The Functional Potential of the Methadone Maintained Person
by
Norman B. Gordon


Dr. Gordon is currently Emeritus Professor of Psychology, State University of New York, College at Oswego, Oswego, N.Y. 13126.

In 1967 the initial investigation of the function potential of methadone maintained patients was begun. At the 4th National Methadone Conference Gordon, Warner and Henderson (1972) reported on their extensive study evaluating the "psychomotor and intellectual performance of ex-heroin addicts," who were the first to be maintained on methadone as part of their treatment for opiate addiction. The conclusions derived from those early studies showed that, receiving methadone as part of the treatment for heroin addiction did not have any adverse affects on either cognitive functioning or perceptual motor learning and performance. A later report (Gordon, 1973) summarized field and laboratory studies of the performance of ex-addicts maintained on methadone, from 1964 to 1972. This paper reviews both the earlier work as well as research by other investigators.

This review is divided into two major sections, Laboratory Studies and Field Studies. The laboratory studies included perceptual-motor, reaction-time and sustained attention tasks, as well as tests of cognitive and intellectual functioning. Field studies were primarily concerned with driving experiences of methadone patients as well as general assessments of job performance, compared with relevant control subjects. There were also one or two studies that assessed patient behavior on-the-job.

Laboratory Studies

Prior to the studies to be reported on, only Isbell and colleagues (1948) had evaluated the effects of chronic administration of methadone in humans, which was conducted with institutionalized addicts to determine the addiction liability of methadone.

Intellectual Functioning

The Isbell study had indicated that methadone might have a detrimental effect on intelligence, therefore, one of the concerns of the early studies by Gordon et al (1972) was to examine intellectual functioning after patients were stabilized on maintenance doses of methadone. The results for 155 patients, whose initial maintenance dose ranged from 70-100 mg/day of methadone taken orally, did not show any departure from expected distributions of IQ scores found in the general population. An absence of cases in the lowest IQ categories was also noted.

Subsequently, Gordon and Lipset (1976) followed up on 30 of the 155 patients who had originally been tested for intellectual functioning, approximately 112 months later. When tested initially, these patients, had been maintained on an average of 79 mg of methadone, and on
follow-up, the average daily dose was 69 mg. The tests used were alternate forms of the Wechsler Adult Intelligence Scale (WAIS). Twenty-five patients showed gains in IQ, one stayed the same, and four showed modest declines. Intellectual functioning in the follow-up, as in the original testing, was normal.

Later studies of cognitive functioning have arrived at similar conclusions. A study by Pugliese (1974) found no difference between age and education matched methadone patients and controls, when they were tested with the Wonderlic, a form of intelligence test. This study was concerned with the employability of methadone patients. A study by Lombardo (1974) also found that when educational level was taken into account methadone patients maintained on 50 or 80 mg per day showed IQs in the normal range.

A study concerned with memory processes by Grevert and colleagues (1977) found that methadone treatment had no effect on memory, in a study that compared memory performance prior to and after three months of treatment.

**Laboratory Studies of Performance**

**Reaction-time Studies**

Studies of reaction-time measure decision time as well as motor response times, which are sensitive to drug effects. The first study by this writer (1970), compared 18 male and 9 female methadone patients stabilized on average daily doses of 100 mg, with matched drug-free recently detoxified heroin addicts, and college students. The task consisted of one simple and two more complex reaction-time (RT) tasks. Methadone patients, both male and female, were either equal to or superior to control subjects on two of the tasks, and on the most complex choice RT task.

Later, Gordon and Appel (1972) studied the RTs of methadone patients when they were 24 hours abstinent from their daily dose and compared their performance when they were one-hour post daily methadone dose. Again, overall results for male and female patients indicated no methadone effect, and RTs were either equal to or superior to relevant control subjects. One interesting finding in the latter study indicated that working patient's RTs were more rapid than those of nonworking patients.

Three additional studies (Chesher, 1985; Kelley, Welch & McKnelley, 1978; Rothenberg et. al., 1977) have appeared which reported on reaction-times of methadone patients in laboratory type tests of attention. Some evidence was found that indicated patients may respond more rapidly than controls.

**Sustained Attention**

Appel (1982) studied the performance of methadone patients on a continuous performance task, where responses were made to an unusual signal after subjects were required to ignore varying strings of regular signals. Different rates of signal presentation were used. Methadone patients did not differ from drug-free ex-addicts or opiate naive subjects. There were differences in response latencies among patients - working methadone patients performed better at the high
signal rates, and had longer latencies and poorer accuracy at the low rates. Nonworking patients made more false positive errors at the high signal rate than the other groups.

Appel and Gordon (1976) used the digit symbol sub-test of the Wechsler Adult Intelligence Scale (WAIS) to study patients' abilities to follow a code in substituting digits for two-dimensional pictorial symbols in a paper and pencil speed test. Working patients did not differ from controls, but nonworking patients experienced poorer performance. No evidence was found that patients who spent the longest times in treatment (8 years) were any poorer than patients who had only been in treatment for 11 months.

Rothenberg et al (1977) has found that methadone patients had faster response times than controls, and that there was no difference in maintenance of attention between patients and other groups of subjects.

**Perceptual-motor Skill**

Isbell et al (1948) had indicated that methadone might slow some aspects of perceptual motor functioning. In early studies (Gordon, Warner & Henderson, 1972), perceptual-motor performance was measured by means of the rotary pursuit test (a task used to measure learning and performance in an eye-hand coordination task), over the period of a year or so. Patients exhibited normal functioning.

Moskowitz and Sharma (1979) reporting on skills performance of patients maintained on methadone for at least six months, concluded that patients failed to show impairment on the most obviously relevant skills performance tasks. These studies represent the most comprehensive evaluation of the performance of methadone patients found so far. A series of eight experiments on various sub-skills related to driving behavior were conducted. They included performance in a driving simulator in which patients and control subjects were subjected to a variety of experiences which required close attention and accurate responses. Tests were conducted just before and two hours after the daily methadone doses of both 60 mg and 80 mg of methadone. While two of the sub-tests gave evidence of a methadone effect, patients compensated by more rapid response times. Methadone is also mentioned in another report (Stapleton, Guthrie & Linnoila, 1986) as having an effect on eye movements, but an assessment of the consequences is lacking. Moscowitz and Sharma (1979) felt that the more rapid reaction-times shown by methadone patients, more than compensated for any potential oculomotor slowing. A final study undertaken by Kelley, Welch and McKnelley (1978) of various functional parameters, also failed to find any important evidence of negative impact on overall functional status.

An interesting study by Ho and Dole (1979) indicates that methadone-maintained persons do not differ from drug-free ex-heroin addicts in their perception of somatic pain, a finding of some significance in terms of functional status.

The general conclusion of available laboratory studies of methadone patients is that there does not appear to be any socially relevant barrier to their ability to perform a variety of tasks such as those found in industrial settings or in driving motor vehicles.

**Field Studies**
Field studies reviewed here have relevance to the question of functional capacity of persons maintained on methadone as part of their treatment for heroin addiction. A recent evaluation study of methadone treatment by Ball and Ross (1991), has found a general relationship between maintenance dose and cessation of heroin use. It appears that the critical dosage level is 71 mg of methadone per day. Those patients maintained on doses lower than 70 mg of methadone, are much more likely to use heroin. The finding implies that daily levels below 70 mg result in incomplete tolerance. This would lead to the suggestion that future studies of functional potential, take into account the methadone dose level needed to maintain tolerance.

The studies reported on below fall into two categories; studies of employability of methadone patients and reports of their performance as motor vehicle operators.

**Employability**

Two studies relate to employability (Double & Koenigsberg, 1977; Yankowitz & Randell, 1977). Both studies indicated that ex-heroin addicts maintained on methadone function quite well as skilled laborers and office workers. This matches the conclusions arrived at in an earlier study (Gordon & Lipset, 1976).

**Driving Behavior**

Driving motor vehicles is an area of considerable public concern, given the widespread misuse of alcohol and other drugs. An earlier review (Gordon, 1976) found that there was little cause for concern about narcotic use generally and specifically for methadone use, when it is used as a maintenance drug. Since the earlier review there are a number of additional reports that have appeared (Babst, Newman, Gordon & Warner, 1973; Blomberg & Preusser, 1974; Maddux, Williams & Ziegler, 1977; Moskowitz & Sharma, 1979; Stapleton, Guthrie & Linnoila, 1986). In these studies, methadone maintained individuals did not differ from age-matched non-drug users or abstinent ex-heroin addicts. The studies reported on both traffic violations and accidents, and report confirmation of interview data collected from patients, by means of the patients' actual motor vehicle driving records obtained from official sources. A recent review by Chesher (1985) finds that based on studies of skills related to driving, or based on epidemiological findings, narcotics, including methadone, generally do not appear to be a source of concern in road crashes.

**Conclusion**

The general conclusion of this reviewer is that there is considerable confidence in the fact that maintenance on methadone at appropriate dosage levels, as part of treatment for heroin addiction, has little if any affect on ability to function in any capacity for which the person is qualified.

The foregoing conclusion should not seem so surprising in view of the fact that even heroin addicts (Caplowitz, 1985) while using heroin, as well as those maintained on morphine as part of their treatment for heroin addiction (Waldorf, Orlick & Reinaman, 1974), were able to be gainfully employed and successful in a wide variety of positions.
Recently it was reported that large doses of opiates are being chronically administered to individuals suffering from otherwise intractable pain (New York Times, 1993). The use of opiates, in the manner reported, for pain management, not only relieves suffering, but enables affected individuals to function normally. The main disability they suffer is stigma for their presumed "addict" status.

The lesson we learn from this, is that addictive behavior, is a construct that is biological in origin and modulated by social and behavioral factors. Narcotics per se can cause physical dependence, tolerance, and craving. However, the social context of a person's narcotic use and way of life determines the nature of addictive behavior. In conclusion, methadone patients who are either building or rebuilding their lives or who are functioning normally within the community are not "addicts" but medical patients being treated for a chronic condition.

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References


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Selective Attention in Opiate Dependent Individuals:
A Pilot Study Investigating the Effects of Endorphin Levels on Attention
by
Ann Rosenberg

Ann Rosenberg, Ph.D. is the Director of Research at the Nassau County Office of Alcoholism and Substance Abuse Services, Long Island, New York.

Introduction

Theorists such as Dole and Nyswander (1976), Goldstein (1972) and others have considered the possibility that there are physiological differences between opiate dependent and non-opiate dependent individuals. This study seeks to explore this possibility. Opiate dependent individuals may have a deficiency of endogenous opioids which they attempt to supplement by the use of opiates (Goldstein, 1976). The present research investigates the effect on attention that occurs by varying systemic levels of endorphins, the internal, or endogenous opioids.

In 1973 three laboratories found evidence of opioid receptors in vertebrate animals, with the highest concentration in the brain (Pert & Snyder, 1973; Simon, Hiller & Edelman, 1973; Terenius, 1973). Investigations followed that led to the discovery of naturally occurring, or endogenous, opioids, called endorphins that bind to these receptor sites (Goldstein, 1976; Hughes, Smith, Kosterlitz, Fothergill, Morgan & Morris, 1975; Terenius, 1975). Goldstein (1976) suggested that opioid receptors were related to emotional responses to pain.
A rich concentration of opioid receptor sites is located in the Locus Coeruleus (LC), an area of the brain that mediates attention (Kuhar, Pert & Snyder, 1973). Investigators found that applying morphine, or producing chemical lesions to the sites in the LC, interfered with the ability of the neurons to fire (Aghajanian, 1978; Pepper & Henderson, 1980; Arnsten, Segal, Loughlin & Roberts, 1981). Other investigators determined that the LC neurons responded selectively to complex, arousing stimuli (13). These studies indicate that the endorphin system plays a broader role than that of relaying information about pain and anxiety. It also plays a role in the processing of attentional information through the LC.

Implication that the endorphin system affects attentional mechanisms leads to questions regarding the effects on processing of simple and complex stimuli. Easterbrook (1959) has theorized that attention to a limited range of cues is preferable for certain tasks. Studies by Kahneman (1973) suggest that performance of a simple task requires limiting attention to a narrow range of cues, and conversely, the ability to attend to a wider range of cues facilitates performance on a complex task.

Naloxone and naltrexone are opiate antagonists; they block the ability of opiates to bind to the receptor sites, and inhibit the effects of opiates. The work of Arnsten (1981) and Arnsten et al (Arnsten, Segal, Loughlin & Roberts, 1981; Arnsten & Segal, 1979) suggests that naltrexone may operate to narrow the range of cues to which individuals attend. This may be desirable for performance on simple tasks, but inhibit performance on complex tasks. Gritz et al (1976) reported that naltrexone facilitated performance of opiate users on a simple task of selective attention. Appel and Gordon (1976) used a task of selective attention, the Digit Span sub-test of the Wechsler Adult Intelligence Score (WAIS), to compare subjects in methadone maintenance treatment with opiate-naive controls, and found no significant difference.

The above theories, discoveries and studies suggest that different levels of endogenous opioids should have an effect on the performance of simple and complex tasks of selective attention. Simply put, individuals with different levels of opioids in their system will respond differently to attentional cues. Opiate dependent individuals may have a deficiency of endogenous opioids (Goldstein, 1976). Treatment modalities for these individuals provide environments that affect systemic endorphins by controlling the use of exogenous opioids. Methadone maintenance treatment provides supplemental opiates, drug free residential treatment prohibits the ingestion of opiates, and treatment with naltrexone blocks the effect of both endogenous and exogenous opiates.

The present study investigates a model that states that: 1) the ability to respond to attentional cues is affected by endorphin levels, 2) this can be observed behaviorally when endorphin levels are manipulated, and 3) the nature of treatment for opiate dependency manipulates these levels.

The hypotheses are based on the theory that performance on tasks of selective attention is dependent on the systemic levels of endogenous opioids. If this is true, 1) methadone-maintained individuals and opiate-naive controls should respond similarly on simple and complex tasks of selective attention, because, though there may be a deficiency of endogenous opioids in this treatment population, methadone supplements this deficiency; 2) abstinent opiate-dependent individuals, who are not provided with opioid supplements should achieve lower scores on both
simple and complex tasks of selective attention than scores achieved by both methadone treated individuals and by opiate-naive controls; and 3) if naltrexone does indeed help narrowly focus attention, individuals in naltrexone treatment should receive higher scores on simple tasks of selective attention than those of individuals in any of the other groups. However, because both endogenous and exogenous opioids are blocked, their scores on complex tasks should be lower than those of all other subjects. There should also be a greater difference in scores on both tasks within this group than those found in all the other groups.

The Study

Three groups consisted of subjects who were in treatment for opiate dependence. Group I consisted of 12 subjects in methadone maintenance treatment, Group II was made up of 12 subjects in treatment at a drug-free residential facility, and the eight subjects in Group III were in naltrexone treatment. Group IV was a control group made up of 12 opiate-naive subjects. All subjects were male and ranging in age from 21 to 44. All subjects were tested for near vision with the Nearpoint Rotochart. They were also tested with the Digit Symbol sub-test of the WAIS for the ability to distinguish and identify the numbers and symbols necessary for completing the various tasks, and to replicate the attentional task used by Appel and Gordon (1976).

Two forms of a paper and pencil Symbol Identification Test were developed by the investigator and evaluated for this research. They were used to evaluate performance on simple and complex tasks of selective attention. Both forms of the tests were administered in counterbalanced order.

Results

The first set of hypotheses contended that there would be no significant differences in scores on both the simple and complex tasks between the methadone maintained subjects and the opiate-naive controls was supported by the data. These results are consistent with research suggesting that opioids are involved in mediating attention, and suggests the need for opiate-dependent individuals to receive supplementation.

The second set of hypothesis claimed that abstinent opiate users would have lower scores on simple and complex tasks of selective attention than methadone-maintained subjects and opiate-naive controls. Although the difference between the scores of the groups were not statistically significant, the results of all the comparisons were in the predicted direction.

The third set of hypotheses is based on the contention that naltrexone narrows the range of cues to which individuals attend by blocking the effects of endogenous opioids. Predictions are that individuals receiving treatment with naltrexone would have higher scores on simple tasks of selective attention than all other groups and lower scores on complex tasks than all other groups. It was also predicted that naltrexone treated subjects would show the greatest differences between scores of simple attentional tasks and scores on complex tasks. As before, all the results were in the predicted direction, but did not reach significance.

Summary
That there were no significant differences between groups overall served to confirm some hypotheses, specifically those that predicted similarities in function between methadone and control groups. But these results, at first glance, may be seen as weak in general, since differences that were found between the groups were not statistically significant.

On the other hand, it would be impossible to dismiss the hypotheses since the results were all in the predicted direction. A closer look at the differences between scores on the simple and complex tasks for all groups reveals consistently predicted trends. The absence of statistical significance may be due to an inadequate sample size. Increasing the number of subjects in each group may yield more significant results by differentiating discrete differences in attention between the groups.

The differences in attentional functioning sought in the present study may be more effectively measured with a combination of behavioral and physiological measures, specifically, highly demanding vigilance tasks combined with physiological measures of evoked potential at the brainstem and cortical levels.

The consistent trends revealed in this study not only prevent dismissal of the hypotheses and the theories that gave rise to them, but are actually indications that this is a fertile area for research. There are benefits in pursuing this investigation, not only for opiate dependent individuals, but also for individuals diagnosed with attentional deficits. Understanding the role of the endorphin, or endogenous opioid system in selective attention is an important step in helping to uncover the causes of some types of attentional deficits and in furthering the understanding of opiate dependency.

References


