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Heroin Add & Rel Clin Probl 2002; 4(2): 11-18 **Research report**

Is craving for heroin and alcohol related to low methadone dosages in methadone maintained patients?

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Summary

The craving for heroin, alcohol and cocaine of 84 heroin-addicted patients under Methadone Maintenance Treatment have been evaluated to highlight possible craving clusters, and to underline contingent correlations with clinical characteristics such as addiction history, positive symptom distress and methadone dosages. The results show a correlation between methadone dosage and a craving for heroin and alcohol. Patients treated with low dosages of methadone show more psychopathological symptoms and a stronger craving for heroin and alcohol. On this basis, the search for an appropriate methadone dosage should be viewed as crucial to the success of the treatment, because it minimizes alcohol and heroin craving, and reduces the risk of psychopathological symptoms during treatment.

Key words: Methadone Maintenance - Methadone dose - Craving

The term craving initially was used to refer to the overpowering urge for opiates experienced by opiate-dependent patients during acute withdrawal [18]. It has subsequently been utilized for describing the desire to use any abused substance at any time. Nevertheless several similarities and differences can be found between the craving for opiate, for cocaine and for alcohol. The association between craving and physical withdrawal symptoms appears to be stronger among opiate-dependent than among alcohol-dependent patients. Among cocaine-dependent patients this relationship is even more tenuous than it is among alcoholics [14]. The subjective experience of "craving" alcohol, cocaine, or opiates has played as significant a role in theories of relapse as it played in theories of drug dependence. Yet a number of retrospective surveys of relapsed alcohol or drug dependent patients call its role into question.

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Psychological distress, family problems, social pressure, interpersonal conflict and the pleasurable effects of the drugs were the most frequently cited explanations by drug addicts for their relapse [3].

The aim of the present study has been to investigate heroin, alcohol and cocaine craving during Methadone Maintenance Treatment Programmes and to focus on contingent correlations with clinical characteristics such as addiction history, positive symptom distress, and the methadone dosages being taken by patients at interview time.

Method

Subjects

Patients diagnosed as affected by heroin addiction, on the basis of the DSM-IV criteria, and under Methadone Maintenance Treatment have been evaluated. Patients enrolled were at different phases of the Methadone Treatment (induction, stabilization, maintenance and detoxification), so as to guarantee the greatest possible variety of different forms of craving.

The sample consisted of 84 patients, 60 men (72.3%) and 24 women (27.7%) with a mean age of 32±6 (ranging from 19 to 50 years).

The stereotypical demographic features of the sample were as follows: male (72.3%), not married (63.5%), with less than 8 years of education (71.1%), and unemployed (51.8%). Their financial situation was, subjectively, considered to be adequate by 53%. Most of the subjects were living with their families (91.6%). Most had been born and were living in Central Italy (95.2). Physical and psychological features included liver diseases (79.5%), odontopathy (42.7%), mood disturbances (65.5%) and anxiety (53.6%). Their social adjustment was generally not troublesome, apart from problems with the law. 48.8% had been arrested at least once. Many were polyabusers (75.6%), with quite frequent abuse of stimulants and cannabinoids (59.5% and 92.9%, respectively). Opiate intake took place more than once a day (61.3%), and almost all the patients (96.3%) had succeeded in interrupting the use of drugs for varying periods of time. Almost all (97.6%) had already been treated, without any significant results. They had come into contact with drugs for the first time when they were about 16 and had started to use them regularly at about 21. The mean duration of their dependence was 145 months; they had first request treatment at the age of 25. They had been under treatment for an average time of 4 years.

Study setting

Patients were recruited in an Italian Public Drug Addiction Outpatient Clinic (SerT) that has been available to heroin addicts since the Seventies in Central Italy. Relapse into heroin use was not a reason for excluding patients from the programme. Reasons for treatment exclusion were the sale of drugs and continued addictive behaviours, with the violation of therapeutic goals, or physical violence at the clinic.

Study design and data collection

This has been a cross-sectional observational study of all patients on the Methadone Maintenance Treatment Programme, lasting almost one year. After informed consent has been given, members of the PISA-SIA (Study and Intervention on Addiction) Group administered rating scales to explore patients' socio-demographic characteristics, addiction history and the psychopathological symptoms, and their craving for heroin, alcohol and cocaine. No members of the PISA-SIA Group belonged to the staff of the Addiction Unit where the study was held or knew the identity of probands. Probands had no reason to expect therapeutic changes or restrictions as a result of what was reported on the rating scales.

Assessment

Addiction History

The characteristics of opioid dependence were investigated through the RSDA (Rating Scale for Drug Addiction) by Maremmani et al. [9]. The RSDA is an observer evaluation questionnaire. It is divided into several areas. The first investigates physical condition at evaluation time (hepatic, vascular and lymph node pathology, gastroenteric disorders, sexual disorders, dental pathologies and HIV infection). The second studies the mental state in terms of psychopathological symptoms in different areas (insight, memory disorders, anxiety disorders, mood disorders, aggression versus others and self-aggression, thought disorders and sensory perception disorders). The third reports socio-environmental conditions at evaluation time (employment, family, sex, socialization and leisure time, and legal problems). The fourth examines lifetime substance abuse (alcohol, opiates, CNS depressants, CNS stimulants, hallucinogens, phencyclidine, cannabis, inhalants, and polysubstance abuse). The fifth examines the clinical picture of substance abuse (age at first use, age during continued use, frequency of drug use, modality, pattern of use, phase, nosology and age at first therapeutic contact), previous therapies, the current therapy and methadone dosage.

The index card automatically provides a total score and ten factor scores. The first five factors record physical problems (number of pathologies), mental problems (number of psychopathological areas with presence of symptoms), polyabuse (number of lifetime substances abused), previous treatments (number of), combined present treatments (number of). The last five factors register categorical (0=absence of problems; 1= presence of problems) social adjustment factors: occupational and family situation, sexual problems, socialization and/or leisure time, and drug-related legal problems. The total score is the sum of all the categorical factors (0=absence of problems; 1= presence of problems).

Inventory Check List (SCL-90)

The SCL-90 [5; 6] is a self-administered inventory consisting of 90 items, each grading from 1 to 5 according to severity. Items are grouped in nine subclasses: Somatic Symptoms; Interpersonal Sensitivity, Obsession-Compulsion, Depression, Anxiety,

Anger-Hostility, Phobic Anxiety, Paranoid Ideation, Psychoticism.

Craving Analogue Visual Scale (CAVS)

The CAVS is an analogue visual scale consisting of three 10-cm long bars, which are displayed in a vertical sequence. The right margin indicates the highest degree of craving for the specified substance, according to the subject's addictive experience. The left margin corresponds to the absence of craving. The intermediate grades of length are proportionally expressed in numerical values along a 1-to-100 scale.

The CAVS has been used for the simultaneous assessment of the subjective intensity of craving for heroin, cocaine and alcohol as experienced by subjects during the administration of their daily methadone dose.

Statistical Analyses

The canonical correlation analysis was performed to compare the craving profile with clinical features (positive symptom distress, RSDA total score and patient's methadone dosage at interview time). SPSS statistical routines were used. The canonical correlation analysis is the best statistical analysis for a comparison between different profiles of behavioural characteristics.

Results and comment

Only 25/84 patients (29.8%) had no craving for heroin. The severity of craving in the other 59 was about 45% of the maximum craving experienced in the past. At the interview, only 7.1% of the patients reported a severity of craving as high as the maximum experienced in the past. 88.1% of the subjects reported no craving for cocaine. Among those who did report craving, values ranged from 5% to 70% of the maximum experienced in the past. A craving for alcohol was not present in 77.4% of subjects; among those who did report craving, values ranged between 1% and 70% of the maximum.

The average methadone dose utilized was 48.60±26.6 (min 5 max 160) mg daily. 25% of the sample were assuming dosages less than, or equivalent to, 30mg/daily. 50% had an intake less than 45 mg/daily, and 75% less than 60 mg/daily.

The positive symptom distress score of the SCL-90 ranges between 16 and 83, compared with a maximum of 90; the intensity of these symptoms is mostly between 1 (mild) and 2 (moderate), anyway ranging from mild to severe. Table 1 shows the SCL-90 factorial scores. The most frequently represented symptoms belong to the depressive and obsessive-compulsive factors. Patients show also somatic symptoms that look like withdrawal symptoms.

Table 2 shows two different profiles of clinical characteristics and craving clusters that maximize the correlation. In the clinical set, patients who assume lower methadone dosages declare a higher number of psychopathological symptoms. Drug addiction history is related neither to psychopathology nor to methadone dosage taken at the

Table 1. Psychopathological symptoms in 84 heroin-addicted patients under methadone maintenance treatment

Symptoms	M	s	Min	Max
Depression	1.21	.79	.08	3.54
Obsessive-compulsive	1.05	.71	.00	2.90
Somatic Symptoms	.96	.66	.08	3.25
Paranoid Ideation	.87	.58	.00	2.33
Anger-Hostility	.77	.68	.00	3.33
Interpersonal Sensitivity	.75	.64	.00	3.00
Anxiety	.74	.59	.00	2.70
Psychoticism	.47	.46	.00	2.20
Phobic Anxiety	.31	.40	.00	2.57

interview time. In the craving set, patients who simultaneously experience a craving for heroin and for alcohol do not report a craving for cocaine. The overall outcome is that when patients are treated with low dosages of methadone, they experience heroin and alcohol cravings and undergo psychopathological symptoms.

Cravings for heroin, cocaine and alcohol are experienced during Methadone Maintenance Treatment. The craving for heroin is strongly related to the craving for alcohol, to low dosages of methadone and to the presence of psychopathological

Table 2. Relationship between clinical aspects and craving for heroin, cocaine and alcohol in 84 heroin-addicted patients under methadone maintenance treatment. Canonical correlation analysis

	Variate 1
Clinical aspects	
Positive symptom distress	.75
RSDA total score	.20
Methadone dosage	-.56
Craving for	
Heroin	.93
Cocaine	-.15
Alcohol	.49
Statistics: Wilk's lambda = .79 p=.03	

symptoms.

Psychopathological symptoms have often been observed during the treatment of heroin addiction, and have been interpreted in different ways [8]. Earlier, we demonstrated that patients with a high number of psychopathological symptoms at the start of treatment need more methadone as a stabilization dosage during a methadone maintenance treatment [4]. In this study, when psychopathology is at low, or very low, level, cravings for heroin and alcohol tend to be absent. On the other hand, craving for cocaine appears, regardless of psychopathology. So, in patients under methadone treatment, cocaine craving may be unrelated both to methadone and to psychopathology.

One hypothesis for the observed cravings for heroin and alcohol should be methadone undermedication. In fact (1), the craving for these two substances is inversely related to the amount of methadone taken; (2) less than 20% of the patients receive a dose of methadone greater than 60 mg/daily, which is considered the minimum effective dose [1; 2; 7; 15- 17].

Moreover, the main trend followed by the Italian Public Services for Drug Addiction (SERTs) is to treat subjects with 40-60 mg of methadone as a standard dose. These dosages are often not sufficient to negativize the urine sample of the patients [1; 2; 7; 15- 17]; we can hypothesize that at these dosages craving is not under control.

Besides, such patients are likely to try to satisfy their craving for opiates by taking any substance capable of influencing the dopaminergic system in some way. They will thus manage to calm their hunger for heroin by alcohol or other substances when insufficient doses of methadone are used [11].

Doses of methadone in excess of 100 mg/die have been indicated as necessary to prevent illicit opiate use, and to stabilize psychiatric symptoms and diminish the abuse of alcohol and benzodiazepines [13]. The presence of craving for heroin, cocaine and alcohol during a methadone maintenance therapy could simply indicate that the treatment is not powerful enough. These conclusions are based on the following results:

1. A craving for heroin develops alongside a craving for alcohol, whereas a craving for cocaine follows a separate path.
2. Craving does not depend on addiction history.
3. A craving for heroin and alcohol correlates with low doses of administered methadone.

The idea that subjects who report persistent craving are undertreated with methadone and need alcohol as a substitute for opiates is supported by the presence of psychopathology correlated with low amounts of methadone. We have noted that psychopathological symptoms and psychiatric comorbidity are sensitive to methadone [4; 10; 12].

References

1. Ball J. C. (1988): The effect of methadone dose on heroin use. *Presented at the Fifth Annual Northeast Regional Methadone Conference.* New York.
2. Ball J. C. and Ross C. A. (1991): *The Effectiveness of Methadone Maintenance*

Treatment , Springer-Verlag, New York.
3. Bauer L. O. (1992): Psychobiology of craving. In J. H. Lowinson, P. Ruiz, R. B. Millman, J. G. Langrod Eds., *Substance Abuse. A Comprehensive Textbook.* Williams & Wilkins, Baltimore.
4. Benko L. B. (2000): Drug-free in Seattle. *Modern Healthcare.* March 27: 56.
5. Derogatis L. R., Lipman R. S., Rickels K. (1973): The Hopkins Symptom Checklist (HSCL): A measure of primary symptom dimensions in psychological measurement. In P. Pichot Ed., *Modern problems in pharmacopsychiatry*. Karger, Basle.
6. Derogatis L. R., Lipman R. S., Rickels K. (1974): The Hopkins Symptom Checklist (HSCL)—A self report symptom inventory. *Behav Sci.* 19: 1-16.
7. Insel T. R., Pickar D. (1983): Naloxone administration in obsessive-compulsive disorder: report of two cases. *Am J Psychiatry.* 140(9): 1219-1220.
8. Jacobs P. E., Doft E. B., Koger J. (1981): A study of SCL-90 scores of 264 methadone patients in treatment. *Int J Addict.* 16: 541-548.
9. Lemere F., Smith J. W. (1990): Hypomanic personality trait in cocaine addiction. *Br J Addict.* 85(4): 575-576.
10. Maremmani I., Canoniero S., Pacini M. (2000): Methadone dose and retention in treatment of heroin addicts with Bipolar I Disorder comorbidity. Preliminary Results. *Heroin Add & Rel Clin Probl.* 2(1): 39-46.
11. Maremmani I., Shinderman M. (1999): Alcohol, benzodiazepines and other drugs use in heroin addicts treated with methadone. Polyabuse or undermedication? *Heroin Add & Rel Clin Probl.* 1(2): 7-13.
12. Maremmani I., Zolesi O., Aglietti M., Marini G., Tagliamonte A., Shinderman M., Maxwell S. (2000): Methadone Dose and Retention in Treatment of Heroin Addicts with Axis I Psychiatric Comorbidity. *J Addict Dis.* 19(2): 29-41.
13. Maxwell S., Shinderman M. (1999): Optimizing Response to Methadone Maintenance Treatment: Use of Higher-Dose Methadone. *J Psychoactive Drugs.* 31(2): 95-102.
14. O'Brien C. P. (1975): Experimental analysis of conditioning factors in human narcotic addiction. *Pharmacol Rev.* 27: 533-543.
15. Parrino M. (1990): *Lettera al Ministro della Sanità Italiana,* NERMTC, New York, NY.
16. Parrino M. W. (1993): Overview: current treatment realities and future trends. In M. W. Parrino Ed., *State Methadone Treatment Guidelines.* U.S. Department of Health & Human Services, Rockville, MD. pp. 1-9.
17. Parrino M. W. (1993): *State Methadone Treatment Guidelines. Treatment Improvement Protocol (TIP) Series, 1,* U.S. Department of Health and Human Services, Rockville, MD.
18. Wikler A. (1948): Recent progress in research on the neurophysiological basis of morphine addiction. *Am J Psychiatry.* 105: 329-338.

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