

## **Craving in Heroin Addicts Maintained on the Opiate Antagonist Naltrexone**

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### ABSTRACT

The level of heroin craving was monitored in patients receiving naltrexone on a regular basis. Meetings and interviews conducted twice weekly attested to a pattern of craving reduction in most but not all the addicts. It was also found that it usually took 3 to 5 weeks for this effect to occur. The possible relationship between drug craving and participation in the naltrexone program is discussed.

In recent years there has been considerable interest in the use of opiate antagonists, and naltrexone in particular, for rehabilitation of drug addicts [1, 2]. Use of this drug is suggested by studies indicating that the discomfort from withdrawal of opiates can last for weeks and even months, thus instigating drug-seeking behavior [3, 4]. Drug craving may also be produced through conditioned responses to stimuli from the addict's environment [5, 6]. If the patient has taken naltrexone, however, use of an opiate will not be reinforcing and the drug-taking behavior might extinguish [7].

Studies thus far assessing the clinical efficacy of naltrexone have been hard to evaluate due to the high dropout rate common to all opiate treatment programs as well as the inherent compliance problems specific to opiate antagonists [8-10]. One aspect of antagonist treatment that needs more examination is its effect on the addict's craving for heroin, since this might have a bearing on the treatment's efficacy.

Naltrexone was initially investigated by the Committee on Evaluation of Narcotic Antagonists (CENA), established within the National Research Council. Its goals were to investigate the feasibility and acceptability of naltrexone, and to assess methods for determining the efficacy of such treatment [10]. In its final report the data suggested that level of craving for naltrexone patients tended to be lower than for placebo patients at the end of the study. Other research supports the notion that addicts taking naltrexone show a decreased desire for heroin, even when it is made available [8, 11].

The level of craving is relevant for two reasons. On the one hand, if craving is reduced the addict is freed to think and act on issues other than drugs while gaining a measure of confidence; on the other hand, this might indirectly affect the treatment outcome in a negative manner. It was initially hypothesized that antagonists would bring about the extinction of drug seeking and taking behavior since it would no longer be rewarded [5]. Some believe, however, that for this to occur an active extinction process must take place [12, 13]. If drug addicts on naltrexone have no desire to use opiates and do not test ("shoot-up") on a regular basis, according to this theory, extinction, i.e., successful rehabilitation, may not occur. Also, once craving is reduced the addict has less incentive to continue taking naltrexone and staying in treatment.

This report describes an attempt to systematically follow the level of craving in heroin addicts on a 9-month naltrexone program. We also wanted to determine how many of our patients tested the antagonist blockade, how frequently, and if testing correlated with a reduction in craving.

## METHOD

Subjects participating in the Naltrexone Treatment Program at the Veterans Administration Hospital Brentwood [14] were volunteers from three groups: a 14-day inpatient heroin detoxification program, former addicts, and methadone maintenance patients who had been in the methadone program at least 6 months, with few absences and currently on 50 mg or less of methadone each day.

After the appropriate detoxification period, patients went through a naltrexone induction schedule of increasing doses until 100 mg was reached. This dose was subsequently given every Monday and Wednesday, with 150 mg ingested (in a liquid vehicle) on Fridays.

In addition to the naltrexone, patients completed various psychological questionnaires at the start of the program and at specified intervals thereafter. These included the Multiple Affect Adjective Checklist, Weak Opiate Withdrawal Scale from the Addiction Research Inventory, an attitude scale measuring "internality-externality," and a symptoms checklist. Blood chemistry and other physiological measures were also periodically taken, as well as weekly urinalyses for each subject. The urine testing was performed on a random basis within each week. A weekly therapy group was also part of the program.

Finally, patients were asked to respond daily as to their level of craving. To record this information they were given copies of a craving scale which consisted of a vertical line marked off in divisions of 10 and going from -100 through 0 to +100. The 0 point was labeled "Take it or leave it." A vertical arrow pointing toward +100 was labeled "increasing craving," while the arrow going toward -100 was labeled "increasing repulsion." This form was originally used in the CENA study [10]. In addition, each scale had space for responses to: "Where are you?," "With whom?," "What are you doing?," and the date.

The instructions for completing the scale went as follows: "We would like you to indicate on this scale how strong your desire is for heroin. The greater your desire the higher up you will mark on the scale. The strength of this desire might be measured by how much you would go through to get a 'fix.' For example, if you would steal for a fix that indicates a considerable craving, while doing it only if someone handed you a free spoon would indicate a lower level of craving. If you imagine you would get disgusted if someone offered you heroin, this would indicate that a negative score is appropriate."

Patients were asked to fill out the "craving scale" whenever they had an urge to use an opiate but also to complete at least one scale each day. As

the program progressed it was discovered that collection of the data on a daily basis was difficult due to the lack of compliance by the naltrexone patients. There was great resistance on their part to filling out the craving scales. As a result, staff arranged two contacts each week (one of these meetings was the weekly therapy group) to question the patients and elicit the appropriate information. The data reported in the next section are based on these two responses per week.

## RESULTS

Table 1 indicates the length of time drug addicts entering our program stayed on naltrexone. This includes all patients entering treatment during the first 10 months. It can be seen that there is basically a bimodal distribution, with nine patients considered long term (over 3 months) and seven short term (1 month or less). There are three entries in between: 1 to 3 months. One patient accounted for both entries in the 1 to 2-month bracket as well as an entry in the 3 to 6-month bracket (i.e., he commenced the naltrexone program three times).

In Table 2 the range of craving scores for each patient is given on a month by month basis over the course of their treatment. The table is divided into three groups based on subject's level of craving at the time of termination from the program. The seven who dropped out of the program during the first month of treatment are not listed. The information elicited from this early dropout group was that their craving continued at a high level throughout participation. Follow-up on five of the seven indicated an immediate return to using opiates after they dropped out (a sixth had transferred to a methadone program closer to his home after 1 week on naltrexone).

Table 1. Length of Time in Treatment

Months	Number of patients
8-9	2 <sup>a</sup>
6-7	0
3-6	7
2-3	1
1-2	2 <sup>b</sup>
0-1	<u>7</u>
Total	19

<sup>a</sup>One of these patients has elected to remain on naltrexone beyond the 9-month term. Currently he is into the 12th month.

<sup>b</sup>Both of these entries, as well as one entry in the 3-6 month row, represent the same patient. He has had two terms of 1½ months and his last term was of 3½ months duration.

Table 2. Level of Craving in Patients on the Program for More Than Two Months<sup>a</sup>

Patient number	Upon entering	Range of craving levels by month								
		1	2	3	4	5	6	7	8	9
1	10/30	-70/-90*	-70/-90	-70/-90	-70/-90	-70/-100	-100	-100/30	-100	-100
8	0	-20	-20	-20/-30	-20	0/-20	-10/-30	-20	-20/-40	-20/-30
12	-100	-100	-100	-100	-100	-100				
3	0/30	-10/25*	0	0	0					
7	0/20	-40/20	-20/10	0	0					
15	20/40	0/40*	0	0						
16	20/50	0/30*	0							
2	20/40	0/40*	0/20	0/20	0/20					
10	30/50	20/40*	20/60	20/80	20/50	20/80				
13	20/40	0/60*	10/40	10/50						

<sup>a</sup>Of the seven who dropped out during the first month, one was transferred to another program and five of the remaining six returned to using heroin immediately after discontinuing naltrexone. Our evidence indicates their craving levels remained high while on naltrexone, even after testing its effectiveness.

<sup>b</sup>Indicates a test of the naltrexone blockade during this period with heroin.

From the table we can see that six of the patients reported that they had no craving for heroin after the first month on naltrexone (as indicated by "0" or negative scores by the second month). This is in contrast to only two indicating no craving at the start of the program. Two others reported a partial drop in craving during this period (Subjects 2 and 7) with one of these going to zero the following month. Only two patients' levels of craving continued as high—in fact slightly higher—as when they started treatment (Subjects 10 and 13). A sign test of changes in craving scores was performed using the mean scores for each month for each subject. The test indicated a significant reduction in craving during the first month on naltrexone ( $p < .01$ ) but not during any successive month.

Finally, note that seven of the subjects in Table 2 actually tested the effectiveness of the naltrexone blockade by taking a "fix." Of these seven, four reported an immediate reduction (although not necessarily an elimination) in desire for heroin and did not test again while on the program. For the other three, there was no reduction in craving the first time they tested. Two of these patients did test a second time and both reported reduced craving (Subjects 2 and 13).

It is difficult to discuss "testing" by the early dropout group since some did not last beyond a week. Three of these subjects indicated that they "shot up" while on naltrexone, after which their craving still existed. In fact, one patient fixed almost every day he was on naltrexone and dropped out at the end of the first week.

## DISCUSSION

Our data appear to support previous evidence [8, 10] that naltrexone treatment reduces the subjective level of craving in patients. Perhaps this is due, as Meyer et al. [15] point out, to its establishment of an  $S^{\Delta}$  condition, indicating that heroin is functionally unavailable. We found, however, that it takes a certain amount of time on the program before this reduction occurs. This period—about 3 to 5 weeks—appears to be necessary for some kind of stabilization to take place. An initial shaky period is evidenced by our almost perfect bimodal distribution with respect to length of time on the program. For the most part it appears that once a patient got past the fourth week, he became accustomed to living with a blockade, and this translated into the elimination of heroin craving.

Another possible explanation for the first month's reduction in craving is

that this is a normal occurrence among detoxified addicts who are able to remain drug-free. Previous studies indicate that a subtle change from primary to secondary abstinence occurs between the fifth and ninth week post-addiction [3, 4] and might coincide with a decrease in craving. In order to test this hypothesis it would be necessary to follow the level of craving for a control group of addicts subsequent to detoxification. This explanation, however, does not account for the subjects reporting a reduced craving immediately following a "fix."

The paradox found in our program as well as other naltrexone programs is that patients drop out (and many times return to opiates) even though they express no craving or desire for heroin. In subsequent interviews (usually during readmittance to the naltrexone program) we find tentative answers. For some the feeling of success and clean living is just too alien—they don't feel comfortable unless things are going poorly for them. With others, they start doing so well that they don't feel they need to continue on naltrexone, when in actuality they still need the protection it affords.

It should be pointed out that not all patients demonstrated a lowering of craving levels. Most, if not all, of those dropping out during the first month never lost their craving. Of the longer term addicts, two continued to have the urge to shoot up. The response of these patients is contrary to the hypothesis that craving correlates with availability [12].

We found that seven of the 10 longer term naltrexone patients tested the blocking effect of the antagonist. Only one tested more than twice. Of these, six reported a reduction in craving as a direct consequence of this act. Reports by three patients who dropped out during the first month indicated their craving remained the same after testing. These data are ambiguous. Certainly for some, the lack of availability as a result of the blocking effect of naltrexone eliminated their craving. It is important again to keep in mind, however, that no control group was followed in this study. Therefore, it is possible that the reduction in craving was a function of other aspects of the treatment, or of the selection process.

One aspect of the reduction in craving is its stability or permanence. Anecdotal information from one patient might be important in this regard. This patient (Subject 1, Table 2) consistently reported a repulsion for heroin, always marking between -70 and -100. During one week he lost his job and was falsely arrested. Immediately after these occurrences, in the seventh month of treatment, his craving went to "10-30." The point to be made is that even someone apparently on the road to rehabilitation and under the "protection" of naltrexone is vulnerable to relapse, as evidenced in the dramatic rise in subjective level of craving.

The results of this study point to a possible way of improving the effectiveness of naltrexone treatment. For example, if patients are kept as inpatients during the first unstable 3 to 5 weeks, i.e., if it is very easy for them to continue treatment, we might expect a drop in craving by the fifth week. Once this drop occurs the probability of the patient staying on naltrexone as an outpatient should be significantly increased.

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