

Heroin Addiction and Related Clinical Problems



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**HEROIN ADDICTION &
RELATED CLINICAL
PROBLEMS**

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Self-reported differences in side-effects for 110 heroin addicts during opioid addiction and during methadone treatment

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Summary

Although methadone maintenance treatment (MMT) has been shown to be effective, poor compliance is always a threat. It has often been pointed out that one variable that inevitably reduces adherence to treatment regimes is the negative side-effects of the treatment. This study examines seventeen known side-effects in a sample of 110 former opiate addicts consecutively admitted to methadone maintenance treatment. Self-reported side-effects were collected through a questionnaire. Despite the considerable increase, from 23 to 74% of the sample, in the proportion that reported individual side-effects between the period of opiate use and that of methadone treatment, the overall result was a significant decrease in eleven symptoms, no change in four and a substantial increase in only two. In some individuals a symptom that is liable to be problematic actually does become problematic, while the same symptom becomes less frequent in the group as a whole. Weight gain is the symptom that increases most in the whole group and needs to be constantly monitored. Other side-effects that remain high and need to be kept under review in clinical practice are nervousness, decreased libido, daytime drowsiness, constipation and perspiration.

Key Words: Methadone; Opioid use; Side-effects; Symptom complaints

1. Introduction

There are numerous studies showing that, compared with opiate addicts not in methadone treatment, methadone maintenance patients live longer [11], stay HIV-negative [3, 4], enjoy an improved quality of life [24] and show a fall in illicit drug use [2, 6], criminality and prostitution [12]. On the other hand, poor compliance with treatment, or none at all, may easily result in an involuntary discharge, and usually raises the risk of death [11, 28]. Haskew, Wolff, Dunn and Bearn [13] found 42% to be partial or poor adherers to their methadone prescriptions during one month. Of the compliers in the study by Grönbladh and Öhlund [10], 86% benefited from the

treatment and showed improvement according to a clinical assessment, whereas only 20% of those who did not fully follow the regime, and were eventually discharged involuntarily, showed any improvement. Non-compliance with treatment may [26] be associated with HIV-related risk behaviour. Dyer and White [9] suggest that the presence of symptoms in methadone clients can help in identifying those who have difficulty with the treatment regime. In a study by Savage, Karp and Curran [21] that compared methadone with l-alpha-acetylmethadol (LAAM), they found side-effects to be the most frequent reason for terminating the treatment for both LAAM, where they accounted for 31% of terminations. and methadone, where the percentage was 23% of those who terminated the treatment in advance.

There are studies on side-effects both on patients who have not previously received opiates, such as those that take methadone and similar substances for pain relief [20] and those who receive methadone as a substitute for earlier opioid use, such as that with injectable heroin [7].

According to the review by Cushman [5], opiate use may increase tolerance, mortality and infectious diseases, coincide with high alcohol use and interfere with the endocrine system, menstrual functions, sexual performance, pregnancy, and the cardiorespiratory, immune and gastrointestinal systems.

Besides withdrawal complaints, the most usual symptoms are those recognized as the side-effects of opioid use. Methadone appears to be associated with almost the same type and the same degree of side-effects as those caused by prescribed injectable heroin, when patients are asked about their experience during the previous week [8]. Of seventeen symptoms (none of them associated with injection), only two proved to allow differentiation between the two groups; these two symptoms were enhanced daytime tiredness/fatigue and problems with urination/passing water. The other fifteen (decreased sex drive, attention problems, memory problems, reduced appetite, enhanced thirst, bellyache, constipation, headache, enhanced appetite, pains in the cardiac regions, numbness in limbs, reduced thirst, breathing difficulties, diarrhoea and increased sex drive) failed to reveal any significant difference. Judson and Goldstein [15] found a tendency ($p=0.07$) towards an increase in side-effect symptoms when using either methadone or heroin. When comparing clients on and off methadone treatment, Judson and Goldstein [15] found that symptom complaints were more common when receiving methadone.

In a sample receiving intrathecal administration of opioids for their pain, endocrine consequences such as decreased libido for both women and men, impotence in men and amenorrhoea/irregular menstruation for women were more common than in the control group [1]. For men the levels of testosterone were significantly lower in the opioid group, and for women the opioid group showed lower levels of estradiol and progesterone, but not to a significant degree. Nyswander [19] concluded that opiates such as morphine diminish the sexual appetite. Schmitner, Schroeder, Epstein and Preston [22] showed that many women with a history of heroin misuse had menstrual dysfunctions at the beginning of

their methadone maintenance treatment. However, during methadone treatment menstruations began to normalize, and this was interpreted as supporting the notion that methadone has less impact on the menstrual cycle than intravenous heroin. In his review, Cushman [5] similarly lists delayed ejaculation as one of the problems to be faced by male heroin addicts.

In their review of the mechanisms behind nausea and vomiting in patients receiving opioid analgesics, Porreca and Ossipov [20] found those common side-effects to be multiple and complex and to have their origin in both central sites of the brain and peripheral sites of the body. According to the review by Cushman, [5] high alcohol consumption was found in 10 to 25% of heroin addicts, in comparison with his control value of 7%.

Stein, Herman, Bishop, Lassor, Weinstock, Anthony and Anderson [23] found that 84 percent of a mixed group of methadone clients had sleep disturbances. This could explain the high percentage (58.9%) that experienced daytime tiredness in a sample of 63 methadone patients in Switzerland [7]. Micturition difficulties (urination problems) were found in 25.4% and headache in 31.7% during the previous week of methadone treatment in a sample selected in Switzerland [7].

Ling, Charuvastra, Kaim and Klett [16] found that, during treatment with methadone or levo-alpha-acetylmethadol, 30 named symptoms and one other symptom were present at various levels from mild to severe in 18 to 81% of the sample. High percentages were, for instance, reported for constipation (81%), anxiety/nervousness (78%), excessive sweating (77%), runny nose (67%). Medium percentages were, for instance, reported for heartburn-gastric distress (46%) and delayed ejaculation (55%), while low percentages were, for instance, reported for diarrhoea (29%) and for edema of the extremities (18%).

Opiate addicts appear to have the same caloric intake as the normal population, but a slightly different dietary pattern [17]. These addicts seem to avoid polyunsaturated fats, fibres and vitamin C, but to have an increased intake of sucrose. In addition, the addicted men are somewhat lighter than their normal counterparts, whereas the weight of the women does not differ significantly. Zador, Wall and Webster [27] suggest that the dietary pattern of methadone clients, with a high sugar and a low fiber intake, may partly explain their problems with constipation. Dürsteler-Macfarland, Stohler, Moldovanyi, Rey, Basdekis,

Gschwend, Eschmann, Rehm [7] reported that 27% of their sample had experienced weight gain during the previous year of methadone treatment. However, as opiates such as morphine [19] reduce hunger sensations, the weight gain may be due to a lower than normal weight during opiate addiction, after which patients' weight tends to normalize. Obesity appears to be more common among long-term methadone patients than in long-term parenteral heroin addicts [18].

Aim

The aim of the study was to compare self-reported side-effects for former heroin addicts both during their earlier opioid addiction and during their present methadone treatment.

2. Method

2.1. Subjects

This study describes 110 former opiate addicts (33 women and 77 men) consecutively admitted to methadone maintenance treatment in Sweden.

2.2. Procedure

Seventeen known side-effects were adapted from earlier research. During a period of three months all consecutive patients admitted to four treatment programmes were asked to anonymously record on a questionnaire the side-effects they had experienced during earlier opioid use and during methadone maintenance treatment. The questionnaire included questions about the following side-effects: (1) diarrhoea, (2) heart burn, (3) menstrual disorder, (4) nausea, (5) runny nose, (6) impotence (males), (7) difficulties in reaching sexual climax, (8) high alcohol consumption, (9) micturition difficulty (difficulty in urination), (10) nervousness, (11) headaches, (12) swelling of hands and feet, (13) constipation, (14) decreased libido, (15) daytime drowsiness, (16) increased perspiration and (17) weight gain.

2.3. Statistics

The McNemar test was used to analyse the change in reported symptoms between the period of heroin use and the current prescription of methadone [25]. All the tests were two-tailed and

were performed using SPSS, version 19 [14].

3. Results

Table 1 shows that eleven of the included symptoms (diarrhoea, heart burn, menstrual disorder [females], nausea, runny nose, impotence [males], difficulties in reaching sexual climax, high alcohol consumption, micturition difficulty, nervousness and headaches) decreased significantly in the group according to their self-report. The decrease varied from minus 19% for headaches to minus 72% for diarrhoea. Four symptoms (swelling of hands and feet, constipation, decreased libido and daytime drowsiness) were statistically unchanged. Two symptoms (increased perspiration and weight gain) showed quite large increases. Perspiration increased by 55%, while weight showed a rise of 641%. Only 11% reported a weight gain during heroin use, whereas the proportion was as high as 82% during methadone treatment.

After the initiation of methadone treatment, only a few patients (15% or less) complained of diarrhoea or heart burn. Rather more, but still fewer than 30%, complained about nausea, difficulties in reaching sexual climax, high alcohol consumption, swelling of hands and feet and impotence (males). A considerable number, but below 50%, complained about menstrual disorder (females), runny nose, micturition difficulty and headaches. A higher proportion, between 50 and 65%, complained about nervousness, decreased libido, daytime drowsiness and constipation. The most frequent reasons for complaint were weight gain and increased perspiration; these two side-effects were reported by over 80% of patients during methadone treatment.

Although most symptoms were less in evidence during methadone treatment, the incidence of side-effects was still notable. As is shown in table 2, there was also considerable individual variation. Of eight symptoms (menstrual disorder [females], nausea, runny nose, high alcohol consumption, micturition difficulty, nervousness, constipation and decreased libido) where there was a considerable fall of 20% or more in those who reported the symptoms during heroin use, there was, in fact, a considerable increase, of 20% or more, in the percentage of patients reporting the same variables during methadone treatment, considering those who had not reported them during heroin use.

There was a considerable number of indi-

Table 1. Self reported side effects for 110 heroin addicts during opioid addiction and during methadone treatment. All tests were Two-tailed. When the expected frequency is less than 5 the binominal test with an exact p is used [25] automatically by SPSS [14].

Side effects	N	Reported during heroin use	Reported during methadone treatment	Difference in percent points (MT minus heroin use)	% change	McNemar test		
						Chi2	df	p<
Diarrhea	110	50 (46%)	14 (13%)	-33.00%	-72%	26.6	1	0.0001
Heart burn	110	40 (36%)	17 (15%)	-21.00%	-58%	13.8	1	0.001
Menstrual disorder (females)	31	21 (68%)	11 (35%)	-33.00%	-48%			p=0.0213
Nausea	110	54 (49%)	29 (26%)	-23.00%	-46%	11.3	1	0.001
Running nose	110	73 (66%)	41 (37%)	-29.00%	-44%	19.2	1	0.0001
Impotency (males)	72	36 (50%)	21 (29%)	-21.00%	-42%			p=0.0026
Difficulties reaching sexual climax	102	42 (41%)	27 (26%)	-15.00%	-36%	5.3	1	0.05
High alcohol consumption	110	44 (40%)	30 (27%)	-13.00%	-32%	4.2	1	0.05
Micturition difficulty	110	60 (55%)	44 (40%)	-15.00%	-26%	5.1	1	0.05
Nervousness	110	71 (65%)	56 (51%)	-14.00%	-21%	5.9	1	0.05
Headaches	110	57 (52%)	46 (42%)	-10.00%	-19%			p=0.0433
Swelling in hands and feet	110	34 (31%)	31 (28%)	-3.00%	-8%	0.1	1	NS
Constipation	110	70 (64%)	71 (65%)	1.00%	1%	0	1	NS
Decreased libido	107	63 (59%)	66 (62%)	3.00%	5%	0.1	1	NS
Daytime drowsiness	100	62 (56%)	72 (65%)	9.00%	16%	3.1	1	NS
Increased perspiration	110	58 (53%)	90 (82%)	29.00%	55%	20.9	1	0.0001
Weight gain	109	12 (11%)	89 (82%)	71.00%	641%	71.3	1	0.0001

Table 2. Self reported side effects for 110 heroin addicts during opioid addiction and during methadone treatment.

During earlier opioid use	N	During present MMT		Change	
		Reported	Not reported	Percentage	Percent changers
Diarrhea					42 %
Not reported	60	5	55	8 %	
Reported	50	9	41	- 82 %	
Heart burn					32 %
Not reported	70	6	64	9 %	
Reported	40	11	29	- 73 %	
Menopause (females only)					52 %
Not reported	10	3	7	30 %	
Reported	21	8	13	- 62 %	
Nausea					46 %
Not reported	56	13	43	23 %	
Reported	54	16	38	- 70 %	
Running nose					45 %
Not reported	37	9	28	24 %	
Reported	73	32	41	- 56 %	
Trouble with erection (males only)					32 %
Not reported	36	4	32	11 %	
Reported	36	17	19	- 53 %	continues

Table 2. Self reported side effects for 110 heroin addicts during opioid addiction and during methadone treatment (Continues).

During earlier opioid use	N	During present MMT		Change	
		Reported	Not reported	Percentage	Percent changers
Difficulties having sexual climax					36 %
Not reported	60	11	49	18 %	
Reported	42	16	26	- 62 %	
Increased use of alcohol					36 %
Not reported	66	13	53	20 %	
Reported	44	17	27	- 61 %	
Difficulty in urination					40 %
Not reported	50	14	36	28 %	
Reported	60	30	30	- 50 %	
Nervousness					30 %
Not reported	39	9	30	23 %	
Reported	71	47	24	- 34 %	
Headaces					23 %
Not reported	53	7	46	13 %	
Reported	57	39	18	- 32 %	
Swelling in hands and feet					26 %
Not reported	76	13	63	17 %	
Reported	34	18	16	- 47 %	
Constipation					41 %
Not reported	40	23	17	58 %	
Reported	70	48	22	- 31 %	
Decreased libido					36 %
Not reported	44	21	23	48 %	
Reported	63	45	18	- 29 %	
Drowsiness in daytime					26 %
Not reported	38	18	20	47 %	
Reported	62	54	8	- 13 %	
Sweating					42 %
Not reported	52	39	13	75 %	
Reported	58	51	7	- 12 %	
Increase in weight					74 %
Not reported	97	79	18	81 %	
Reported	12	10	2	- 17 %	

viduals that moved in either direction between opioid use and methadone maintenance treatment. The variables could roughly be divided into four groups according to the number of individuals that changed with respect to a given symptom. Three variables – headaches, swelling of hands and feet and drowsiness in daytime – showed the lowest proportion of changers (23 to 26%). In the next group, which showed rather more changers (30 to 36%), there were twice as many variables – six in all: nervousness, heart burn, trouble with

erection (males only), difficulties in reaching sexual climax, increased use of alcohol and decreased libido. Even more changers (40 to 46%) were found in the next group, again comprising six variables: difficulty in urination, constipation, diarrhoea, sweating, runny nose and nausea. Lastly, in the group with the highest proportion of changers (52 to 74%) there were only two variables – menopause (females only) and increase in weight.

4. Discussion

The main finding in the present study is the considerable changes recorded in self-reported side-effects. Of the seventeen side-effects that were measured, three showed changes of 23 to 26%, six revealed changes of between 30 and 36%, a further six displayed changes of between 40 to 46% and two experienced substantial changes as high as 52% and 74%, respectively.

The high levels of the symptoms reported during heroin use and methadone treatment is consistent with earlier studies [16, 19].

On an aggregated group level, eleven of the seventeen symptoms that were investigated (diarrhoea, heart burn, menstrual disorder [females], nausea, running nose, impotence [males], difficulties in reaching sexual climax, high alcohol consumption, micturition difficulty, nervousness and headaches) decreased significantly in the group according to patients' self-report. Four symptoms (swelling of hands and feet, constipation, decreased libido and daytime drowsiness) were statistically unchanged. Two symptoms (increased perspiration and weight gain) showed quite large, statistically significant increases. The substantial increase in weight may to some extent be due to the fact that opiates such as morphine [19] alleviate the hunger sensations and the harsh environment that opiates addicts have to undergo. Thus, the weight gain may be a result of a below-normal weight during opiate addiction, which tends to return to normal during methadone treatment. It should be noted that the gain in weight continues even when former addicts reach their normal weight. This finding is in accordance with the fact that obesity appears to be more common among long-term methadone patients than in long-term parenteral heroin addicts [18].

The various different symptoms associated with the sexual system [19] are as important today as they were 55 years ago, and should be given special attention; these symptoms may be treated with sex-hormones, because of their low levels in opiate users [1].

The results of the present study show quite a large difference when compared with those of Dursteler-Macfarland, Fischer, Mueller, Schmid, Moldovanyi and Wiesbeck [8], who found only two symptoms that differed between patients on methadone and patients who were taking prescribed injectable heroin (enhanced daytime tiredness/fatigue and problems with urination/passing water), while the other fifteen (decreased

sex drive, attention problems, memory problems, reduced appetite, enhanced thirst, bellyache, constipation, headache, enhanced appetite, pains in the cardiac regions, numbness in limbs, reduced thirst, breathing difficulties, diarrhoea and increased sex drive) produced no significant difference. This highlights the notion of Cushman [5] that some complications of opiate use are due to biochemical influences, while others derive from the addict's life-style. Thus, one of the limitations of the present study is that there is no way of differentiating between the consequences of an addict's life-style and the side-effects of the substance alone. In any case, in clinical practice clinicians will meet patients who in most instances will compare their former life as an addict with their present life as a patient receiving methadone. From that point of view, the present study may have a somewhat greater ecological validity but a lower internal validity.

5. Clinical implications

Although there are significant percentage decreases in reporting most side-effects during methadone treatment compared with illicit opioid use, there is a substantial individual variation that needs to be taken into account in clinical practice. In some individuals a symptom that is liable to be problematic actually does become problematic, while the same symptom becomes less frequent in the group as a whole. Weight gain is the symptom that increases most and needs to be attended to. In particular, there is likely to be a need for dietetic counselling. Other side-effects that remain frequent are increased perspiration, nervousness, decreased libido, daytime drowsiness, and constipation. The strengths of the present study are founded on the clinically relevant comparison between an addict's former life as an addict and his/her present life as a patient on methadone; this comparison ensures a high ecological validity. Its internal or pharmacological validity is weaker because the study was not designed to address the other important question of whether it is the substance itself, or the whole of an addict's life-style that is responsible for the symptoms that are found during heroin use. In the same way the study was not intended to separate the effects of the substance from those due to patient-related life-styles during methadone treatment.

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Contributors

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Conflict of interest

One of the authors is associated with the treatment reported. None of the authors have any other relevant conflict of interest to report in relation to the present study.

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Latent suicidality in heroin addicts

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Summary

According to the transactional analysis (TA) theory of personality development and the development of psychopathology, any behaviour that indirectly or directly threatens someone's physical integrity could be a manifestation of the 'Don't exist' injunction and the script decision to die young. A 'don't exist' injunction is defined as a parental message that challenges a child's right to live, and that can be sent directly or indirectly, verbally or nonverbally, intentionally or unintentionally. An (early) script decision is defined as a compromise between the various authentic needs and requirements of the environment. The theoretical assumption on which this work is based is that a mentioned injunction and script decision to die young could be present in the population of heroin addicts, considering their continuous and repeated self-destructive behaviours and, typically, short lifetimes. The main objective of this work was to check the assumption that the 'Don't exist' injunction and the script decision to die young are theoretical concepts that are available for measurement through questionnaires and have the potential to discriminate heroin addicts from non-clinical examinees. The general research method that was selected was non-experimental, correlation research; the sample consisted of 50 heroin addicts and 50 non-clinical examinees. Its results confirm the hypothesis that both measured theoretical concepts have the potential to discriminate heroin addicts from non-clinical examinees. Heroin addicts have, to a statistically significant degree, a more strongly marked "Don't exist" injunction, together with the script decision to die young. This finding may be related to the theoretical assumptions of several authors in the TA – assumptions which include the concept that psychoactive substances allow a person to implement the script decision to die young.

Key Words: transactional analysis; "don't exist" injunction; script decision to die young; heroin addicts.

1. Introduction

One of the key theoretical concepts within Transactional Analysis is the concept of the Life Script. Eric Berne, the founder of this theoretical model, defines the Script as a person's life plan, based on the decisions made in childhood, reinforced by parents, confirmed by life events and culminating in the chosen alternative. Berne believed that life is not possible without a Script, in other words that the Script is an expression of a being who has, in a way, been programmed and predetermined, and is thus part of the proc-

ess of identification and internalization (3). C. Steiner defined the Script in a similar way, as a rigid, self-destructive plan that allows for very little deviation from the previously determined steps (27). S. Woollams defines the Script as the current or actual plan of a person, which he or she has shaped by implementing a series of decisions made in childhood, and those decisions are viewed by him/her as the results of an interpretation of significant events within one person's experience (30). Essentially, it is considered that the Life Script is the unconscious life plan a child creates up till the age of seven – a plan that person

will follow impulsively throughout his/her adult life, and which has been shaped by parental, familial, social, cultural and religious influences. It is assumed that the Life Script gives meaning to the world, provides a definition and protection of oneself, as well as definitions of other people and of the individual's relations with them. However, the Script is also a constraint, in the sense that an adult person will not enact some of what would otherwise be realistic possibilities, if they are not included in her or his Script.

The Life Script is mainly founded on Script Injunctions and Script Decisions.

Script Injunctions are defined as all those direct and indirect, verbal and non-verbal, intentional and unintentional parental messages by which certain human rights of a child are denied, and which lead to chronic non-functionality in vital areas of life (17). It is considered that injunctions limit freedom by complicating a child's development, sometimes even his/her whole life. It is assumed that they are often left in a non-verbal form, in other words, that they are conveyed on a *psychological* level of communication. Apart from verbal and non-verbal ways of conveying injunctions, it is believed they can be communicated through social learning and by suggestion. That means that a parent, in setting him- or herself up as an example, is showing a son or daughter how, for instance, not to think in stressful situations. An example of that is a parent who, while in a state of panic, acts aimlessly on seeing that his/her child has cut him- or herself and is bleeding. Suggestion implies that parents are trying to explain to a child how to understand something or what to do (28). The reason for parents communicating injunctions is most probably some sense of inadequacy, their confusion, dissatisfaction, or feelings of misery, anguish, disappointment, anger or frustration (14). Bob and Mary Goulding first defined the list of "injunctions" in 1966 and have supplemented their definition several times while rewriting it (13). One of the variants of this list includes the following injunctions: "Don't exist!", "Don't be important!", "Don't be who you are! (Don't be you!)", "Don't be a child!", "Don't grow up!", "Don't succeed! (Don't make it in your life)" "Don't be close!", "Don't belong!", "Don't think!" (either about a forbidden topic or in any way different from that of their parents), "Don't feel!" (forbidding certain feelings, or feelings that differ from those of their parents), "Don't be well!" (or "Don't be sane!") and "Don't" – an injunction against any of a va-

riety of activities conveyed by an overprotective mother. The existence injunction denies a child's right to live at all (13).

An early (Script) decision is defined as a compromise solution in the Life Script of a child in a situation of existential or psychological impasse. Or as a compromise between a child's needs and the demands of the environment. It is supposed that the Script is a response to the messages that have been communicated, but one that is based on a child's limited ability to process reality. Most commonly, early decisions really have an adaptive function; they come to constitute a strong reinforcement of a child's tendency to hold on to that decision (27). It is considered that there is an unlimited number of decisions that a child can take as a response to injunctions, apart from the possibility that a child might not believe in a given injunction and therefore decide to reject it, or might find somebody who challenges that injunction, believing that person instead (14). It is believed that a child takes a set of Script decisions, depending on its constitutional abilities, temperament, and interpretations of how to deal with demands from the environment (19). A script decision on early death indicates that a person has decided that he/she will die young. The Gouldings have extended their original list of six deadly decisions to seven: "If things get too bad, I'll kill myself!"; "If you don't change, I'll kill myself!"; "I'll show you, even if it kills me!"; "I'll kill myself and you'll be sorry!"; "I'll kill myself and make you realize that you love me!", or "I'll make you kill me!"; "I'll catch you, even if I get hurt doing that!" ("I will get back at you, even that kills me!" [i.e.: I will always keep even with you, even if it kills me.]) "I must always (or repeatedly) be on the verge of death for you to love me!" (13, 14).

Analysing the theoretical concept of Life Script, we come across the assumption that any behaviour which directly or indirectly jeopardizes someone's physical integrity is actually a manifestation of the existence injunction and Script decision on early death. For example, the author L. Achimovich speaks about the suicidal Script in people with anorexia nervosa, which he considers to be delayed suicide, since refusing to eat leads to an early death (1). In the same study he emphasizes the high prevalence of depression and suicidality in these patients' parents. At the same time, he stresses the generally higher mortality rate of the members of the family of those who suffer from this disorder, and draws the con-

clusion that the suicidal Script exists on the family level. When it comes to addiction to psychoactive substances, in certain authors we find the assumption that they enable someone to reach an early decision to kill him- or herself (26, 9, 8). L. Craig speaks in favour of a similar view, namely that heroin users, among other things, take a pre-conscious decision to die (8). The Gouldings also claim that users of psychoactive substances apply their existence injunction and their early decision to commit suicide or homicide (9).

Investigations into Scripts and injunctions have mostly been carried out through qualitative techniques, such as semi-structured interviews, projective techniques and clinical observations (25, 3, 6, 24). Only one attempt to examine them through questionnaires has been reported (23). The authors of this paper have confirmed in their previous study that the concept of injunctions can be investigated through the examination of questionnaires, bearing in mind that one advantage of questionnaires is that they have the potential to allow differentiation between a clinical and a non-clinical population (12, 4). So far, Script Decision research has mainly been limited to examination by qualitative techniques, except that Woollams construed an Early Decision Scale, which aims to discover the level of acceptance of permissions and injunctions, on the supposition that it is on that basis that a decision is taken about the content of the Script Decision (30). No research into the two concepts mentioned above has been conducted in the population of heroin addicts or on the contents of their Life Script.

Apart from the testing of these two concepts' potential to discriminate non-clinical examinees from heroin addicts, this kind of research can, to some extent, contribute to a better understanding of the problem of heroin addiction. That could also have an impact on the contents of prevention programmes, as well as to actively contribute to therapeutic work with addicts. Prevention programmes could be drafted in a different way from that currently used, which is as much focused on the individual's early development, as on his or her development in adolescence, which is now the dominant focus of a majority of existing prevention programmes. As far as psychotherapeutic work is concerned, it could be confirmed that heroin addicts have, to a statistically significant degree, a more marked existence injunction and decision about early death, which could easily influence the contents of psychotherapy procedures; those procedures could,

in fact, be enriched by new elements that would go to modify existing therapeutic procedures. In addition, this research will provide two instruments that aim to verify the existence of parental injunctions and a Script Decision on early death, so allowing the evaluation of psychotherapeutic work even with suicidal clients.

2. Methods

2.1. Aim

The general aim of this inquiry is that of examining the assumption that the existence injunction and the decision on an early death are accessible to questionnaire measurement and have the potential to discriminate non-clinical examinees from heroin addicts. The general research method that has been selected is non-experimental correlational research. Two key dependent variables are the existence injunction and the decision on an early death; they become operational at the moment when examinees answer the Questionnaire on Parental Messages (URP) and the Questionnaire on the Script Decision (USO) (5).

2.1. Instruments

2.1.1. URP Scale (Questionnaire on Parental Messages)

It has the aim of recording the expression level of the existence injunction, by determining the level of exposure to parental messages and actions which deny the right to live, since that child, in growing up, has accepted them as a part of his/her picture of the self. It has 25 items, phrased as expressions of attitudes that test examinees' level of agreement on a five-point Lickert scale. The index of reliability of the Scale, expressed in Cronbach's alpha coefficient was 0.92 (5).

2.1.2. USO (Questionnaire on the Script Decision)

It has the aim of evaluating the level of expression of thoughts, feelings, behaviours and attitudes towards an individual's self and own life, by raising the question of whether and how a person? has made a decision on early death. This scale too has five points and is of Lickert type. It contains 26 items. The index of reliability of this scale, expressed in Cronbach's alpha coefficient, was 0.78 (5).

2.3. Sample

The sample was designed for convenience of use and included 100 examinees, 50 from a non-clinical population, and 50 from a clinical population of heroin addicts. One criterion for the inclusion of examinees in the non-clinical group was the absence of previous or current psychiatric treatment, whether ambulatory or in a hospital setting – a finding that had been determined on the basis of an interview with each examinee. Admission into the diagnostic group of heroin addicts was determined by competent psychiatrists who had decided on their classification on the basis of a diagnostic interview and by applying diagnostic criteria drawn from ICD-10 (29).

2.4. Statistical Analysis

Statistical analysis of the data was conducted using software SPSS 18.0.

3. Results

3.1. Descriptive characteristics of the sample on the URP and USO scales

As can be seen from Table 1, both scales have a mean smaller than the theoretical average mean – in other words they are ‘heavy’, because less capable of discriminating in the sphere of low scores. The distributions shown by both scales display a curvature to the right. In the context of an inquiry into heroin addicts, this kind of score distribution can be accounted for by hypothesizing conscious and unconscious censure in answering questions, with the aim of minimizing the individual’s psychopathology and providing socially acceptable answers.

3.2. Examination of the differences between a non-clinical population and heroin

addicts on the concept of existence injunctions

In examining the potential of the Script Injunction concept to differentiate non-clinical examinees from heroin addicts, a statistically significant discriminant function was found (Wilks’ Lambda=0.24; Chi/square=149.84 df =25 p<0.001). This discriminant function is statistically significant at a level of p<0.001, which means that it can be said that the difference between the non-clinical and the clinical group, as assessed on the scale, exists without any possibility of errors in measurement.

Examination of the matrix of the discriminant function structure shows that it is determined by the following items (Table 2):

The discriminant analysis extracted is determined by 15 items, which, given their contents, question the right to existence. It can be seen from the position of the groups’ centroids that the group of addicts systematically obtained higher scores on these items (centroids: Non-clinic=-0.78; Heroin Addicts = 3.92).

To a statistically significant degree, the higher receptiveness to the messages denying the right to live that was recorded in heroin addicts than in the non-clinical component of the sample can speak in favour of the assumption that heroin addicts act on an existence injunction (9). According to Transactional Analysis, every form of psychopathology includes the existence of injunctions (2, 27, 22, 14, 13), and the data obtained can be taken as a confirmation of the TA assumption on the existence injunction in heroin addicts.

The results obtained speak clearly in favour of the examined concept’s potential to discriminate non-clinical examinees from examinees who have developed heroin addiction.

It is evident that the items regarding brutal physical punishment have proved to be non-discriminative, a finding that is not in accordance

Table 1. Distribution of scores on URP and USO scales (N=50+50)

	URP non-clinical	URP heroin addicts	USO non-clinical	USO heroin addicts
Mean	37.09	59.00	37.12	60.05
St. Deviation	15.9	19.5	14.0	19.7
Skewness	0.32	0.23	0.31	0.23
Kurtosis	-0.32	-0.74	-0.71	-0.77

Table 2. Excerpt from the matrix of the discriminant function structure

They used to tell me I would end up in the grave-yard prematurely.	.62
They used to tell me they were ashamed about me being their child.	.58
My father or my mother would often tell me that I was scum or a spiv.	.49
They used to kick me out of the house when they got mad with me.	.42
They were telling me: «You'll cost me my life».	.36
My parents were behaving as if I did not exist.	.36
They used to tell me I was a complete failure.	.35
They went on telling me «Nothing good will ever come from you».	.34
They used to tell me: «Drop dead»!	.34
My mother used to say: «I should never have had you»!	.32
My father or my mother used to tell me: «I wish I could kill you!».	.32
They used to tell me:«I can't bear to look at you!».	.31
They used to tell me:«You're the worst!».	.31
When criticizing, they used to curse me.	.30
They used to tell me:«If you make a mistake, you had better kill yourself!».	.30

Table 3. Excerpt from the matrix of the discriminant function structure

I have had more than three car accidents in my life.	.52
It would be easier for my parents if I weren't there.	.41
I sometimes think my parents would prefer it if I were dead .	.41
I am a trouble for everyone.	.38
I sometimes think there is no point in me living.	.35
I went on putting out cigarettes on my hand or some other part of my body.	.33
I would like to disappear.	.33
People sometimes annoy me so much that I would jeopardize my life to force them to change.	.31
My mother would be more successful in life if she didn't have me.	.31
I sometimes think it would be best if I got sick and died.	.30
I am sorry I was born in the first place.	.30
I kept on hitting my fist or head against some hard object or a wall.	.30
I kept on cutting myself.	.30
I hate myself.	.30
I have the impression that everything is my fault.	.30
Only if I got seriously injured would others start paying attention to me.	.30

with theoretical expectations. We shall discuss this in detail in the final discussion on our results.

3.3. *Examination of the differences between the non-clinical population and the group of heroin addicts on the concept of the decision on early death*

A statistically significant discriminant function was obtained on this concept, too (Wilks' Lambda=0.22; Chi/square=156.74 df =26 p<0.001).

The discriminant function is statistically significant at a level of p=.000, and, as stated

earlier, that finding means that the difference between the non-clinical and the clinical group on the scale exists without any possibility of errors in measurement.

Moving on now to examine the matrix of the discriminant function structure, that is made visible and is determined by the items that appear in Table 3.

On an isolated discriminant function, the score recorded for addicts is higher to a statistically significant degree (centroids: Non-clinical=-0.82; Heroin Addicts = 4.11).

As can easily be seen, heroin addicts systematically show higher scores on items included

in the USO scale.

The results obtained are in accordance with the theoretical assumptions, that heroin addicts act on a Script Decision on early death (26, 9, 8). The results of numerous inquiries, including those situated outside the transactional theoretical model, can be interpreted as a confirmation of previously stated assumptions. In those inquiries indicators have been found that speak in favour of the view that those who abuse drugs are often depressive, indulge in suicidal ideation or have already attempted to commit suicide (7, 21, 16). At this point, the question arises, in connection with all the points made so far, of the order in which the various processes unfold, and we shall talk about that in greater detail in the final discussion of our results. It is evident that this examined concept too has the potential to discriminate non-clinical examinees from heroin addicts.

4. Discussion

By comparison with the non-clinical population, heroin addicts have, to a statistically significant degree, an existence injunction and a decision on early death that are more clearly expressed. The results obtained are in agreement with the theoretical assumptions that users of psychoactive substances are influenced by an existence injunction and a Script Decision on early death (26, 9, 8). Looking at these questions in a broader perspective, it should be borne in mind that the founder of Transaction Analysis, Eric Berne, stresses the view that injunctions lead to chronic dysfunctions in vital areas of life (17). If, in the context that has been specified above, we take into consideration the existence injunction that has been recorded in the memory of heroin addicts, it is clear that it could hardly be expected to be functional in preserving their own lives. The data that speak in favour of the stated assumptions and the findings obtained are as follows. Several longitudinal researches on substance-related disorders point to the fact that most addicts die before the age of 50, the cause officially recorded being "overdose" in 21.6% of these cases, and "homicide" or "suicide" in 19.5% (16). Furthermore, the annual mortality rate of heroin addicts is sixfold to twentyfold that of their peers in the general population (10). As to the research carried out on the suicide rate of drug addicts in the United Kingdom, longitudinal studies indicate it is significantly higher than in the general population (69 per 100,000 inhabit-

ants). In 45% of these cases, the cause of death was recorded as "overdose" (20). Longitudinal research on the correlates of suicide attempts in heroin addicts shows that 11.6% of addicts actually commit suicide. Suicidal ideation and previous suicide attempts have been shown to be the most reliable predictive indicators (11).

It has been confirmed that both the concepts examined can be accessed through questionnaire measurement, and that they do have the potential to differentiate non-clinical examinees from heroin addicts.

When it comes to the existence injunction, it is extraordinary that the items regarding various forms of physical punishment did not turn out to possess any capacity to discriminate. It is obvious that the results obtained indicate that verbal aggression and more subtle psychological rejection are more effective factors in this clinical group. It is possible that what has been stated above derives from the size of the two groups selected within the sample, since the study has been carried out, in the interests of convenience, on a small sample of addicts undergoing detoxification treatment in hospital. It might be, on the other hand, that the subsisting conveyed messages identified by items included in the described scales, and which by their contents deny the right to life, are just a dysfunctional parental response pattern to the addictive behaviour of their offspring, even if, in giving instructions to examinees, it was stressed that they were supposed to give answers about messages they had received in childhood, before they ever developed addiction. It is, most certainly, necessary to carry out more comprehensive and voluminous research about different modalities of conveying messages by which the right to life is denied, and which are active in the population of addicts. It would be important to take into consideration the severity of the addiction, since it is assumed that addicts with a severe form of addiction manifest gradual, delayed suicidal behaviour which has been predisposed by the existence of the suicidal Life Script, while that predisposition cannot be expected in people with less severe forms of addiction. Comparison with subjects who have attempted to commit suicide or have developed other forms of self-destructive behaviour would also be helpful, as it would permit the exclusion of comorbid psychiatric disorders that is a necessary requisite to be carried out during the screening of all those being examined as potential examinees.

Finally, we have mentioned the question

of what precedes what, covering suicidality as a feature preceding addiction, or addiction as occurring before manifest suicidality. Longitudinal follow-ups of adolescents from risk groups before they develop addictive behaviour would certainly answer that question. If we thought within the framework of the transactional theoretical model, so as to implement the aim of testing the hypothesis that heroin addiction is actually one of the manifestations of the suicidal Life Script, a significant step forward would be made if examinees' parents could be included in the study, because of the crucial role played by social learning and trans-generational conveyance of Script pathology. If it were true that elements of the suicidal Script, especially the existence injunction and the decision on early death, were recorded in them too, we could then think with greater certainty of heroin addiction as being a form of latent, delayed suicide, as well as other forms of risk and self-destructive behaviour that are entailed by the same assumption. According to some authors (31), indirect self-destructive behaviours can be defined as voluntary actions that bring a significant element of risk to that subject's life or health. They cover a wide range of behaviours, from high-risk sports and unprotected sex to taking drugs, drunk driving or Russian roulette. Although those taking part in this game consciously accept a high probability of injury or even death, they have recourse to a kind of defence that refuses to describe those kinds of actions as having any suicidal intention. Many researchers put forward the view that these behaviours have the psychodynamic function of denying or struggling with mental pain that would otherwise lead to states of helplessness and depression by following the route to temporary pleasure (18). This research can certainly make a contribution to the task of initiating the empirical testing of numerous psychodynamic hypotheses on latent suicidality, not only in the case of heroin addiction, but in other partly manifest self-destructive behaviours.

5. Conclusion

In general, we can draw the conclusion that the assumptions that were scheduled for testing as the main aim of this study mostly received the kind of confirmation that could have been expected.

Compared with non-clinical examinees, heroin addicts have, to a statistically significantly

degree, a more clearly expressed existence injunction and decision on early death – an outcome that is in full accordance with the assumptions of the transactional theoretical model.

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Patients who use alcohol during MMT receive lower doses of methadone, show fewer positive urine analyses for opioids, and suffer from PTSD more frequently

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Summary

The objectives of the study were to identify the prevalence of alcohol use, to find out differences in sociodemographic characteristics, the frequency of PTSD, percentages of invalid war veterans, the average methadone dose and number of positive urine analyses on opioids among patients undergoing methadone substitution treatment who use alcohol from those who abstain. We found that 42 (25.77 %) out of 163 participants had an AUDIT score > 7, indicating alcohol use. The two groups did not differ in terms of sex, age, education, employment, marital status or percentages of war veterans. The statistically significant differences recorded were: lower average dose of methadone, fewer positive urine analyses for opioids and a higher incidence of PTSD among the patients undergoing methadone substitution treatment who were using alcohol. Conclusions: The patients who use alcohol have a lower average dose of methadone, fewer positive urine analyses for opioids and a more frequent presence of PTSD. The risks arising from alcohol abuse and possible PTSD in these patients call for greater attention in everyday practice.

Key Words: methadone maintenance treatment; alcohol use; methadone dose; PTSD

1. Introduction

Many patients in methadone maintenance treatment (MMT) abuse multiple drugs. Those who are addicted to opioids frequently use benzodiazepines, cannabinoids and alcohol.

Alcoholism is a common problem among people in methadone programmes (2). The frequency of alcohol use is 48.8% among subjects entering a MMT (9).

Some reports in the literature show that alcohol use was either greater or unchanged during MMT. Moreover, several studies suggest that alcohol consumption in patients who interrupt methadone treatment rises, probably to obtain relief from the symptoms of narcotic craving without relapsing into the use of heroin (3).

On the other hand some authors report that the administration of methadone in heroin-

addicted patients without alcohol dependence reduces the intake of alcohol (3).

Alcohol is a frequent co-intoxicant in methadone-related deaths, while mortalities attributed to methadone intoxication alone were a rare finding (6).

The use of cannabis or benzodiazepines, a higher risk of relapse into illicit drug use and of discharge from treatment was significantly associated with alcohol use (15).

The aim of the study was to identify the prevalence of alcohol use, especially that of heavy alcohol use indicating alcohol addiction, to find out differences in sex, age, education, employment, marital status, incidence of PTSD, percentages of invalid war veterans, the frequency of positive urine analyses for opioids and the average dose of methadone among patients undergoing methadone substitution treatment who use

alcohol and those who abstain from it.

2. Methods

2.1. Design

This was an open prospective study of comparative, analytic type conducted in 2010.

2.2. Setting

The cohort was recruited from one drug addiction treatment centre in Bosnia Herzegovina (canton of Zenica-Doboj).

The participants were recruited by their psychiatrist in the methadone centre, and data were collected using an interviewer-administered questionnaire, which included the Alcohol Use Disorders Identification Test (AUDIT), with a score of >7 considered as an “alcohol use disorder”; some data were collected from the medical records in the drug addiction treatment centre (1).

Inclusion criteria: Patients in a methadone programme could be considered for inclusion after stabilization of the methadone dose.

Exclusion criteria: patients who had been in a methadone maintenance programme for less than two months were excluded.

2.3. Data collection and statistical analysis

The sample was divided into two groups depending on a patient’s AUDIT score: The patients who were using alcohol (those with an AUDIT score of 8 or more) were assigned to the first group, and those who were abstaining from alcohol (with an AUDIT score of 7 or less) were assigned to the second. This allowed us to determine the prevalence of alcohol use among patients in MMT.

For both groups the average dose of methadone from medical records at the moment of interview was recorded. The numbers of urine analyses that were positive and negative for opioids was recorded for each patient in both groups tested in 2010.

The data were organized in the Microsoft Excel spreadsheet programme and the statistical analysis was carried out using the SPSS software programme.

We compared differences in sociodemographic characteristics (sex, age, education, employment, marital status), medical and substance

use characteristics (presence of PTSD, percentages of invalid war veterans, average dose of methadone and frequency of positive urine analyses for opioids among patients in these two groups).

The T-test was used to find the differences between the average age and methadone dose in the two groups. The χ^2 test was used to find differences for other parameters while comparing the two groups.

3. Results

The sample had 163 patients in MMT; of these, 7 were females (4.29%) and 156 males (95.71%).

Results are reported in table 1.

We found 42 (25.77%) out of 163 participants who had an AUDIT score > 7 , indicating alcohol use; these patients belonged to the first group. Of these, fifteen (9.2% of the total number) scored 20 or more, so indicating a probable alcohol dependence. There were no females in the first group.

The second group consisted of 121 patients; seven of them (5.79%) were females. They had an AUDIT score of 7 or less, so indicating no alcohol use disorders.

The mean age in the first group was 31.59 ± 7.85 years and 31.74 ± 7.35 in the second group ($p=0.842$). In the first group the average dose was 49 mg and in the second 55.35 mg.

The total number of urine analyses on opioids was 3,075. Out of 700 tests carried out in the first group, 273 (39%) were positive. Out of 2,375 tests in the second group, 1,078 (45.39%) were positive.

Five patients (11.91%) proved to have PTSD in the first group and seven (1.65%) in the second group.

4. Discussion

4.1. Prevalence of alcohol use

Alcoholism is a common problem among people in methadone programmes. In our study, out of 163 participants 42 (25.77%) – every fourth patient – had an AUDIT score > 7 , indicating alcohol use. Fifteen (9.2%) scored 20 or higher, indicating probable alcohol dependence. Our results are in agreement with those of other authors.

Bihari reports that alcoholism affects as many as half of such patients, noting that “many

Table 1. Differences between methadone treated patients with (Group 1) and without (group2) alcohol misuse

	Group 1 N=42	Group2 N=121	T/chi	p
Age	31.59±7.8	31.74±7.3	1.25	0.842
Methadone dose	49.00±28.7	55.35±29.7	3.52	0.026
Sex (Males)	42 (100.0)	114 (94.2)	2.53	0.111
Education				
Primary school	10 (23.8)	34 (28.1)	1.45	0.483
Secondary school	32 (76.2)	84 (69.4)		
College	0 (0.0)	0 (0.0)		
Faculty	0 (0.0)	3 (2.5)		
Employment				
Active	26 (61.9)	75 (61.9)	0.67	0.880
Non-active	8 (19.0)	26 (21.5)		
Provisional active	5 (11.9)	15 (12.4)		
Retired	3 (7.2)	5 (4.2)		
Marital status				
Single	28 (66.7)	78 (64.5)	2.01	0.365
Married	8 (19.1)	33 (27.3)		
Widower	6 (14.3)	10 (8.3)		
Divorced	0 (0.0)	0 (0.0)		
Invalid war veterans	2 (4.8)	6 (5.0)	0.13	0.716
PTSD	5 (11.9)	2 (1.7)	5.67	0.017
Opioid positive urines samples	273 (39.00)	1078 (45.39)	9.70	0.007

methadone-maintained patients need to be treated simultaneously for alcoholism” (2). Stastny and Potter report that, of 170 patients who were assessed by using the self-administered alcohol screening test (mSAAST), fifty-three (31.9%) patients scored 7 or more on the mSAAST scale, indicating actual or potential drinking problems (14). Rittmannsberger et al. have reported that, alcohol consumption during methadone maintenance treatment (MMT) often becomes a problem: 52% of their patients were positive in response to ‘alcohol indicators’ and 32% fulfilled more severe criteria for alcohol abuse (10). Senbanjo et al. report that approximately one-third of the sample (57/192) were AUDIT-positive (score ≥ 8) (13). Chen et al. found the high prevalence rates of alcohol use problems, indicated by hazardous drinking at 31.4% (7).

Ryder et al. found that 14% of patients scored 20 or higher, indicating probable alcohol dependence (12).

In terms of age there is no statistically significant difference between the two groups. Mean age was 31.59 ± 7.85 years in the first group and 31.74 ± 7.35 in the second ($p=0.842$).

Domenicali et al. report a mean age of 33.16 ± 7.53 years (3).

Sex: in our sample there were only 7 females in the MMT and all of them had an AUDIT

score of less than 8, but there was no statistically significant difference between males and females.

Stastny reports that there was a slight tendency for alcohol use to be male. (14) Jackie Lind reports that “These clients showed a tendency to be predominantly male“. (7)

Education level, marital status and employment: there was no statistically significant difference between the two groups.

Invalid war veterans: by “invalid war veterans” we mean people wounded as soldiers in the last war in Bosnia (1992-1995) who receive compensation for their disability from the State. They numbered 8 out of 163 patients. The percentage of invalid war veterans in our sample was 4.91%. There was no statistically significant difference between the two groups.

Dose: the patients in the methadone programme who were using alcohol were taking a lower dose of methadone than those who were not. In the first group the average dose was 49 mg and in the second 55.35 mg. This difference was statistically significant.

In 1999 Ottomanelli found that, “contrary to the expectation that methadone patients who consumed excessive amounts of alcohol would require higher dosages of methadone, it was found that non alcohol-abusing methadone patients requested the higher dosage levels” (8).

Many authors have found a reduction in alcohol intake during MMT. In a study which excluded alcohol-dependent subjects, Addolorato, Domenicali et al. found that short-term methadone administration reduces alcohol consumption in non-alcoholic heroin addicts (3).

PTSD: 7 out of 163 patients in the sample were suffering from PTSD. The percentage of these patients in our sample was 4.29%; more precisely, 11.91% of our sample had PTSD and were using alcohol, while 1.65% had PTSD while abstaining from it. This difference was statistically significant.

Posttraumatic stress disorder (PTSD) is frequently linked with substance abuse. The self-medication hypothesis suggests that some people may use illicit substances in an attempt to self-treat psychiatric symptoms (18).

Comorbidity between alcohol use and posttraumatic stress disorder has been well documented. The results have indicated that both alcohol use disorder (AUD) and alcohol problems were associated with greater PTSD symptom severity. Women who have histories of alcohol problems may be at higher risk of severe PTSD in response to interpersonal violence than those without any history of AUD or alcohol problems (4).

Ross et al. reported that, of those in their sample who were heroin users, 42% had a lifetime history of post-traumatic stress disorder (11).

The factors associated with depression in the treatment groups (MMT) investigated by Teesson et al., were: PTSD, attempted suicide in the last 12 months and severe physical disability (16).

In a sample of methadone maintenance patients, the prevalence of lifetime PTSD was found to be 20% for women and 11% for men. The most common stressors reported were rape for women and seeing someone hurt or killed for men (17).

For female methadone patients being treated with methadone, an untreated trauma-related disorder can be a hidden factor that hinders treatment response and leads to treatment complications, such as depression, polysubstance abuse, or treatment drop-out (5).

In any case, there are studies which have failed to confirm the relationship between PTSD and alcohol use in methadone maintenance programmes (18).

Frequency of positive urine analyses on opioids: in all, 3,075 urine analyses were performed for opioids; of these, 43.93% were posi-

tive. The patients who were using alcohol had a positive result in 45.93% of these analyses, whereas those who were abstaining had a positive result in only 39%. This difference is statistically significant.

In conclusion, we found that alcohol was used by 25.77% of the patients undergoing methadone treatment in our sample (counting those with an AUDIT score > 7); and 9.2% of these patients had an AUDIT score of 20 or higher, which indicated probable alcohol dependence.

The two groups did not differ in terms of sex, age, education, employment, marital status or percentage of war veterans.

The statistically significant differences recorded were: the lower average dose of methadone, fewer positive urine analyses for opioids, and the greater incidence of PTSD among the patients undergoing methadone substitution treatment who were using alcohol ($p < 0.05$).

These findings can be explained by the cumulative, reinforcing effects of alcohol with respect to methadone. PTSD seems to be an additional risk factor in the use of alcohol during methadone treatment.

Both alcohol and PTSD require greater attention in everyday practice. These findings need further research, especially in the case of high doses of methadone.

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Further evidence of no relationship between anxiety-depressive mental status and dual diagnosis in heroin addicts entering treatment

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Summary

Psychiatric symptoms are generally the rule among heroin addicts requesting treatment, and are not always the expression of an associated mental disorder. In a previous study we investigated the mental status of 1,090 Italian heroin addicts at the beginning of treatment, and its relationship to relevant demographic and clinical data through the use of standardized instruments. We concluded that the presence of depressive–anxious symptomatology in the clinical presentation appears to be unrelated to ‘dual diagnosis’. In this study we tried to replicate our previously reported study in a sample of 591 Slovenian heroin addicts (462 males and 129 females aged between 18 and 52). The results showed that psychomotor excitement was the most frequent psychiatric symptom among Slovenian heroin addicts looking for treatment; it was linked with a lower severity of drug addiction history. By contrast, the presence of depressive features in the clinical presentation of Slovenian heroin addicts appears to be a reliable indicator of general addiction severity. Psychomotor excitement and psychosis, but not depression, predict the presence of an actual dual diagnosis, in agreement with our previous study and providing further support for the view that it is important for clinicians to be able to identify major as well as minor psychomotor excitement and psychotic symptoms in heroin addicts presenting for treatment.

Key Words: Mental status; heroin addiction; dual diagnosis; anxiety; depression

1. Introduction

Substance use and other mental disorders interact in various ways [8]. Psychiatric illness and substance use share several features: substance use may induce or mask a concurrent but independent psychopathology, thus making it difficult to discriminate between them [11]. The use of addictive substances generally causes a wide variety of psychiatric symptoms, and various different psychiatric syndromes may be mimicked. The psychopathology of addiction is almost always characterized by craving, a withdrawal-re-

lated discomfort or a fear of withdrawal symptoms to come [11]. Thus psychiatric symptoms are generally the rule among heroin addicts demanding treatment and are not always the expression of a “non substance use” mental disorder [12].

Recently we studied the mental status of 1,090 Italian heroin addicts (831 males and 259 females aged between 16 and 51) at the beginning of treatment, and its relationship to relevant demographic and clinical data through the use of standardized instruments. We concluded that the presence of depressive–anxious symptomatology

in the clinical presentation in heroin addicts appears to be unrelated to 'dual diagnosis' [12].

This finding supported our idea that the persistence of an important psychopathological manifestation in subjects with an addiction who are undergoing treatment may depend on the persistence of addiction rather than the presence of other mental disorders. The inclusion of some components of mood, anxiety and impulse control dimensions in substance-use disorders will help clinicians to re-evaluate the appropriateness of the treatment delivered for addiction before turning to the treatment of another assumed associated mental disorder [19].

In this study we tried to replicate our previous reported study [12] in a sample of Slovenian heroin addicts.

2. Methods

2.1. Sample

The study included 591 heroin addicts, who had requested treatment during the period 2003-2008 at an outpatient drug treatment service in Slovenia (Centre for Treatment and Prevention of Illegal Substance Use at Izola, specialized in the treatment of "dual diagnosis heroin addicts"). All patients received a diagnosis of opioid dependence with physical dependence (according to DSM III/IIIR/IV criteria), and gave their informed consent for study participation.

The average age of the patients was 29 ± 6 years old (range 18–52). Most of the patients were male ($N=462$, 78.2%) and single ($N=507$, 85.8%), with less than 9 years of education (70.7%); 267 (45.2%) were students, of whom 143 (53.5%) had left school. The remaining 324 (54.8%) were non-students; of these, 216 (66.7%) were unemployed.

The males in the group were older than the females (30 ± 6 vs 27 ± 6 , $T=5.63$, $p<0.001$). Males and females differed too in their employment rate (17.5% of males were students and 39.0% were unemployed; 33.3% of females were students and 27.9% were unemployed; $df = 3$; chi-square 15.93; $p = 0.00117$). There were no statistically significant differences between males and females with respect to marital status.

2.2. Instruments

Addiction-related information was collected by means of the Drug Addiction History

Rating Scale (DAH-RS, [10]) administered by a psychiatrist.

The DAH-RS is a multi-scale questionnaire comprising the following categories: demographic data, physical health, mental health, substance abuse, treatment history, social adjustment and environmental factors, clinical characteristics as frequency of drug use, patterns of use, previous treatments, and current treatments. Items are set up so as to elicit dichotomous answers (yes/no).

For the purpose of standardised registration by means of DAH-RS, psychiatric disorders are investigated on the basis of the DSM-IV decision trees for differential diagnosis. Each decision tree starts with a set of clinical features. When one of these features is a prominent part of the presenting clinical picture, the clinician can follow the series of questions to rule in or rule out various disorders. The questions are only approximations to the diagnostic criteria and are not meant to replace them. Three decision trees have been used: 'differential diagnosis of psychotic disorders' (initial clinical features: delusions, hallucinations, disorganised speech, or grossly disorganised behaviour), 'differential diagnosis of mood disorders' (initial clinical features: depressed, elevated, expansive or irritable mood; two separate items record the presence of depression and/or any tendency towards the bipolar spectrum as testified by an elevated, expansive or irritable mood), and 'differential diagnosis of anxiety disorders' (initial clinical features: symptoms of anxiety, fear, avoidance, or increased arousal).

As for bipolar spectrum diagnoses, a history of previous hypomanic episodes, as well as temperamental characteristics, was explored using the criteria listed in the Semistructured Interview for Depression (SID) [4]. All information was gathered from the patient and at least one close relative (usually parents/siblings); in addition, all available clinical records were carefully examined. An inquiry into temperamental attributes was made in exploring the habitual state of the patient during periods free from affective episodes; the information gathered came both from the patient and from significant others. Our operational criteria for affective temperaments were the University of Tennessee [1] modifications of the Schneiderian descriptions [28]. The SID, developed as part of the Pisa-Memphis (now San Diego) collaborative study on affective disorders, has been used with over 2,500 patients at the time of writing; its reliability for diagnostic assessment of patients and their temperaments

has been documented elsewhere [20, 21].

2.3. Statistical analyses

To describe a patient's mental status, we used the following DAH-RS items: awareness of illness, consciousness disturbances, memory deficits, anxiety states, depression, sleep disturbances, eating disturbances, excitement, violence, suicidality, delusions and hallucinations.

A factor analysis was performed on these DAH-RS items for 591 patients in order to identify possible composite dimensions. The initial factors were extracted by means of principal component analysis (type 2) and then rotated according to varimax criteria in order to achieve a simple structure. This simplification is equivalent to maximizing the variance of the squared loading in each column. The criterion used to select the number of factors was an eigenvalue greater than 1. Item loadings with absolute values greater than 0.4 were used to describe the factors. This procedure makes it possible to minimize the correlations between the factors, so allowing their optimization as classificatory tools for each subject. The factorial scores were then standardized as z-scores to facilitate comparisons between scores among the factorial components. All the subjects were then grouped into different subtypes on the basis of the highest z-scores obtained for each factor (dominant factor). We compared clinical features within the various dominant factor groups by means of one-way ANOVA followed by the Student–Neuman–Keultz F-test for metrical variables and the chi-square test for

category variables.

Statistical analyses were carried out using the SPSS package (version 4.0 by SPSS Inc). As this is an exploratory study, statistical tests were considered significant at the $p < 0.05$ level.

3. Results

Only 28 (4.7%) patients showed awareness of their illness, which means that this group conceptualize themselves as having a self-maintaining disease caused by previous exposure to heroin, and are in need of some long-term relapse prevention. A total of 185 (31.3%) reported depressed mood, and 122 (20.6%) reported preoccupation with somatic functions or an experience of spontaneous anxiety. Sleep disorders were reported by 183 subjects (31.2%), and (hypo) manic or mixed excitement was displayed in a prominent way by 230 (38.9%) patients at the time of evaluation; 200 (33.8%) felt or showed aggressive behaviours and/or had been violent recently; 106 (17.9%) had engaged in self-injurious acts. Appetite had increased or decreased in 90 (15.2%) subjects. Memory disturbance occurred in 43 (7.3%) subjects. The symptoms that featured least were delusions ($n = 31$; 5.2%), altered states of consciousness ($n = 25$; 4.2%) and hallucinations ($n = 36$; 6.1%).

Significant gender-related differences for psychic impairment at treatment entrance were revealed by univariate analysis (Table 1).

Females were more likely to display eating disturbances, states of anxiety, depression, violence, psychomotor excitement, suicidal thoughts

Table 1 - Mental status of 591 Slovenian heroin addicts at beginning of treatment

	Total N (%)	Males N = 462	Females N = 129	Chi-square	p Value
Awareness of illness	28 (4.7)	25 (5.4)	3 (2.3)	2.13	0.143
Consciousness disturbance	25 (4.3)	20 (4.4)	5 (3.9)	0.04	0.835
Memory disorders	43 (7.3)	36 (7.8)	7 (5.5)	0.83	0.361
Anxiety state	122 (20.7)	85 (18.5)	37 (28.9)	6.62	0.010
Depression	185 (31.5)	132 (28.8)	53 (41.4)	7.41	0.006
Sleep disturbances	183 (31.2)	140 (30.5)	43 (33.6)	0.44	0.504
Eating disturbances	90 (15.3)	58 (12.6)	32 (25.0)	11.78	0.000
Psychomotor excitement	230 (39.2)	173 (37.7)	57 (44.5)	1.96	0.160
Violence	200 (34.1)	158 (34.4)	42 (32.8)	0.11	0.733
Suicidality	106 (18.1)	69 (15.0)	37 (28.9)	13.22	0.001
Delusions	31 (5.3)	20 (4.3)	11 (8.6)	3.61	0.057
Hallucinations	36 (6.1)	24 (5.2)	12 (9.4)	2.98	0.083

and behaviours, and delusions. On the whole, Slovenian women tended to have a higher level of psychic impairment at treatment initiation.

Principal component factor analysis of the selected 12 items of DAH-RS yielded a three-factor solution, with a loading greater than 0.40 (Table 2).

The first factor reflects a ‘depressive–anxious’ dimension (memory deficits, anxiety state,

employed. They had fewer somatic comorbidity, and social and leisure major problems. They showed a stable modality of heroin use and more frequently they were found to be in stage 2 of the addictive process (transition from recreational use to patterns of use consistent with addiction). They were oldest at first heroin contact, when they started their continuous use of heroin and when they got their first AOT (Opioid Agonist

	F1	F2	F3
Awareness of illness			
Consciousness disturbance			0.58
Memory deficits	0.47		
Anxiety state	0.72		
Depression	0.80		
Sleep disturbances	0.78		
Eating disturbances	0.66		
Psychomotor excitement		0.93	
Violence		0.93	
Suicidality			
Delusions			0.91
Hallucinations			0.90
Eigenvalue	3.92	1.65	1.27
<i>% Variance</i>	32.7	13.8	10.6

depressed mood, sleep and eating disturbances), which accounted for 32.7% of the variance. The second factor, accounting for 13.8% of the variance, reflects a psychomotor excitement dimension (hypomanic/manic or mixed state, aggressiveness and violence). The third factor, which reflects a ‘psychotic state’ dimension including altered consciousness, delusions, and hallucinations, accounted for 10.6% of the total variance.

On the basis of the highest z-scores obtained for each factor (dominant factor) we clustered all the subjects into three groups. The dominant ‘depressive–anxious’ group comprised 115 subjects (19.5%), the dominant ‘psychomotor excitement’ group 360 (60.9%), and the dominant ‘psychotic state’ group 110 (18.6%). Comparisons between these groups (Table 3) revealed significant differences.

Depressive–anxious heroin addicts were less frequently employed and reported household major problems. At treatment entry, they were using more hallucinogens and showed a junkie modality of heroin use;

Psychomotor excited heroin addicts were less frequently students and more frequently un-

Treatment).

Psychotic heroin addicts more frequently received combined treatments and, at treatment entry, were also found to be using more CNS stimulants. They showed a ‘two worlders’ and ‘loners’ modality of heroin use. They were youngest when they started to use heroin continuously and when they got their first AOT (Opioid Agonist Treatment).

Lastly, predominantly ‘depressive–anxious’ patients were less likely to be rated as having a ‘dual diagnosis’ when going through a more thorough psychiatric evaluation by means of DSM and SID. Baseline conditions of dominant psychomotor excitement and psychosis are more likely to correspond to the otherwise assessed presence of an addictive and autonomous psychiatric disorder (dual diagnosis).

4. Discussion

A current major depressive episode was reported in 16–34% of patients seeking treatment [3, 5, 23-25, 27]; that percentage was higher than among those without any treatment [29]. Females

were more likely to have a current major depressive episode [29]. In this study 19.5% of patients fell into the dominant 'depressive-anxious' group, including depressed mood together with anxiety states, sleep disturbance and altered appetite. This percentage was lower than that reported in our previous study on Italian heroin addicts [13] but the depressive-anxious dimension, built in as a factor, continued to be the best represented (32.7% of total variance). In Slovenian heroin addicts the depressive-anxious factor proved to be related to the severity of addiction history, but was not linked to a concomitant dual diagnosis.

The 'psychomotor excitement' dimension, which, incidentally, accounted for aggressiveness and self-injurious behaviour, was prominent in a clear majority of these subjects (60.9%). On clinical and psychopathological grounds, psychomotor excitement is usually related to the presence of dual diagnosis, with special reference

to the bipolar disorder. It should be noted that the prevalence of this factor in our sample is far higher than the rates of manic/hypomanic and mixed states previously reported in the literature, which ranged from 0.1% [24, 26] to 5.5% [16, 17], but also higher than in the sub-sample recruited in our university psychiatric setting (51-55%) [9, 15]. In this study we confirm that patients with dominant psychomotor excitement were more likely to be assessed as having a dual diagnosis than predominantly depressive-anxious patients. Subjects who presented prominently as psychotic on entering treatment were less well represented (18.6%). Other authors agreed, reporting low rates for psychosis among heroin addicts [2, 18, 22]. These subjects too are more likely to be affected by a dual diagnosis than depressive-anxious ones.

Lastly, in this study, heroin-dependent patients tend to have a very poor awareness of their

Table 3 - Differential characteristics of heroin addicts with different psychopathological syndromes at the initiation of their treatment

	Depressive group N = 115	Psychomotor excitement N = 360	Psychotic state N = 110	chi/F	p	Contrasts
Age	30±7	30±6	28±6	1.53	0.215	
Sex (males)	92 (80.0)	287 (79.7)	79 (71.8)	3.34	0.187	
Marital status (single)	94 (81.7)	310 (86.1)	101 (91.8)	4.87	0.087	
Occupation				43.23	<0.001	
Student	35 (30.4)	53 (14.7)	36 (32.7)			1,3#2
Left school	37 (32.2)	74 (20.6)	28 (25.5)			1,3#2
Employed	11 (9.6)	75 (20.8)	21 (19.1)			2,3/1
Unemployed	32 (27.8)	158 (43.9)	25 (22.7)			2#1,3
Somatic comorbidity	52 (45.2)	103 (28.6)	54 (49.1)	21.00	<0.001	1,3#2
Work major problems	66 (57.4)	213 (59.2)	61 (55.5)	0.50	0.775	
Household major problems	73 (63.5)	284 (78.9)	77 (70.0)	12.05	0.002	2#1
Loving major problems	14 (12.2)	58 (16.1)	21 (19.1)	2.04	0.359	
Social and leisure major problems	45 (39.1)	60 (16.7)	49 (44.5)	45.86	<0.001	3#1#2
Legal problems	92 (80.0)	173 (48.1)	56 (50.9)	36.77	<0.001	1#2
Polyabuse	110 (95.7)	340 (94.4)	107 (97.3)	1.53	0.463	
First treatment	17 (14.8)	50 (13.9)	19 (17.3)	0.75	0.687	
Combined treatment	27 (23.5)	71 (19.7)	43 (39.1)	17.03	<0.001	3#2
Alcohol use	106 (92.2)	349 (97.8)	108 (98.2)	9.49	0.008	
CNS Depressant use	96 (83.5)	296 (83.6)	100 (90.9)	3.74	0.153	
CNS Stimulants use	98 (87.5)	253 (80.0)	98 (92.5)	10.34	0.005	3#2
Hallucinogens use	102 (91.9)	244 (79.7)	93 (89.4)	11.68	0.002	1#2
Cannabinoids use	113 (99.1)	353 (98.9)	109 (100.0)	1.22	0.541	
Inhalants use	23 (20.4)	47 (13.5)	19 (17.6)	3.41	0.181	
Frequency of Heroin Intake (1-5)	4.14±1.5	4.51±1.0	4.41±1.1	2.33§	0.310	

continues

Table 3 - Differential characteristics of heroin addicts with different psychopathological syndromes at the initiation of their treatment (continues)

	Depressive group N = 115	Psychomotor excitement N = 360	Psychotic state N = 110	chi/F	p	Contrasts
Modality of use (a)				52.44	<0.001	
Stables	11 (10.2)	94 (33.9)	17 (16.3)			2#1
Junkies	58 (53.7)	66 (23.8)	29 (27.9)			1#2
Two worlders	25 (23.1)	93 (33.6)	43 (41.3)			3#1
Loners	14 (13.0)	24 (8.7)	15 (14.4)			
Periodic self-detoxification	107 (95.5)	343 (96.6)	103 (93.6)	1.90	0.385	
Stages of heroin addiction (b)				11.90	0.018	
Stage 1	23 (21.7)	41 (14.2)	21 (20.4)			
Stage 2	20 (18.9)	85 (29.5)	16 (15.5)			2#1,3
Stage 3	63 (59.4)	162 (56.3)	66 (64.1)			
Clinical Typology (c)				2.79	0.593	
Type 1	30 (27.5)	80 (24.8)	27 (25.0)			
Type 2	14 (12.8)	29 (9.0)	14 (13.0)			
Type 3	65 (59.6)	214 (66.3)	67 (62.0)			
Age at first contact (years)	19±3	20±4	19±4	5.57	0.004	2#3
Age at onset of continuous use	21±4	21±4	20±4	5.06	0.006	2#3
Dependence length (months)	78±62	63±43	70±46	3.67§	0.159	
Age at first treatment	22±4	23±5	21±4	3.36	0.035	2#3
Dual diagnosis	21 (18.3)	194 (53.9)	95 (86.4)	104.98	<0.001	3#2#1

§Kruskal-Wallis 1-way anova

(a) 'Stable' or 'conformist' heroin addicts lead an existence that is apparently acceptable to social conventions. 'Junkie' heroin addicts are 'destructive' or 'violent' addicts; they are immersed in their drug sub-culture, and live in places and situations that are often at the limits of the law, or may even be in open conflict with rules or conventions. 'Two worlder' heroin addicts do not care about their criminal activities or living together with other addicts, but often have a regular job. 'Loner' heroin addicts are not involved in the drug culture, do not have a stable job and in most cases live on State subsidies rather than on the proceeds of criminal activities [7].

(b) The development of addiction may be considered to consist of three stages: (1) acute (immediate) drug effects; (2) transition from recreational use to patterns of use consistent with addiction; and (3) end-stage addiction, which is characterized by an overwhelming desire to obtain the drug, a diminished ability to control drug seeking and reduced pleasure from biological rewards [6].

(c) Type 1 or 'reactive' heroin addicts show psychosocial stressors before using heroin. Type 2 or 'self-therapeutic' heroin addicts report psychiatric stressors before using heroin. Type 3 or 'metabolic' heroin addicts show no psychosocial or psychiatric antecedents [14].

illness.

5. Conclusions

This study shows that psychomotor excitement is the most frequent psychiatric symptom among Slovenian heroin addicts looking for treatment, and that it forms part of the most highly represented clinical state. A dominant psychomotor excitement state is linked with a lower severity of drug addiction history. Psychomotor excitement and psychosis both predict the presence of an actual state of dual diagnosis. It is therefore

very important for clinicians to be able to identify major as well as minor psychomotor excitement and psychotic symptoms in heroin addicts presenting for treatment, because it is likely that these patients are affected by another independent mental disorder (i.e. qualify as dual diagnosis patients), and that the second disorder deserves specific clinical attention and treatment. By contrast, the presence of depressive features in the clinical presentation of Slovenian heroin addicts appears to be a reliable indicator of general addiction severity, and to be a common comorbid condition in the average addict. In conclusion,

our data indicate something that conflicts with the general tendency to identify dual diagnosis from baseline depression patients and ascribe psychomotor excitement or psychosis to intoxication from psychoactive substances. Depressive-anxious symptoms are more likely to exist in parallel with addiction, whereas psychomotor excitement and psychotic symptoms are likely to spring directly from a state of dual diagnosis.

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Requiring stabilized heroin addicts to stop successful agonist opioid treatment before liver transplantation can shift patients over a cross-acting (alcohol) substance abuse

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Summary

Methadone Maintenance Treatment patients are significantly under-represented in most liver transplant programmes, but the number of patients receiving agonist opioid treatment (AOT) is increasing, and few data are available at the moment when patients are selected for surgery. We present a case in which an Italian patient affected by heroin dependence and successfully treated with AOT had to stop opioid medical treatment to be able to enter a liver transplantation programme. He successfully discontinued AOT, received a liver transplant and continued not to abstain from heroin in the post-transplant period. Unfortunately, he engaged in alcohol use, so shifting over into another cross-acting substance abuse disorder, and endangering his newly restored liver functions. He was a non-responder to alcohol abuse treatment and, while he was abstaining from alcohol, he reported a craving for heroin. We reintroduced opioid agonist treatment, so obtaining a non-relapsing condition regarding heroin and a significant patient recovery on alcohol abuse, with a complete liver function normalization. We suggest that successful agonist opioid treatment should be continued even when transplantation is needed, not only to avoid the risk of relapse into heroin use, but also to avoid the risk that the patient may shift over into another substance abuse disorder (in this case, alcoholism). The shift from heroin to alcohol also means the transition from a highly curable disease, as heroin addiction is, to one that is hard to cure, as alcoholism is, which implies a greater risk to endangering the new liver function with respect to the continuation of AOT.

Key Words: Opioid Agonist Treatment; liver transplantation; shift from heroin dependence to alcoholism

1. Introduction

Methadone Maintenance Treated (MMT) patients are significantly under-represented in most liver transplant programmes, but the number of patients receiving agonist opioid treatment (AOT) is rising, and few data are available at the moment of selecting patients for surgery.

HCV-related cirrhosis is the most common reason for liver transplantation, and the parenteral use of street drugs is the most common way of acquiring hepatitis C, so that, unsurprisingly, a significant proportion of AOT patients have

chronic hepatitis C. The feasibility of hepatitis patients in need of AOT becoming candidates for a liver transplant is a controversial issue, and some transplant centres require patients to withdraw from this type of therapy before the transplant process can move forward. As a result, stable patients with end-stage cirrhosis who are receiving AOT are left in a most awkward situation: they must either discontinue medication, and accept the side-effects of withdrawal, but with the risk of recidivism in the use of street opiates – an absolute contraindication for transplantation – or continue with AOT, but risk their exclusion from

the transplant programme [6].

In this paper we present a case in which a heroin-dependent Italian patient successfully treated with AOT had to stop opioid medical treatment to enter a liver transplantation programme. He discontinued AOT, received a liver transplant and continued to abstain from heroin in the post-transplant period. Unfortunately he engaged in alcohol use, so shifting over into another cross-acting substance abuse disorder and endangering his newly restored liver functions. He was a non-responder to alcohol abuse treatment and, while abstaining from alcohol, reported a craving for heroin. We reintroduced opioid agonist treatment, so avoiding any relapse into heroin use and recovering from his alcohol abuse; the outcome was complete liver function normalization. We suggest that a successful agonist opioid treatment should be continued even when transplantation is needed, with the double aim of avoiding the patient's relapse into heroin use, and also the patient's shift over into another substance abuse disorder (such as alcoholism).

2. Case Report

Mr F. B. is a Caucasian, 65-year-old single male, a liver-transplanted patient, now living on welfare benefits, who had presented at the Vincent P. Dole Dual Diagnosis Unit, Department of Psychiatry, Santa Chiara University Hospital, Pisa (Italy); on that occasion he requested treatment for his current alcohol abuse. At our first diagnostic evaluation the patient was affected by a severe form of alcohol abuse, and he also presented a major depressive episode. After the complete diagnostic evaluation he received a lifetime diagnosis of bipolar II disorder, heroin dependence and alcohol dependence according to DSM-IV TR criteria.

As a 21-year-old he had started heroin use by sniffing, and he rapidly developed tolerance to it, with a consequent need to increase dosages. At the age of 24 he was using heroin by injection; in that period HCV infection was often contracted through the exchange of needles. As a separate issue, his liver condition called for his hospitalization, so that the progression of HCV infection and organ functioning could be properly evaluated.

Over time, he was given opioid agonist treatment according to the Dole and Nyswander methodology [4], with a complete remission of addictive behaviours. Despite this, his liver func-

tion worsened, due to HCV progression.

When he was 46, cirrhosis and liver failure were diagnosed, so his need for liver transplantation became evident. The transplant programme required him to stop AOT before surgery could be performed.

Thus, he successfully discontinued AOT and, at the age of 48, did undergo surgery; he continued to abstain from heroin in the post-transplant period. Unfortunately, from 48 up to 65 he started and increased his use of alcohol, which led to clinical deterioration. His liver function was once again at risk, and he engaged in street methadone use before entering our treatment programme. Alcohol detoxification through the prescription of benzodiazepines and gamma-hydroxybutyrate (GHB), together with social support, failed. F.B. refused the use of disulfiram and naltrexone. F.B.'s use of street methadone persuaded us to reintroduce stable opioid treatment with buprenorphine at 24 mg/day. The current major depression episode (DSM-IV TR criteria) was treated with mood stabilizers and antidepressants

During buprenorphine maintenance treatment F.B. did not relapse into heroin use. Once he had become completely detached from alcohol use, he recovered from his depressed mood, and his liver function improved. After a one-year follow-up, liver functional parameters had returned to normal values, and his drug tests were negative for opioid and alcohol.

3. Discussion

To be admitted into a liver transplant programme, F.B. had to stop a successful AOT. He discontinued methadone but shifted to alcohol abuse, with a craving for heroin testified by street methadone use. He did not relapse into heroin use, but, due to his abuse of alcohol, the risks to his liver functions became even more severe. His liver transplant was needed because of HCV infection progression.

HCV infection is a clinical disease that is often (64-88%) associated with heroin addiction [2, 5]. Hepatitis C and related hepatic insufficiency cause 9% of all deaths associated with MMT. In any case, the presence of severe chronic hepatopathy is not a clinical counterindication for beginning and/or continuing MMT, and MMT should not constitute a limitation on transplantation [14]. The belief that people suffering from hepatitis C are intolerant to methadone, or are

more sensitive to unspecified hepatotoxic effects of methadone itself, is unmotivated: methadone treatment has a positive impact on the liver function of patients with HCV-related liver disease, with plasma transaminase levels proving to be higher in non-treated patients than in those receiving methadone treatment [9]. Furthermore, long-acting opioids seem to improve the outcome of the viral infection, as suggested by the ability of methadone and buprenorphine to significantly reduce the relapse rate of patients undergoing interferon and ribavirine treatment [13]. Long-acting opioids are not toxic to the liver, whether in treating an acute condition or in long-term administration [8]. Liver transplantation can be safely performed in methadone-maintained patients [7]. In a 1999 study, 185 case files of methadone-maintained transplanted patients were reviewed; these patients' life expectancy was close to that of other categories of transplanted patients [7]. The relapse rate after transplantation was 12%, which is, anyway, lower than that among transplanted abusers who were not on methadone treatment [3].

It should be made clear that transplantation can only be carried out if alcoholic patients continue to treat their alcoholism before and after liver surgery [16].

F.B. did not use alcohol before or during AOT, and he started to use alcohol after methadone discontinuation. He failed to respond to treatment for alcohol abuse. To date, we know that, when correctly handled, agonist opioid treatments are crucial in inducing a cessation of illicit opioid abuse and a high level of retention in treatment. These treatment patterns are positively correlated with a curtailment of alcohol and cocaine abuse, and the absence of the psychosocial complications associated with such abuse [11]. On the other hand, the abuse practised by alcohol- and/or heroin-dependent people could reflect the destabilization of the opioid system resulting from undermedication or premature methadone discontinuation. In other words, heroin abuse and alcohol abuse might share a common metabolic pathway [1, 12, 15]. This case report points to alcohol abuse as one possible pathological outcome of the impairment of the opioid metabolism underlying heroin addiction. Alcohol-abusing heroin addicts seem to suffer from a metabolically acquired problem, which derives from the pre-conditioning brought about by opiate abuse, and later prompts either opiate- or alcohol-seeking behaviour in an addictive way. The accomplish-

ment of this metabolic destiny through a shift from heroin to alcohol use is subtle, as it may be mistaken for the remission of opiate addiction, whereas it appears to be just another pathological dynamic leading to opiate use extinction. Like the so-called masked depressive syndromes, alcohol abuse in former heroin addicts can be considered a masked form of heroinism, or a sign of enduring opiate dysfunction disguised as remission. The shift from heroin to alcohol also means the transition from a highly curable disease, as heroin addiction is, to one that gives a poor response to treatment, as alcoholism is.

F.B.'s use of street methadone is telling evidence of the dysfunction of the opioid system in his case, and may be considered a sort of self-medication that was resorted to because of the impossibility imposed on him of continuing MMT before and after transplantation [10]. In conclusion, F.B.'s former history of opioid dependence may well have influenced the severity of his alcohol abuse and liver failure after methadone discontinuation and liver transplantation. At this point, it is hardly surprising that the reintroduction of AOT allowed the patient to control his alcohol intake after he had failed to respond to standard treatment for alcohol abuse.

In our opinion and according to this case report, surgical teams should not require the interruption of a successful AOT either before or after transplantation. As this case report has demonstrated, any such obligation is liable to endanger a patients' safety, increasing both the risk of a relapse into heroin use, and also the risk of shifting over to an abuse of alcohol that certainly puts the liver functions at far greater risk than continuing a successful AOT. In any case, an expert on AOT should be consulted about the advisability of modifying or stopping a patient's AOT before a decision is taken on liver transplantation.

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HEROIN ADDICTION & RELATED CLINICAL PROBLEMS

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Suboxone® switch data: A regional experience

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TO THE EDITOR: Suboxone® is a fixed-dose tablet containing buprenorphine HCl and naloxone HCl dihydrate at a ratio of 4:1. Suboxone® was developed to have an efficacy and safety profile similar to that of Subutex® (buprenorphine HCl) in the treatment of opioid dependence.

When Suboxone® is administered sublingually, the naloxone component shows sub-therapeutic absorption and bioavailability, but the buprenorphine component is absorbed normally, as it is from Subutex®. On the other hand, when Suboxone® is injected intravenously, naloxone quickly precipitates withdrawal symptoms in opioid-dependent users, so strongly attenuating the subject's previous perception of enjoying the drug.

Suboxone® is therefore a formulation that is much less liable to misuse through injection than Subutex®, which explains why most patients in Italy who were on treatment with buprenorphine alone (Subutex®) were switched to Suboxone® to enhance the safety of their take-home therapy.

In Italy a lot of attention has been dedicated to the need to 'prepare the patient'. In most drug addiction centres where the switch to Suboxone® therapy was made, the patients were divided into groups and were properly informed regarding:

- * the pharmacological characteristics of the new combination;
- * that buprenorphine in Suboxone® works in the same way as buprenorphine in Subutex®;
- * the sub-therapeutic absorption of naloxone when it is taken sublingually;
- * the risk of triggering a withdrawal syndrome when the combination is taken by intravenous injection;
- * the possibility of receiving increased medication as take-home therapy and for longer periods through the use of the buprenorphine/naloxone combination.

The step of preparing patients was preceded by a specific and thorough training of all the professionals in the drug addiction centres, first of all to share common action guidelines.

Suboxone® was first made available in Italy in 2008. I had two years of experience with Suboxone®; this therapy was implemented on my patients, and, especially because of my role as regional consultant, on patients who were attending other drug addiction services.

In my Region (Latium), more than 600 patients who had initially been on Subutex® maintenance therapy were switched to Suboxone®, and were provided with weekly (or fortnightly) supplies of medication to take without supervised administration. Most patients switched to Subox-

one® at the same dose of buprenorphine; only a few of them needed a higher dose of Suboxone® during the switch. For this group of patients, the average mean doses of Subutex® and Suboxone® at transfer were 14.8 mg and 16.5 mg, respectively.

In my opinion, this need to increase the dose to be taken was most likely due to the anxiety and lack of confidence of the physicians and patients involved (particularly because of the naloxone present in Suboxone®). After stabilization these patients returned to their previous base maintenance dose. None of them appeared to have been destabilized by unsupervised dosing of Suboxone®, and the medication was well tolerated.

Now, after this initial two-year experience, the switch is proceeding well, and at this time no dose increases are required when transferring from Subutex® to Suboxone®. Both physicians and patients are now more familiar, better informed and more confident about the characteristics of Suboxone®.

Interestingly, after the switch we observed a fall in the average maintenance dose of approximately 15-20%. These data can be accounted for by the fall in the proportion of drug misuse and diversion.

Some common adverse events were experienced by 5% of patients; these were mainly gastrointestinal pain, headache and dyspepsia. When there was an immediate return to therapy with Subutex®, the subsequent data showed that there was no apparent relationship between the average daily dose of Suboxone® and the reporting of adverse events, and that common adverse events were of exclusively psychosomatic origin. Three consecutive weeks of treatment with Suboxone® led to the extinction of the common adverse events observed.

Regarding misuse patterns, I suspect that a few subjects probably attempted to inject Suboxone®, but without reporting their major adverse reactions; more importantly, they did not experience euphoria. All of them stated that they would not inject Suboxone® again, thereby supporting

the concept that Suboxone® reduces potential intravenous misuse and diversion in this population that has an experience of taking buprenorphine.

Overall, the conclusions to be drawn from my clinical experience with Suboxone® can be summarized as follows:

The presence of naloxone in Suboxone® is designed to reduce intravenous misuse and diversion without compromising the sublingual activity of buprenorphine. For that reason, switching from Subutex® to Suboxone® does not increase the withdrawal symptoms of opioid-dependent patients;

Suboxone® has an efficacy and safety profile that is comparable with that of Subutex®;

High-dose adjustments proved to be unnecessary when patients were switched from Subutex® to Suboxone®;

The few subjects who tried to inject Suboxone® one time only reported no major side-effects and did not experience euphoria. In any case, they were unwilling to inject Suboxone® again;

Frequent (5%) mild adverse events were reported; a few treatment discontinuations were observed, too. All such events were considered to be the result of anxiety about being forced to switch to Suboxone® without receiving sufficient information and/or counselling;

The therapeutic switch of patients from Subutex® to Suboxone® at the same dose is both safe and effective; it has the advantage of lowering the risk of misuse and diversion within this population that has an experience of taking buprenorphine.

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**HEROIN ADDICTION &
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What concept of 'spectrum' is useful in addiction medicine?

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TO THE EDITOR: The concept of a 'spectrum' was originally formulated in physics, where it indicates a series of qualitatively different phenomena that apparently result from a quantitative continuum; for example, the series of different colours that are formed when a beam of white light passes through a prism [22].

In psychiatry, a few authors have borrowed this concept to describe syndromes that, while remaining distinct on clinical-symptomatic grounds (depression and alcoholism), are underpinned by a common pathogenic factor [2, 44]. In the case of schizophrenia spectrum disorders, the hypothetical common denominator is their genetic family basis [4, 25, 26, 41]; depression spectrum disorders are characterized by their capacity to respond to the same pharmacological treatments [24], and dissociative spectrum disorders by the presence of common psychopathological traits [36, 40].

In the recent literature the term 'spectrum' has been used with a different meaning – one that refers to a wide area of psychiatric phenomena that are all associated with a single mental disorder [7, 20] and that include – to adopt a dimensional approach – nuclear, atypical, and subclinical symptoms, along with related behavioural dysfunctions, which may precede, overlap with or be residual after the full clinical expression of the major disorder.

This conceptualization has not yet been accepted by conventional psychiatric nosology; in particular, DSM-IV R makes use of a categorical approach that classifies personality disorders along a different axis from the corresponding clinical disorders [1]. Even so, some researchers have focused on the idea of a continuum where attenuated phenotypes lie at the opposite extreme to full-blown disorders; on that basis they have reconsidered several psychiatric diseases.

Regarding panic disorder, the Structured Clinical Interview for Panic Agoraphobic Spectrum (SCI-PAS) has been widely validated in an Italian multicentric study that compared psychiatric patients meeting DSM-IV criteria for panic disorder with cardiovascular patients and with healthy volunteers. This instrument was able to assess the lifetime presence of symptoms and other clinical features considered to comprise the panic-agoraphobic continuum, with good internal consistency, discriminant validity, and inter-rater reliability [6].

The same approach has been used with social anxiety and obsessive-compulsive disorders. The corresponding instruments – Structured Clinical Interview for Social Anxiety Spectrum (SCI-SHY) and Structured Clinical Interview for Obsessive Compulsive Spectrum (SCI-OBS) – have been validated both through the use of interviews and in self-report formats. The degree of agree-

ment between the two versions was very good, with a certain tendency for subjects to under-report some phobia-related problems in the interview version. Given the high level of agreement between the domain scores in the two formats made available by the instruments, and the fact that scores were virtually identical when the self-report version was administered first, the authors recommend the use of the self-report versions in clinical and research settings [14].

Recently the same authors, proceeding within a dimensional conceptualization, have also studied the stress response disorders arising from life events, putatively including the DSM-IV diagnosis of post-traumatic, adjustment and acute stress disorders, and the complicated grief. The Structured Clinical Interview for Trauma and Loss Spectrum (SCI-TALS) has been validated both in its interview and in its self-report versions, showing good reliability and validity. The validation process, while supporting the existence of a specific grief-related condition, suggests the idea that different forms of stress response share similar manifestations [13, 15].

It is generally accepted that Bipolar Disorders too constitute a clinical spectrum that includes various subtypes, based on the presence of hypomanic episodes, family history for mood disorders, pharmacological hypomania, and cyclothymic or hyperthymic temperament. On the basis of this hypothesis, a new instrument for the assessment of lifetime symptoms related to mood spectrum disorders – the Structured Clinical Interview for Mood Spectrum (SCI-MOODS) – has been elaborated and widely validated, both in the interview and the self-report format. The SCI-MOODS instrument was found to discriminate between patients with mood disorders and subjects belonging to two control groups, as well as between bipolar and unipolar patients [12, 18].

In line with other validated instruments for the assessment of mood, anxiety, loss and traumatic spectra, some authors have tested and validated the Structured Clinical Interview for the Spectrum of Substance Use (SCI-SUBS), a new instrument that is capable of exploring the interactive pathway between substance abuse and psychiatric disorders. This interview has shown satisfactory internal consistency and construct validity in a population consisting of psychiatric outpatients with and without substance abuse comorbidity, non-psychiatric subjects with opioid dependence and normal controls [38].

Two years later the validity and reliabil-

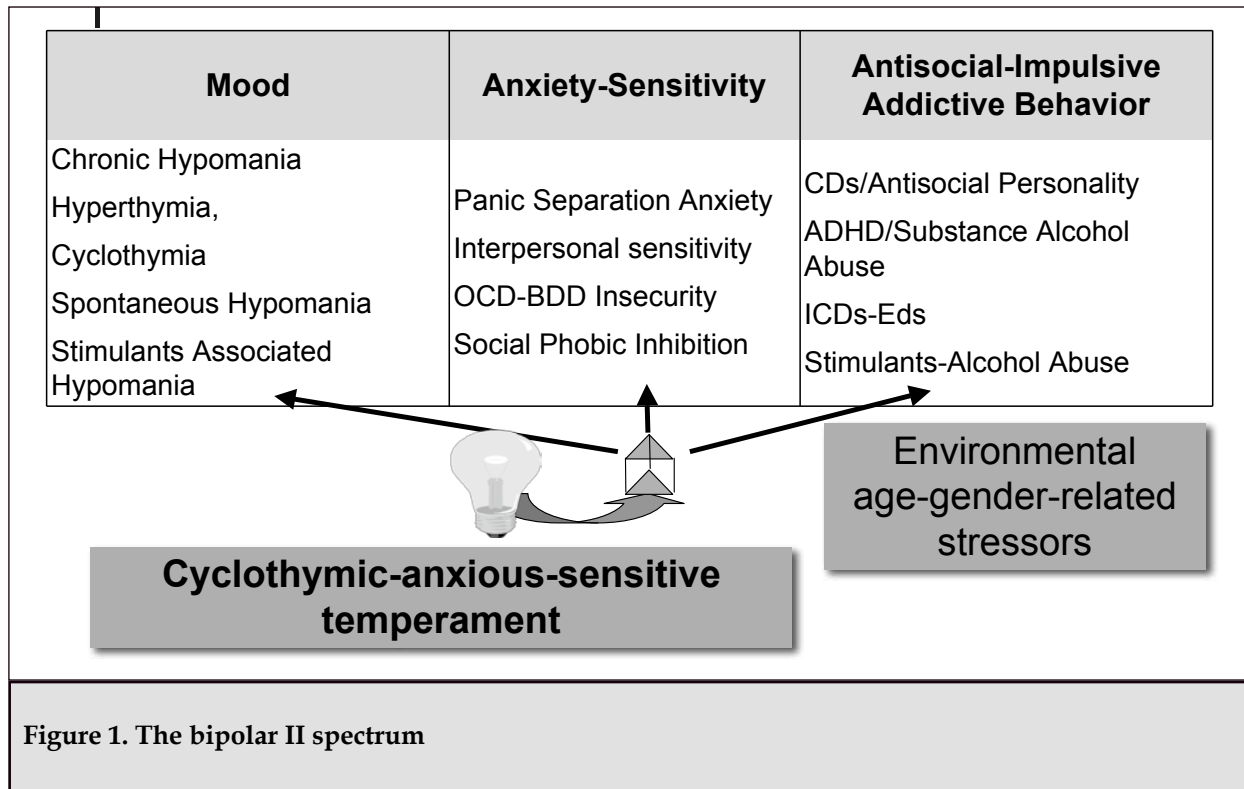
ity of the Structured Clinical Interview for the Psychotic Spectrum (SCI-PSY) were tested in a sample of psychiatric patients belonging to several diagnostic groups as a new instrument developed to assess the psychotic spectrum. SCI-PSY comprises a subset of the DSM-IV criteria for psychotic syndromes, but also a number of features derived from clinical experience and from a review of the phenomenological descriptions of psychoses [37].

In summary, in the past decade some researchers have used a dimensional approach to identify – whether in psychiatric patients or in healthy subjects – the presence of psychopathological traits belonging to different areas, ranging from mood and anxiety spectrum disorders to substance use and psychotic disorders. While mood, anxiety and obsessive-compulsive disorders have been shown to exist in attenuated forms characterized by sub-threshold manifestations [10, 21, 42], the same cannot be said of addiction and psychosis.

Substance use disorders are thought to be characterized by the impairment of the physiological process of attachment [19, 33, 39] that represents the neuroendocrine basis of the mother-infant bond [9, 23, 43]. By investigating alcoholic inpatients' attachment system, it has been possible to distinguish three degrees of severity of the illness [11]. In any case, it is our opinion that, when the attachment system is affected by an addiction process, it turns out to be qualitatively different compared with a well-functioning attachment system. According to this theory attachment should be conceptualized as a quality rather than a continuum.

In the case of psychotic disorders, the issue of their psychopathological nature has been the topic of even more heated debate. Neither the dimensional nor the categorical representation of psychosis have proven to be superior in discriminating between known risk factors for the development of a psychotic disorder. Most of the authors believe that a combination of dimensional measures with categorical diagnoses may turn out to be a productive strategy in conceptualizing psychotic illnesses [3, 16, 17].

As far as substance abuse disorders are concerned, some authors have provided much evidence in pointing out their correlation with bipolar disorders not only at the clinical level [5, 8, 28, 29, 31, 32], but also at the affective, temperamental levels. Cyclothymic temperament has been reported to represent the temperamental



profile of heroin addicts and alcoholics [30, 34]. These observations underline the possible role of bipolarity in the pathogenesis of substance use disorders, and to view the bipolar spectrum as the psychic substrate for the development of a substance-resorting attitude [27, 32, 35].

We intend to apply the concept of a 'spectrum' to substance use disorders in the same way as it was initially introduced in psychiatry. Addiction, together with mood and anxiety disorders, impulse control disorders and eating disorders, could belong to syndromes that differ from each other clinically, but are all underpinned by a common factor that is displayed in the cyclothymic temperamental disposition (figure 1). In other words, the cyclothymic temperament might turn out to be the nuclear structure from which the addiction process arises, whenever substances are present and available.

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