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Brief report

Chronology of illness in dual diagnosis heroin addicts:
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ABSTRACT

Background: Recent celebrity deaths have been widely reported in the media and turned the public attention to the coexistence of mood, psychiatric and substance-abuse disorders. These tragic and untimely deaths motivated us to examine the scientific and clinical data, including our own work in this area. The self-medication hypothesis states that individuals with psychiatric illness tend to use heroin to alleviate their symptoms. This study examined the correlations between heroin use, mood and psychiatric disorders, and their chronology in the context of dual diagnosis.

Methods: Out of 506 dual diagnosed heroin addicts, 362 patients were implicated in heroin abuse with an onset of at least one year prior to the associated mental disorder (HER-PR), and 144 patients were diagnosed of mental illness at least one year prior to the associated onset of heroin use disorder (MI-PR). The retrospective cross-sectional analysis of the two groups compared their demographic, clinical and diagnostic characteristics at univariate and multivariate levels.

Results: Dual diagnosis heroin addicts whose heroin dependences existed one year prior to their diagnoses (HER-PR) reported more frequent somatic comorbidity ($p \leq 0.001$), less major problems at work ($p = 0.003$), more legal problems ($p = 0.004$) and more failed treatment for their heroin dependence ($p < 0.001$) in the past. More than 2/3 reached the third stage of heroin addiction ($p < 0.001$). Their length of dependence was longer ($p = 0.004$). HER-PR patients were diagnosed more frequently as affected by mood disorders and less frequently as affected by psychosis ($p = 0.004$). At the multivariate level, HER-PR patients were characterized by having reached stage 3 of heroin dependence (OR=2.45), diagnosis of mood disorder (OR=2.25), unsuccessful treatment (OR=2.07) and low education (OR=1.79).

Limitations: The main limitation is its retrospective nature. Nonetheless, it does shed light on what needs to be done from a clinical and public health perspective and especially prevention.

Conclusions: The data emerging from this study, does not allow us to determine a causal relation between heroin use and mental illness onset. However, this data, even if requiring longitudinal studies, suggest that self-medication theory, in these patients, can be applied only for chronic psychoses, but should not be applied to patients with mood disorders using heroin.

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1. Background

The high comorbidity rate of Substance Use Disorders (SUD) with other mental health disorders has been highlighted in a number of trials conducted in clinical samples and in general population (Grant et al., 2004; Kessler et al., 1994; Kessler et al., 1996; Regier et al., 1990; Swendsen and Merikangas, 2000).

The link between heroin addiction and bipolar disorder is generally accepted both in inpatient and outpatient settings (Maremmani

et al., 2000a; Maremmani et al., 2000b; Maremmani et al., 1994; Maremmani et al., 2004; Maremmani et al., 2012; Maremmani et al., 2005; Maremmani et al., 2000c) and has been extended from the full-blown disorders to the affective temperaments, which, according to Akiskal and Mallya's conceptualization, reflect the substrate genetic for manic-depressive illness (Akiskal, 1983; Akiskal, 1989; Akiskal et al., 1989; Akiskal and Mallya, 1987; Cassano et al., 1989; Maremmani et al., 1994; Maremmani et al., 2009), and possibly underlies the genetic predisposition, particularly for irritable and hyperthymic types (Greenwood et al., 2012).

Psychosis and heroin addiction are associated with withdrawal psychosis (Levinson et al., 1995) as well as comorbid dual diagnosis (Maremmani et al., 2011).

Considering this high comorbid ratio, many authors have attempted to shed light on the nature of dual diagnosis. A possible explanation is provided by the 'self-medication hypothesis', according to which substance abuse could function as an attempt to alleviate the emotional suffering arising from the ensuing psychiatric illness (Khantzian, 1980; Khantzian, 1985; Khantzian and Treece, 1985). This hypothesis is supported by the fact that, among substances of abuse, opioids seem to engender therapeutic effects rather than psychopathological ones (Maremmani et al., 2014).

The role of the 'self-medication hypothesis' in dual diagnosis heroin-addicted patients can be addressed by studying the temporal priority between the onset of the substance abuse and that of the mental illness.

Studies have suggested that anxiety disorders, passive-aggressive disorder, behavioral disorders and ADHD may generally precede substance abuse disorders, while mood disorders are generally secondary to substance abuse disorders (Kessler, 2004). However, there remains a lack of conclusive data to explain these temporal relationships.

In the present study, dual diagnosis heroin-addicted patients were examined based on the temporal relationship based upon the onset of substance use. When the onset of heroin abuse was implicated at least one year prior to the associated mental disorder, the patient was described as "primarily affected by heroin use disorder" (HER-PR). When the onset of mental disorder existed at least one year prior to the associated heroin use disorder, the patient was described as "primarily affected by mental disorder" (MI-PR). If there was less than one year between diagnoses of either condition, then the patient was not assigned to either category. Therefore, this study examined the correlations between mood disorders and chronology of illness in dual diagnosed heroin addicts.

2. Methods

2.1. Study design

This is a cross-sectional study of heroin-dependent dual diagnosis patients requesting treatment at Pisa University Hospital in the last two decades. Once diagnosis and chronology of illness were confirmed, we divided patients into two groups: HER-PR and MI-PR. We then compared their demographic, clinical and diagnostic characteristics at univariate and multivariate levels.

2.2. Sample

A total of 506 dual diagnosis heroin dependent outpatients were enrolled in the study. All patients satisfied the DSM diagnostic criteria for Opiate Dependence and another mental illness and signed informed consent for participation in the study.

The mean age was 29.61 ± 5.9 sd in years (ranging from 17 to 45 years). The majority of patients were males ($n=376$; 74.3%), never married ($n=369$; 72.9%), reported less than 9 years of education

($n=330$; 65.2%). 217 (42.9%) and were unemployed at the time of clinical assessment. 109 (21.50%) reported poor economic status; 76 (15.0%) were living alone.

According to the timing of the onset of heroin use and mental illness, 362 (71.5%) were characterized as heroin-dependent priority patients (HER-PR) and 144 (28.5%) were characterized as mental ill priority patients (MI-PR). All patients were Italians and were only included once in the analyses.

2.3. Instruments

The DAH-Q (Maremmani and Castrogiovanni, 1989) is a multi-dimensional questionnaire that comprises 8 areas: demographic data, physical health, mental status, social adjustment and environmental factors, substances abused, substance abuse modalities (heroin intake, modality of use, stages of illness, nosography), treatment history and addiction history (age at first contact, age at onset of continuous use, dependence length and age at first treatment). The questionnaire collects information on 10 different areas: somatic comorbidities, abnormal mental status, work problems, household problems, sexual problems, socialization and leisure time problems, drug-related legal problems, poly-substance abuse, previous treatment, combined treatments. These dimensions are encoded using a dichotomous approach (present/absent), thus this instrument allows the collection of categorical and metric variables.

We encoded the modality of use as follows: 1-stables, 2-junkies, 3-two worlders, 4-loners according to Lahmeyer's classification (Lahmeyer et al., 1988). "Stables" are opioid addicts who have adopted conventional values, hold legitimate jobs, are generally law-abiding and do not associate with other addicts. "Hustlers", otherwise called "junkies" or "criminal addicts", are closely identified with an addict subculture, are not legitimately employed, and subsist on the proceeds of criminal activities. "Two-worlders" addicts engage in criminal activities and associate with other addicts, but are also legitimately employed. "Loner" addicts are not involved either in the addict subculture or the conventional culture. They are usually unemployed, and live on welfare benefits rather than on the proceeds of criminal activities. These uninvolved addicts may have severe psychological disorders.

The development of addiction may consist of three stages: 1-acute (immediate) drug effects (Honeymoon Stage); 2-transition from recreational use to patterns consistent with addiction (Increasing Dose Stage); and 3-end-stage addiction, which is characterized by overwhelming desire to obtain the drug, diminished ability to control drug-seeking and reduced pleasure from biological rewards (Revolving Door Stage) (Kalivas and Volkow, 2005).#

Diagnostic process consisted in two steps: first we analyzed the temporal priority (at least 1 year interval) between continuous use of heroin and presence of depressive, manic or psychotic episode, according DSM-IV diagnostic criteria. After that, psychiatric disorders were investigated on the basis of the various DSM diagnostic criteria and the "Decision Trees for Differential Diagnosis" performing a longitudinal diagnosis. Three decision trees were used: "Differential Diagnosis of Psychotic Disorders", "Differential Diagnosis of Mood Disorders" and "Differential Diagnosis of Anxiety Disorders". To reduce the diagnostic ambiguity between intoxication-related symptoms and spontaneous mental disorders, patients were not enrolled during the acute phases of withdrawal or intoxication. Whenever further clinical information emerged from later interviewing, diagnoses were reviewed.

2.4. Data analysis

The comparison of HER-PR and MI-PR patients was performed by the means of Student's *t*-test for continuous variables. Categorical variables were compared using the Chi-square test.

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