skills which are related to those required to drive a motor vehicle with safety. The tests used for the study were chosen for their relevance to driving as well as for the distinctive properties of the opioids.

The interaction between methadone and two other drugs commonly used by clients on a methadone program were also examined. These were (i) alcohol, to produce a mean blood alcohol concentration at peak of 0.064 g per 100 ml blood and (ii) a therapeutic dose of the benzodiazepine, diazepam (15 mg).

The test battery proved to be sensitive to the effects of alcohol and diazepam at the doses used. There was however, no evidence for an effect of the acute dose of methadone on any of the experimental groups of clients on the methadone program. These results suggest that these clients enrolled on the methadone maintenance programme should not be considered as impaired in their ability to perform complex tasks such as driving a motor vehicle.

Both alcohol and diazepam produced a significant decrement in the performance on the test battery by the control groups and the stabilized methadone clients. However, there was no difference in the intensity of this effect between the groups. There was no evidence for an interaction between methadone and either alcohol or diazepam in the group of methadone clients stabilized on the program.

INTRODUCTION

The use of methadone in the treatment of opioid dependence was first described thirty years ago (Dole and Nyswander 1965) and it remains to be the most widely used pharmacological agent for such treatment. In Australia there are at present approximately 13,000 people on methadone maintenance, about 9000 of whom are in New South Wales; and most of these are in the Sydney Metropolitan Area.

One of the positive outcomes of the methadone maintenance programme is the behaviour change which permits in many cases, the return of the client to the workforce. However, employment for many on the methadone program involves driving trucks, buses, taxis or trains or the operation of factory machinery. It is of no little interest therefore to know if
methadone, as used in the methadone program, is likely to impair the skills of these people in performing these tasks.

The present study was designed to examine the effects of methadone, as used in a methadone maintenance programme, on the performance of driving-related skills.

METHODS

The Tests of Human Skills Performance

The skills of primary interest in this study are those related to driving a motor vehicle. Three tests were chosen for the study.

A Divided Attention Task (Southern California Research Institute)

This comprises two tasks which are conducted simultaneously; a compensatory tracking task (CTT) and a visual search task (VST).

The complete task is computer presented on five separate viewing screens placed in the form of the five spots on a die. The tracking task appears on the central screen.

The tracking task takes the form of a fixed reference mark (a divided narrow vertical bar) in the screen centre and a horizontally moving cursor (a smaller bar fitting between the fixed bars) which moves randomly back and forth. Subjects use a control stick located at their preferred hands to attempt to maintain the moving cursor level with the reference bar.

Simultaneously with attempting to control the tracking task, a visual search task (VST) is presented in the form of a matrix of 24 numerals shown on the four separate peripheral screens, 6 numerals to a screen. The numerals are changed randomly, but from time to time a “target” numeral appears (the numeral “2”). When the target numeral is detected by the subjects on any of the screens, they are required to press one of the four corresponding response buttons located at their non-preferred hands. If the correct response is made the target numeral changes to a “0”. If a response is incorrect, no change in the display occurs.

The duration of each test run is 12 minutes plus a 15 seconds warm-up period (during which responses are not recorded). There are 48 visual search “targets” during each trial with an inter-stimulus interval mean of 15 seconds; range between 7 and 23 seconds.

The computer samples and maintains a record of the tracking error, which is the difference between the stimulus signal and the response. At the end of a trial the absolute tracking error is calculated. This is the error of the response from the zero position. The mean response time to correct target stimulus responses was taken as the measure for the visual search task.

Critical Tracking Task (Systems Technology Inc. California)

A critical tracking task is a form of compensatory tracking which continually increases in instability and difficulty during the trial. The rate of increase in the instability of the task is directly related to the number and extent of errors made by the subject. At some point the instability of the system is beyond the capacity of the subject to control, and at that point the
trial ends. The basic theory and validation of this task is provided by (Jex et al. 1966; Kelley 1969; McDonnell and Jex 1967). One measure (lambda) is recorded, being an index of the ability of the subject to stabilize the controlled instability of the system.

A Vigilance Task (The Mackworth clock)

Vigilance is obviously an important factor in driving, particularly in light traffic when attentional demands on the driver are lower. This test was included to measure the response of drowsiness, sometimes referred to a “nodding”, which may accompany the administration of methadone.

The Mackworth Clock test presents on the screen, twenty four dots in a circle like the digits on a clock. Each dot ‘flashes’ in clockwise sequence. A target stimulus occurs when the flashing skips a dot. The subject must press a key on the response board when a target occurs. The task has a duration of forty five minutes. The reaction time for each hit is recorded, as are misses and false positives. During the 45 min of the test, 20 stimuli are presented.

The Study Population and the Control Group(s)

There are a number of variables which are associated with the behaviour of an individual enrolled on the methadone program, only some of which are related to the pharmacological effect of the drug methadone. The selection criteria for volunteers in the study rests solely on their membership of the methadone program. Membership is dependent upon a history of destructive use of heroin.

However, this criterion will embrace subjects with different degrees of exposure to methadone. Therefore, it was decided to include three groups of methadone clients according to their exposure to the drug. These groups also provide the opportunity to examine the effect of an acute dose of methadone on individuals with differing degrees of opioid tolerance.

Methadone: Stabilized Clients

As methadone programs have been underway in the State of New South Wales for some years, the greater proportion of clients enrolled in a program will have been stabilized on a dose of the drug and will exhibit a substantial degree of tolerance to most of the effects of methadone and of other opiates. Earlier studies (Moskowitz and Robinson 1985; Robinson and Moskowitz 1985) have indicated that the skills performance of stabilized methadone clients do not differ from those of matched non-opioid using controls.

A fundamental pharmacological principle of the methadone program is that of the cross-tolerance which exists between methadone and morphine. However, cross tolerance to the opioids does not extend to other central depressant drugs. Clients in the methadone program commonly use alcohol and benzodiazepines and the possibility of an interaction between these drugs and methadone was investigated.
The stabilized group comprised those clients who had been maintained on the same dose of methadone for at least six months. Members of this group attended the laboratory on four occasions. On occasions 1 and 2, the test battery was completed before and after the daily methadone dose. On the third and fourth occasions, tests were conducted before and after methadone as well as a dose of alcohol (on occasion 3) and diazepam (occasion 4).

**Methadone: Clients Beginning on the Program; their first dose**

If methadone is to exhibit an acute effect on skills performance one would expect it to be most noticeable after the first dose or when the dose taken is increased. The acute effect of the drug would be expected at this time and before tolerance had been developed to the dose taken.

Volunteers for the second experimental group were drawn from those clients beginning the methadone program. Members of this group were given their first and third dose of methadone at the laboratory. These volunteers attended the laboratory on two days only, and were tested before and after taking their first and third daily dose of methadone.

**Methadone: Clients Undergoing a Dosage Increase**

Clients in the earlier stages of their treatment frequently require and upward adjustment of their dose of methadone. Volunteers for this group were those who were receiving an increase in their dose of methadone of 10 mg per day.

These volunteers attended the laboratory on two occasions, the first when they were tested before and after their usual dose and the second occasion, before and after their increased dose.

**The Control Groups**

(a) Ex-user controls

In view of the findings of (Craig 1990; Hagland and Furland 1978; Kleinman 1978) that people who use heroin differ in a number of significant respects from those who do not, it is necessary to use as controls a group of volunteers who are ex-opiate users and who currently are drug free. These were recruited by a “snowball” technique by asking each volunteer to encourage a friend who had been a user of heroin, to participate in the study.

(b) Non-user controls

In view of an initial difficulty in recruiting ex-user controls who were willing to participate in the study, we included a group of non-user controls. These volunteers were recruited from University students and from those enrolling for unemployment benefits.
Procedure

Volunteers were recruited from three Sydney metropolitan methadone centres. The purpose of the study, the nature of the treatments and the tests were explained to all volunteers and their informed consent obtained. All volunteers signed a form to confirm their informed consent.

All subjects were conveyed to and from the laboratory by taxi. Upon arrival at the laboratory the tests were demonstrated to them and a practice run on each was given as described below. The tests were conducted in the same order throughout the experiment, with divided attention first, the critical tracking next and the Mackworth clock, the task of longest duration, was last.

Practice on the Test Battery

Each test was fully described to the volunteers who then had a brief practice run under supervision to ensure that the task was fully understood. A complete run on the task was then completed before continuing with the description of the next test.

For the volunteers of Group 1 (the stabilized clients) who attended the laboratory on four occasions, the data for the first testing occasion was regarded as practice on the test battery and was not used in the analysis. However, as the clients in Groups 2 and 3 had not reached a stable dosage of methadone and could not be described as being in a stable state, we could not, for ethical reasons, ask these clients to defer their first dose or their increased dose of methadone more than necessary for the sake of the experimental design. For this reason, we did not devote a full days testing to practice on the tests. The practice on the test battery for Groups 2 and 3 was, as described above, a complete run on each test after they had shown a full knowledge of the nature of the test.

Test Schedule

Each volunteer received their designated dose of methadone at the laboratory and after a wait of one hour to allow for drug absorption, the tests were repeated.

On the third test day, when alcohol was consumed by the stabilized methadone group and both of the control groups, the procedure after the completion of the pre-drug test run was as follows:-

<table>
<thead>
<tr>
<th>Activity</th>
<th>Time Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone taken</td>
<td>0 mins</td>
</tr>
<tr>
<td>Wait</td>
<td>0 mins to 20 mins</td>
</tr>
<tr>
<td>Alcohol consumed</td>
<td>20 mins to 40 mins</td>
</tr>
<tr>
<td>Wait</td>
<td>40 to 60 mins</td>
</tr>
</tbody>
</table>

Subjects were then submitted to breathanalysis (Drager 7110) after which they then completed the post-drug run on the test battery.

On the fourth day of the experiment, when the dose of diazepam was given, all volunteers received this drug (by mouth) at Zero minutes; i.e. ehrm the methadone group received their methadone. Testing began after an absorption period of one hour had elapsed.
RESULTS AND DISCUSSION

Methadone Doses
The mean dose for all of the methadone clients was 70 mg (range 15 to 150 mg). The mean for the stabilized group was 85 mg (range 40 to 150 mg); the group receiving a dose increase, 67 mg (range 40 to 135 mg); and the group beginning on the program, 38 mg (range 15 to 60 mg).

Blood Alcohol Concentrations
The mean blood alcohol concentration measured twenty minutes after the completion of drinking, which in turn had been undertaken over a period of twenty minutes were as follows.

(a) For all 64 volunteers : 0.064 g per 100 ml blood (± 0.015 S.D.)
(b) For the controls; 0.062 g% (± 0.012 S.D.)
(c) For the methadone maintenance group; 0.060 g% (± 0.012 S.D.)
(d) For the ex-user group; 0.072 g% (± 0.016 S.D.)

Data Analysis
The dependent variable used in all comparisons was a composite score reflecting overall performance. The individual test scores were standardized and combined as follows:-

\[ \text{Mean absolute tracking error} + \text{visual search reaction time (of Divided Attention)} + \text{Mackworth clock misses - Critical tracking lambda} \]

A numerical increase in the composite score therefore represents poorer performance.

Group 1. Stabilized Clients and Controls
The initial analyses were planned to compare the performance of the various methadone groups before and after their prescribed dose of methadone with that of the control and ex-user groups.

There were three within-subject effects of potential interest:

(i) Pre-dose versus post-dose
(ii) The presence or absence of alcohol
(iii) The presence or absence of diazepam

All planned analyses were conducted using a groups x repeats ANOVA program based on the regression model.

Performance for these groups are compared for the second third and fourth days of testing; i.e. the effects before and after (a) methadone alone, (b) methadone with alcohol and (c) methadone with diazepam.

Since there was no clear prediction as to the outcome of the study, critical F values (the value of F which is required to determine significance at the 95% probability level) for each
family of contrasts were determined using the method recommended by Hall and Bird (Hall and Bird 1986). Subjects used in this analysis comprised 26 stabilized methadone clients; 19 normal controls and 19 ex-users.

There was no difference in the group comparison between the normal control group and the ex-users (Obtained F=0.05; Critical F=6.3). Therefore the composite scores for the all of the control groups were combined for the subsequent within subject analyses.

The contrast comparing the performance scores before and after the acute dose of methadone on day 2 with that of the combined control groups revealed no differences ( Obtained F=0; Critical F=17.25), indicating there to be no effect of the acute dose of methadone.

All groups, of course, received alcohol and diazepam on Day 3 and 4 respectively. The repetition x drug contrasts, reveal that very strong effects in the direction of impaired performance were seen over all groups for both ethanol ( Obtained F=41.01; Critical F=13.1) and diazepam ( Obtained F=31.92; Critical F=13.1). However, neither the group x repetition x ethanol, nor the group x repetition x diazepam interaction approached significance. This indicated that although both ethanol and diazepam significantly impaired performance of all groups tested, there was no difference in the extent of this impairment between the methadone and the control groups.

The other group contrast of interest is that of the methadone stabilized group v all of the control groups. This indicated that there was a difference in the overall performance scores between these groups over the six testing occasions on Days 2, 3 and 4. This difference, which just achieved significance ( Obtained F=6.39; Critical F=6.30), indicates that both the normal controls and the ex-user groups performed better overall than did the stabilized methadone group. However, an examination of the other contrasts indicates that this difference cannot be explained by the effect of the acute dose of the drug methadone. Furthermore, one needs only to examine the level of significance of this measure with that of the effect of alcohol or diazepam to compare the intensity of these effects. The extent of the alcohol impairment also provides a measure of the sensitivity of the test battery, as this significance was described for a mean blood alcohol concentration of 0.064 g%.

**Group 2. New Clients and Increased Methadone Dose Groups**

The performance of the groups of new clients, taking their first dose of methadone, and those taking an increased dose of methadone were compared with the performance of the normal controls and the ex-users, as for the first analysis. However, in these comparisons, the first two days of testing of the control groups were used to assess the relative performance measures. The two methadone groups of course were only tested on two days (see Methods).

Subjects used in this analysis comprised 10 new clients taking their first and third doses of methadone, 22 taking an increased methadone dose on the second day, 18 normal controls and 17 ex-users. These numbers were those for whom a complete set of data were available for analysis.

The group difference contrasts indicated that there were no differences between performance measures of the two control groups. The data for both control groups were therefore combined for subsequent analysis for differences between the control groups and the two methadone groups. These contrasts indicated there to be no significant difference in
the overall performance, i.e. across all testing occasions, between the controls and the methadone groups. There was however a trend (in this case, non-significant) suggesting that both of the methadone groups performed less well overall on the tests than did the control groups.

The repetition contrasts examining the pre-post differences of all groups (i.e. both controls and both methadone groups) on days 1 and 2 indicated there to be no effect on day 1, but a significant effect on day 2 ($F=14.61; \text{Critical } F=8.57$). However, the interaction of group x repetition and the pre/post scores both for day 1 and day 2, revealed no trend at all to significance. These analyses indicate that the effect described above for the day 2 pre/post differences could not be attributed to the effect of the daily dose of methadone. In fact, the pre/post differences observed were in the direction of worsened performance of the post scores for all groups.

Finally, from this analysis, the group x repetition x test day x pre/post scores interaction showed there to be no differences between methadone groups and the combined control groups which even approached significance. There was therefore, no effect of the acute dose of methadone for either the new client or the increased dose groups, when compared with the control groups, neither of which received any drug.

**Overall Performance of the Methadone Groups**

Due to the differences in overall scores noted between the control groups and the groups taking methadone (in particular the stabilized group, where the difference just reached significance) we conducted a further analysis, post hoc. All of the analyses above indicate that the differences cannot be due to the acute effect of the drug methadone. Four variables were identified for post hoc analysis which might be expected to influence overall performance on the tests (for details of this analysis, see (Chesher et al. 1989)). These were subject’s age, gender, educational attainment and the dose of methadone.

These post-hoc analyses revealed that the only variable included in this regression equation which significantly related to the overall score was the dose of methadone. However, as none of the members of the two control groups was taking methadone, the term “dose” means only the “presence” or “absence” of methadone.

As the analyses above indicate that the between-group difference cannot be explained by the acute dose of methadone, it is entirely arguable that the differences in overall performance between methadone clients and the controls can be interpreted in a manner which does not involve the consideration of any impairment of skills by methadone or any of the opioid drugs used by these individuals. Those who become heroin-dependent have been shown to differ in a number of ways from those who do not (Hagland and Furland 1978; Kleinman 1978). There has also been an increase in the evidence that personality disorders play a possible aetiological role in opioid dependence. For example, Craig (Craig and Olson 1990) using DSM-III criteria, considered that “drug addicts have an array of personality disorders concomitant to their substance abuse”. The role of unemployment as a factor in skills performance was examined by Appel and Gordon (Appel and Gordon 1976) who compared performance of high dosage methadone maintenance clients on the digit symbol substitution task of the WAIS with employed and unemployed clients. They noted, unexpectedly, that the scores of the unemployed group, although within the normal range,
were significantly lower than those for the employed group. The authors discussed possible reasons for the differences.

**SUMMARY**

The test battery was sensitive to the effects of alcohol (mean BAC 0.064g%) and diazepam (15mg by mouth). There was no evidence for an effect of the acute dose of methadone on any of the experimental groups of clients on the methadone program.

The insensitivity of these tests of skill performance to the acute effect of methadone on the clients within the methadone maintenance program indicate that these clients should not be considered as impaired in their ability to perform complex tasks such as driving a motor vehicle.

Both alcohol and diazepam produced a significant decrement in the performance on the test battery by the control groups and the stabilized methadone clients. However, there was no difference in the intensity of this effect between the groups. There was no evidence for an interaction between methadone and either alcohol or diazepam in the group of methadone clients stabilized on the program.

The overall scores on the test battery showed a trend to poorer performance by the methadone clients. This trend just reached significance for the stabilized group of methadone clients. However, the intensity of this difference was very considerably less than that achieved by alcohol at the mean BAC of 0.064g%. It is considered that this small difference can be interpreted in a manner which does not involve the pharmacological effects of methadone. It is suggested that factors including unemployment, life-style, social and personality disorders could play a contributory role.

**REFERENCES**


Chesher GB, Lemon J, Gomel M, Murphy G (1989) The effects of methadone, as used in a methadone maintenance programme, on driving-related skills. National Drug and Alcohol Research Centre, University of New South Wales, Australia


McDonnell J, Jex J (1967) A “critical” tracking task for man-machine research related to the operator’s effective elay time. Part II: Experimental effects os a system input spectra, control of stick stiffness, and controlled element order. NASA, CR-674
