Conditioned Responses to a Videotape Showing Heroin-Related Stimuli

Stephen I. Sideroff,* Ph.D.

Murray E. Jarvik, M.D., Ph.D.

Department of Psychiatry
School of Medicine
University of California
Los Angeles, California 90024

Veterans Administration Hospital Brentwood
Los Angeles, California 90073

Abstract
Heroin addicts on 0 or 2 mg of methadone and finishing a 14-day detoxification program, and control subjects were shown a videotape of heroin-related stimuli. Psychological questionnaires were completed before and after the videotape, while physiological responses were monitored during viewing. It was found that the experimental subjects had an increased level of anxiety, depression, and subjective level of craving following the stimulus presentation, with the controls showing no similar change in these measures. In

*To whom requests for reprints should be addressed at 530/151D, Veterans Administration Hospital Brentwood, Wilshire and Sawtelle Boulevards, Los Angeles, California 90073.
addition, the experimental group had significant increases in heart rate and galvanic skin response compared with controls. The results present some of the first objective evidence of conditioned abstinence occurring in addicts exposed to stimuli closely related to those found in the natural environment.

INTRODUCTION

Conditioned effects of heroin use have long been postulated as a primary cause of relapse. Wikler (1961, 1965) suggested that addicts, returning to their old environment, come in contact with stimuli previously associated with withdrawal pain. This produces a conditioned state of withdrawal which, while perhaps less severe than the genuine withdrawal pain, still reproduces some aspects of the “sick” feeling. In addition, there is evidence of a physiological imbalance resulting in an opioid need (protracted abstinence), persisting for as much as a year after opiate termination (Wikler and Pescor, 1970). The resultant psychological and physiological state can lead to drug-seeking behavior—the behavior the addict has learned will alleviate the pain. While readily acknowledged, this readdiction theory has been supported only by anecdotal evidence and animal studies (O’Brien, 1975; Goldberg et al., 1969).

In an effort to demonstrate experimental support for this theory, O’Brien et al. (1975) conditioned abstinence symptoms in humans in a laboratory setting. Pairing a tone and odor to a naloxone-induced abstinence response, they reported conditioned abstinence responses in five of their eight subjects. Yet their stimuli were quite distinct from the naturally occurring conditioned stimuli the addict typically encounters in his environment.

Furthermore, while conditioned abstinence had been demonstrated in monkeys, it has been shown that this effect undergoes rapid extinction (Goldberg et al., 1969). On the other hand, in a clinical study on the effectiveness of naltrexone, an opiate antagonist, Sideroff et al. (in preparation) report that most instances of strong desire for drugs correspond to stimuli associated with the heroin “high.”

But perhaps this dichotomy is academic, since an addict is always the “sickest” (in terms of abstinence pain) right before the next “fix,” i.e., his behavior is cyclical. Thus the conditioned stimuli associated with withdrawal are likely to be identical to those associated with “shooting up,” the high, and the heroin itself. This total conditioned Gestalt might best be called “craving.”

It would thus be incumbent on researchers into this problem to examine the conditioned effects of stimuli surrounding the actual acquisition, pre-
paration, and administration of heroin. Teasdale (1973) presented addicts with slides of drug-related scenes such as the syringe, a person injecting, and an "outfit." He found some indication that these slides increased anxiety and confusion on a self-rated mood scale. More objective measures, however, were not available.

The present experiment was an attempt to come as close as possible to replicating the actual stimuli the addict encounters in his own environment. In addition, physiological measures were taken as an objective means of determining the effects of the stimuli on the addict.

METHOD

Subjects

The subjects were 16 patients from the Veterans Administration Hospital Brentwood. The experimental group consisted of eight subjects from a 14-day inpatient detoxification program. At the time of their participation, they were either at 2 or 0 mg of methadone. The control subjects consisted of two patients who had only snorted heroin, plus six patients who did not have drug habits but were equated with the drug patients with respect to education and socioeconomic status.

Procedure

Subjects were asked to sit in an easy chair in front of a television monitor. They were then connected to a Beckman Type R Dynograph via electrodes to record heart rate and galvanic skin response (GSR) as well as a thermocoupler attached under the nose to monitor respiration.

They were then asked to answer the Weak Opiate Withdrawal (WOW) Scale of the Addiction Research Center Inventory (Haertzen et al., 1970), the Multiple Affect Adjective Checklist (MAACL), Symptom Checklist, a brief drug history, and a Craving Scale (this consisted of a vertical line marked off in increments of 10, from —100 through 0 to 100; "0" was labeled "take it or leave it"; an arrow going up marked "increasing craving," and an arrow going down marked "increasing repulsion"). They were also given blank paper and colored magic markers and asked to draw a person on one page and an expression of their feelings at the moment on a second page. This same series of tests was again administered to the subject at the conclusion of the experiment.

After completion of the questionnaires, the subjects were asked to relax
for a few minutes. They were then shown a 6-minute videotape (VT) depicting scenes of heroin preparation and "shooting up," including the actual injection of the drug. There was a 5-minute baseline period before and after the VT presentation, as well as a 1-minute break at 4 minutes into the film.

Upon completion of the second set of questionnaires, the experimenter sat down and talked with subjects, answering any questions they might have as well as making observations on physical appearance. Follow-up meetings were made to assure that there were no long-lasting effects from the VT.

RESULTS

Pre-VT questionnaire scores from the experimental group were compared with those of the control subjects. The only test yielding significant differences was the WOW (p < .05), with means of 13.25 and 10.7, respectively. In addition, anxiety levels of the MAACL were elevated for both groups in comparison to normative data (Zuckerman and Lubin, 1965).

For statistical purposes, the questionnaire data were handled by subtracting the pre-VT score from the post-VT score for each subject. Thus a positive number indicates an increase in the measure being examined, while a negative number demonstrates a decrease in that measure. Figure 1 shows the results for the WOW questionnaire, the MAACL, and the Craving Scale. The numbers represent mean difference scores for the two groups. As can be seen, there was little difference between pre and post scores for either group on the WOW. Mann-Whitney comparisons between the experimental and control group yielded no significant difference (p > 0.1).

In the subjective level of craving, however, one can see a large increase in craving by the experimental group, with no comparable response in the control group. Comparisons between the experimental and control groups indicated a significant difference (p < 0.01).

Also in Fig. 1 are the mean difference scores for the MAACL's levels of anxiety, depression, and hostility. It can be seen that subjects in the experimental group showed increases in their level of anxiety and depression. These differences were found to be significantly different from those of the control group using the Mann-Whitney Test (p < 0.01). No significant difference was found for the measure of hostility (P > 0.1).

Turning to the physiological data, we see percent heart rate changes from baseline (Fig. 2) for each minute of the experiment for the two groups. [Baseline heart rate was not statistically different between the experimental and control groups; analysis of variance, (p > 0.1).] Note that the 5th, 8th,
and 9th minutes are control, with no VT being shown. It can be seen that the experimental group response is an acceleration in heart rate during each minute of the VT, while the control group response is primarily a deceleration. An analysis of variance conducted on the heart rate percentage changes yielded significant differences for the 1st, 4th, and 6th minutes between experimental and control groups. ($p < 0.05$).

Fig. 2. Percent heart rate changes from baseline during each minute of VT presentation as well as a 2-minute post-VT period.
Figure 3 presents similar data for respiration rate. Although the graph indicates that the group of detoxing patients has consistently higher respiration rates during the first 4 minutes, these differences were not statistically significant (analysis of variance, $p > 0.05$). This was probably due to the high degree of variability within groups.

Finally, a Mann-Whitney analysis of the number of GSR responses (each 2-mm deflection of the Dynograph pen was counted as a response) between the control and experimental groups indicated the latter group made a significantly greater number of responses ($p < 0.01$).

Experimenter observations before and after the VT indicated subjects in the experimental group yawning, sniffing, and being generally more tired-looking at the end of the experiment. This, however, was not a double-blind procedure.

**DISCUSSION**

The major findings of the present experiment were that drug addicts terminating a 14-day detoxification program demonstrated significant psychological and physiological changes to the presentation of heroin-related stimuli. These changes included an increase in anxiety, depression, and subjective level of craving, as well as an increase in GSR and heart rate acceleration. When these responses are studied in conjunction with the observed post-VT behavior in the experimental group (yawning, sniffing, half-closed eyelids), it appears that some form of conditioned abstinence
response was demonstrated (Himmelsbach, 1939). These data, particularly
the reported increase in level of craving, support the contention that the
conditioned effects of heroin are a major cause of relapse in addicts (Meyer et
al., 1976; Wikler, 1965).

While other studies have, to some extent, demonstrated this phenomenon
(O'Brien et al., 1975; Teasdale, 1973), the present study is the first to show
both psychological and physiological changes to stimuli so closely resem-
bling drug-related stimuli of the addict's environment.

As discussed in the Introduction, the conditioning of environmental
stimuli to the withdrawal state cannot be considered in isolation. Since the
addict experiences the strongest abstinence "pain" just prior to his next "fix,"
we would expect the same stimuli to be conditioned to both withdrawal and
to the "high" resulting from heroin injection. It is interesting to note,
therefore, that the conditioned responses demonstrated in this report are
similar to those associated with withdrawal and not with an opiate "high."
This might be a function of the type of person viewing the VT. If they were
patients seriously trying to go drug-free, it is probable that the presentation
of heroin-related stimuli would produce anxious responses. One fear at the
outset of the experiment was that patients might be tested who were
detoxifying simply to return to the street at a lower heroin dose. This
hypothetical subject, it was assumed, would respond quite differently from
the subject seriously trying to go drug-free. It is left to future experiments to
determine if a conditioned "high" constellation of responses can be dem-
onstrated.

The reported data should be considered with caution until further
research is performed to assess their reliability as well as the range of addicts
to which the data are applicable. Subsequently it would be important to
determine if these conditioned responses indicate degree of susceptibility to
relapse. One might expect that addicts demonstrating the greatest condi-
tioned responses to the VT are most likely to go through conditioned
withdrawal when they return to their home environment after being
detoxified. To verify this hypothesis, follow-up studies need to be carried out
on subjects taking the VT experiment to determine the correlation between
conditioned responses and "latency to relapse." The possibility of a resultant
"readdiction liability" score has important implications for treatment pro-
grams. The test procedure might be used to (1) assess the readiness of a patient
to leave a treatment facility (2) evaluate the efficacy of a treatment program,
and (3) be the basis for desensitization procedures. A program should then be
provided to train personnel to operate and understand psychophysiological
equipment and integrate these procedures within a treatment program.
ACKNOWLEDGMENT

This research was funded in part by USPHS Biobehavioral Research Support Grant No. RR 05756–04.

REFERENCES


HIMMELSBACH, C.K. Studies of certain addiction characteristics of (a) dehydromorphine ("Paramorphin"), (b) dehydrodesoxymorphine ("Desomorphine"), (c) dihydrodesoxycodine-D ("Desocodeine"), and (d) methylidihydromorphone ("Metopen"). J. Pharmacol. Exp. Ther. 67: 239–267, 1939.


