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The influence of Comorbid Personality Disorder on patients in Heroin-Assisted Treatment: Pilot data on clinical outcome

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Summary

Background: The diagnosis of a comorbid personality disorder (PD) is very common in patients with drug dependence. However, it is unclear whether differences between opioid-dependent patients with and without co-occurring PD influence diamorphine-assisted substance abuse treatments. **Methods:** Twenty-six patients with a diagnosis of opioid dependence (according to DSM-IV) in a stable heroin-assisted treatment (HAT) were included in this pilot study. The SCID II was used to assess the personality disorder diagnosis. At baseline, history of substance abuse (ASI), depressive symptoms (BDI) and childhood trauma (CTQ) were measured. At a 12-month follow-up, the clinical course was assessed with the Opiate Treatment Index (OTI), and substance abuse as well as depressive symptoms were newly assessed. **Results:** Fifty percent (n = 13) of the patients were diagnosed with at least one personality disorder. Patients with co-occurring PD experienced more depressive symptoms at baseline ($p < 0.05$), were more traumatized ($p < 0.01$) but had a shorter treatment history of heroin-assisted treatment ($p < 0.05$) and less cannabis abuse ($p < 0.05$) than those without a PD. At the 12-month follow-up, patients with comorbid PD showed worse overall psychological adjustment ($p < 0.01$). **Conclusion:** Patients with co-occurring PD had more severe psychopathological symptoms. These findings indicate that even within a heroin-assisted treatment group, patients with opioid dependence suffering from an additional PD may represent a sicker clinical subgroup, which could benefit from disorder-specific treatment.

Key Words: Addiction; opioid dependence; personality disorder; Antisocial Personality Disorder; heroin-assisted treatment; diamorphine; Substance Use Disorder; comorbidity.

1. Introduction

It is well known that psychosocial and physical impairments are common among patients with substance abuse. In recent years, several studies have focused on the relationship between drug addiction and other mental disorders. A high prevalence of comorbid psychiatric symptoms in patients with substance use disorders (SUDs) has been a consistent finding [26, 28, 34]. In opioid dependence, a chronic relapsing disorder that is characterized by a compulsion to seek and use opioids [30], affective disorders and personality disorders (PD) are the most widespread comorbid types of mental disorder [7, 18, 48].

Several authors have suggested that affective instability and impulsivity underlie the development of both conditions — PD and SUD — and thus explain much of their comorbidity [6, 45]. Furthermore, both PD and SUD are often associated with early adverse life experiences (e.g., childhood physical/sexual abuse and a dysfunctional family), which may also contribute to the development of psychopathology [8].

Comorbid PDs occur in about 60% of individuals with substance abuse [25, 37, 44]. PDs of Cluster B (Borderline PD, Antisocial PD, Histrionic PD,

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Narcissistic PD) are those most frequently diagnosed [25, 35, 44]. The relevance of antisocial PD (ASPD) in SUD has already been shown: antisocial behaviour is a predictor of developing opiate dependence, and ASPD is related to multiple substance use [23]. To date, however, other than ASPD, the association between SUD and PD has been little investigated prospectively, so prospective outcome evaluations are important. In addition to the findings on ASPD, recent work has demonstrated the important role of borderline PD (BPD) and schizotypal PD in the course of co-occurring SUD [21, 53]. Moreover, even patients with remitted BPD were shown to have a high vulnerability to substance relapse [53].

Although a lifetime diagnosis of a comorbid mental disorder does not seem to affect the long-term course of opioid dependence linearly [50], personality pathology is a serious problem in opioid-dependent patients. Personality disorders have a major negative impact on patients' subjective quality of life, including their physical, mental and social functioning [14, 24, 41]. Moreover, comorbid PD in patients with SUD was found to be associated with a greater involvement in the following factors: illegal drug use, psychopathology, impulsivity, aggressive behaviour, isolation and depressiveness [37], as well as in greater global impairment [44]. Those with opiate addiction often manifest antisocial temperament configuration (a high level of novelty seeking, difficulties in reward dependence). Patients with opioid dependence and with PD differ significantly in their interpersonal style [11] and their personality profile [14] from those without PD, as was to be expected.

In summary, the research literature provides evidence that comorbid PD, especially BPD and ASPD, renders the psychopathology and clinical outcomes of SUD more serious [27, 31, 32, 36, 54, 56]. Addiction severity and psychiatric comorbidity explain the greatest amount of Quality of Life variance in a clinical sample of patients with alcohol, drug and dual dependence [10]. Other studies do not support the notion that individuals with BPD and SUD display more severe BPD features than individuals with BPD alone [29]. Overall, a certain paucity of evidence remains about whether comorbid PD exacerbates SUD features and generates greater psychopathology.

Thus, the aim of the current study has been to compare opioid-dependent patients receiving heroin-assisted treatment, with and without a comorbid personality disorder, in terms of psychopathological symptoms at baseline and clinical course of illness at a 12-month follow-up.

We tested the following specific hypothesis: that despite a stable heroin-assisted treatment with closely comparable setting variables, patients with opioid dependence and with PD would score higher than those without PD in depression symptoms and lower in psychological adjustment.

2. Methods

2.1. Study sample

Twenty-six patients (17 male, 9 female) were included from among patients of the University of Basel Psychiatric Hospital's Division of Substance Use Disorders (heroin-assisted treatment, HAT). They were aged 23-58 years (mean age = 41.0, SD = 6.8), met the DSM-IV diagnostic criteria for opioid dependence, and had been in HAT for a mean period of 6.9 years (SD = 4.5). All patients got regular supportive meetings (during the 12-month follow-up period too) with mental health workers, but no specialized or manual treatment for PD.

The sample was part of an experimental study design with n=28 heroin-dependent patients. N=2 were missing according to the SCID II testing; for details, see [52]. Exclusion criteria included a positive breath-alcohol test and a history of major mental disorders (other than SUD and PD) (e.g., schizophrenia). All patients received written information on the examination protocol and gave their written consent. The study was approved by the local ethics committee (EKBB).

2.2. Procedure

At baseline, the personality disorder diagnosis was assessed by applying the German version of the Structured Clinical Interview for DSM-IV, Axis II (PD); SCID-II [15, 17, 55]. Interviewers were first trained to improve their reliability. Prior to this study, personality disorder diagnosis had not been evaluated with a standardized instrument, although patients had been in the treatment for many years. When heroin-maintained patients fulfilled the inclusion criteria, their history of heroin and other illicit substance use was assessed by applying the semi-structured interview according to ICD-10 research criteria.

At a 12-month follow-up, the Opiate Treatment Index (OTI) [12] was used to assess the course of patients' substance use and related problems. To evaluate changes, the Addiction Severity Index (ASI) [43] as well as the Beck Depression Inventory (BDI) [2]

were used once again.

2.3. Clinical measurements

The SCID-II is a two-stage instrument for assessing PDs. It consists of a screening questionnaire and a structured interview. Its excellent inter-rater reliability varies between 0.77 and 0.94 (the mean kappa value for all PD = 0.84), indicating that the SCID II provides a reliable and valid tool for diagnostic purposes in clinical practice as well as in research [33].

The Opiate Treatment Index (OTI) is a multidimensional instrument for evaluating the effects of opiate treatment. It includes six scales, which assess the following independent outcome domains: drug use, HIV risk-taking behaviour, social functioning, criminality, health and psychological adjustment. For each of the scales, an alpha coefficient of $\alpha = 0.38 – 0.83$ was calculated. Correlations with the Addiction Severity Index (ASI) [43] provided a validity of 0.42-0.70. As the OTI has excellent psychometric properties, it can be used as a reliable and valid instrument for both clinical and research goals [12].

Depressive symptoms were measured by applying the Beck Depression Inventory (BDI) [2, 22]. The Childhood Trauma Questionnaire (CTQ) [1, 3] was helpful in assessing the number and severity of patients' trauma experiences. Both instruments are well-established tools for determining clinical symptomatology.

2.5. Statistical analyses

For comparison of means, the Student t-test and, where appropriate, a non-parametric test (Wilcoxon signed-rank test) for independent samples were used. Frequencies were analysed by means of the Chi-square test (Fisher's exact test). All analyses were computed by utilizing the statistical programme SPSS 19.0. Graphs were created with SigmaPlot 11.0. The two-tailed significance level was set to $p \leq 0.05$. Power analysis indicated that the number of patients was sufficient for detecting probabilities of 80% (for R= 0.7) or 95% (for R = 0.8).

3. Results

3.1. Sociodemographic and clinical variables at baseline

Half of the patients (n=13) were diagnosed with an additional PD; the majority revealed an antisocial PD (see Table 1). No significant differences were observed in sociodemographic variables, but patients

Table 1 : Socio-demographic and clinical characteristics of the study sample (n=26) and subdivided for patients with and without a co-occurring personality disorder (PD)

	Patients (n=26)	Without PD (n=13)	With PD (n=13)	p
Age, *mean (SD)*	41.0 (6.8)	42.2 (7.8)	39.8 (5.6)	0.379
Gender, n (%)				
Female	9 (34.6)	4 (30.8)	5 (38.5)	1.000
Male	17 (65.4)	9 (69.2)	8 (61.5)	
Relationship, *n (%)*	8 (30.8)	4 (30.8)	4 (30.8)	1.000
Education in years, *mean (SD)*	10.4 (2.6)	10.9 (1.5)	10.0 (3.3)	0.762
Currently Employed, *n (%)*	10 (38.5)	6 (46.2)	4 (30.8)	0.688
Disability pension, *n (%)*	9 (34.6)	5 (38.5)	4 (30.8)	1.000
Age at first-time heroin use, *mean (SD)*	18.8 (3.3)	19.3 (3.6)	18.3 (3.1)	0.456
Duration of heroin use, *mean (SD)*	20.5 (6.6)	22.5 (5.9)	18.5 (6.8)	0.114
Duration of HAT in years, *mean (SD)*	7.5 (4.9)	9.6 (4.0)	5.4 (4.8)	0.023*
Doses of DAM (mg/day), *mean (SD)*	327.3	293.1 (103.5)	361.5 (135.6)	0.161
Current substance abuse				
Cocaine, *n (%)*	13 (50)	4 (30.8)	9 (69.2)	0.115
Cannabis, *n (%)*	8 (30.8)	7 (53.8)	1 (7.7)	0.030*
Tobacco, *n (%)*	26 (100)	13 (100)	13 (100)	-
Numbers of cigarettes/day, *mean (SD)*	21.2 (9.4)	22.5 (8.4)	20.0 (10.4)	0.418
BDI Sum at baseline, *mean (SD)*	16.2 (8.3)	12.8 (7.7)	19.6 (7.7)	0.032*
Personality Disorders, *n (%)*				
Paranoid PD	2 (7.7)		2 (15.4)	
Schizoid PD	1 (3.8)		1 (7.7)	
Antisocial PD	7 (26.9)		7 (53.9)	
Borderline PD	3 (11.5)		3 (23.1)	
Avoidant PD	5 (19.2)		5 (38.5)	
Obsessive-Compulsive PD	1 (3.8)		1 (7.7)	

Note. SD= Standard Deviation HAT = Heroin-assisted treatment; DAM = Diacetylmorphine (heroin); *p<0.05, **p<0.01

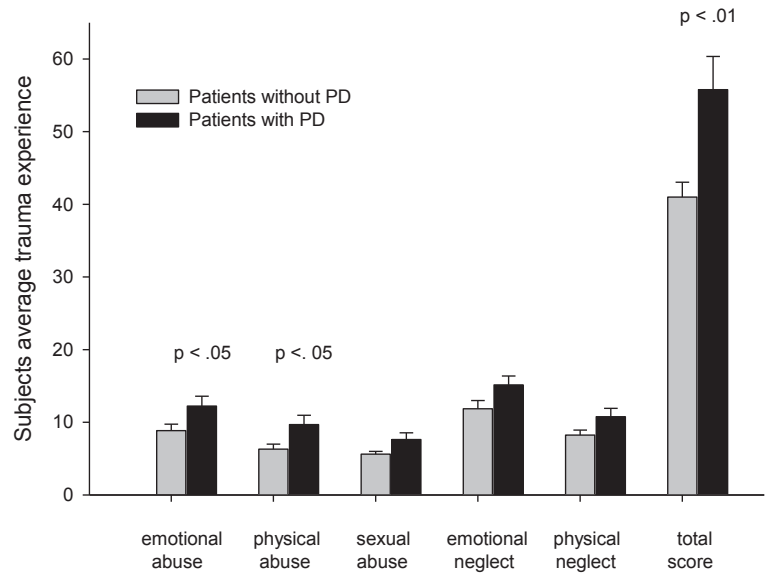

Figure 1. Trauma experiences in patients with and without co-occurring personality disorder (PD) as measured by Childhood Trauma Questionnaire (CTQ) [1, 3]

with comorbid PD scored significantly higher on the BDI depression index (p<0.05).

Looking now at various forms of substance abuse, patients with PD had a significantly shorter duration of heroin-assisted treatment (HAT) (p<0.05) and less cannabis abuse (p<0.05)

Figure 1 shows the scores for both groups on the CTQ. Patients with comorbid PD reported more emotional (p=0.049) as well as physical abuse (p=0.032), and scored higher on the total index (p=0.009). Effect sizes were large.

3.2. Follow-up after 12 months

At the 12-month follow-up, there were no significant differences in additional drug use between opioid-dependent patients with PD and those without PD (see Table 2). Patients with comorbid PD still had higher scores on the BDI, but the difference was no longer significant. However, on the OTI these patients scored significantly worse on psychological adjustment (p<0.01) and showed a slight but not significant trend towards worse social functioning (p=0.052), but with less HIV risk-taking behaviour (p= 0.057). Effect sizes were large in this case too.

4. Discussion

The present pilot study examined whether opioid-dependent patients with a co-occurring PD differ from those without a co-occurring PD in psychological characteristics, and whether they might thus constitute a specific subgroup in opioid dependence, so making possible the prediction of a clinical course.

Table 2 : Clinical characteristics of the patients at 12-month follow-up

Measurements	Without PD (n=13)	With PD (n=13)	p
Substance abuse at 12 month			
Cannabis, n (%)	4 (30.8)	4 (30.8)	1.000
Cocaine, n (%)	3 (23.1)	6 (46.2)	0.400
BDI Sum at 12 month, mean (SD)	10.2 (7.0)	15.7 (9.0)	0.097
Opiate Treatment Index (OTI)			
Drug use, mean (SD)	23.4 (6.1)	21.5 (10.2)	0.545
HIV risk-taking behavior mean (SD)	6.8 (2.6)	4.9 (2.0)	0.057
Social functioning, mean (SD)	12.8 (7.7)	18.4 (6.2)	0.052
Criminality, mean (SD)	0.2 (0.6)	0.6 (1.0)	0.204
Health, mean (SD)	6.9 (4.4)	8.2 (4.9)	0.481
Psychologial adjustment, mean (SD)	16.5 (8.8)	28.5 (12.1)	0.003**

Note. SD= Standard Deviation ; HAT = Heroin-assisted treatment; *p<0.05, **p<0.01

In a 12-month follow-up exploration, we found significant differences between patients with and those without co-occurring PD in their psychopathological symptom burden. This was the main result of our pilot study.

In agreement with previous research [12], we found no significant differences between the sociodemographic data pertaining to patients with, and those without co-occurring PD, so suggesting that these variables were not, or at best, were less decisive, predictors of clinical severity. It is, however, true that Kokkevi and colleagues [25] found that patients with substance dependence and with a comorbid antisocial PD were significantly younger than those without a comorbid antisocial PD when they began to use illicit drugs.

Psychological status was worse in the group of patients who had opioid dependence and also had a comorbid PD. The most common PDs were Antisocial PD (26.9%), Anxious (avoidant) PD (19.2 %), Borderline PD (11.5%) and Obsessive-Compulsive PD (11.5%). In this group, in accordance with our hypothesis, depressive symptoms, as well as general psychological maladjustment, were significantly more manifest than in those without any co-occurring PD. This difference turned out to be clinically relevant. Moreover, these patients showed considerably more trauma experiences. This suggests that emotional and physical abuse are especially relevant factors, not just in the etiology of SUD, but most notably in the development and maintenance of severe PD and other mental symptoms [13].

In previous research, HAT was consistently found to be an effective treatment for severe opioid dependence in a variety of countries [5, 19, 20, 38, 40, 46, 47, 49].

Interestingly, patients with opioid dependence but without co-occurring PD and showing a better overall psychological state had a significantly longer treatment history of heroin-assisted treatment (HAT). This confirms previous research findings that opioid-dependent, non-comorbid patients show higher response rates for HAT, compared with patients who have a psychiatric comorbidity [42]. Patients with personality disorders frequently drop out of therapies prematurely.

Axis II comorbidity seems to be more deleterious than Axis I comorbidity, in terms of the clinical course of opioid dependence. It is possible that a longer treatment history of heroin-assisted treatment (HAT) in patients without co-occurring PD is an indicator of higher stability and not of higher morbidity. Another explanation could be that the emotional instability that underlines the proneness to an addictive disorder belongs more to Axis-II premorbid conditions than to Axis-I full-blown pathology comorbidity.

Our pilot findings (mean duration of controlled agonist opioid treatment) indicate that HAT, with its psychosocial treatment elements and risks, may contribute to a globally successful therapy outcome even for patients with chronic opioid-dependence and with serious additional psychological problems. In addition to the reduction of substance use problems, patients' mental state (possibly including severe psychiatric disorders like PD) seems to improve over time as well. It is unclear whether the phasic opioid stimulation provided by heroin-assisted treatment, while able to reverse withdrawal and drug-seeking behaviours, may not be able to treat important aspects of addiction psychopathology, as it is just a similar phasic opioid stimulation of street opiate use.

The following limitations in the present study must be considered: First, it could be that neither patient group was large enough to allow possible group differences to be discovered. Therefore, the small sample size in our study (N = 13 for each group) could be an explanation for the statistically less than significant results recorded for the clinical outcome variables. Furthermore, we did not discriminate between patients with different comorbid (specific PDs e.g., ASPD alone and ASPD with comorbid BPD) and important exclusion criteria (major mental disorders (other than SUD and PD). Various different PDs may be accompanied by different neurobiological correlates and other disorder-specific factors [4, 39], and this could have produced a bias affecting the findings of our study. In an earlier study by our group, we found normally modulated affective reactivity (startled responses) in patients with heroin-dependence and with ASPD [51]. It could be that heroin-assisted treatment itself has an impact on the psychopathology of opioid addicts.

Lastly, the main result of our study – the differences found in 12-month outcomes –was based on only one instrument (OTI) not performed at baseline. It might therefore be true that differences in the OTI domains could have been there at baseline, before baseline, during the 12 month interval, and at 12 months (or any combination of these).

Despite these limitations, our pilot study provides initial evidence of some specific characteristics in patients with opioid-dependence and with an additional PD (especially ASPD (53.8% in the PD

group, together with higher criminality rates), which suggests there may be clinical possibilities for the treatment of SUD. Low anxiety sensitivity could indirectly mediate the relationship between ASPD and opioid dependence.

The present investigation is a pilot study of psychological differences between patients with opioid-dependence and with PD (especially ASPD) and those without co-occurring PD that are in a stable substitution treatment (HAT). In addition to the opioid substitution itself, patients with opioid dependence and with comorbid PD may draw benefits especially from broad treatment interventions, including more PD-specific psychotherapy (e.g., dialectical behaviour therapy, mentalization-based treatment, transference-focused psychotherapy, schema therapy). Moreover, treatment of comorbid PD could be an additional therapy goal in patients with SUD in the future. It was shown that BPD constitutes a high vulnerability factor for SUD relapse [53], and that it has a negative impact on the course of affective and anxiety disorders as well. The social and psychological consequences are significant, too. Patients with ASPD in methadone maintenance were over five times more likely to receive physical disability benefits than patients in methadone maintenance without ASPD [9]. ASPD is also a predictor of criminal behaviour in patients with drug abuse [16]. But the heterogeneity of the PD population is difficult to interpret meaningfully, as that population comprises quite a range of different disorders.

In order to prevent relapse in drug use, it may therefore be clinically crucial to treat the co-occurring PD in patients with SUD.

5. Conclusions

The current study suggests that, even in a heroin-assisted treatment setting, there is a specific, clinically worse subgroup of opioid-dependent patients mainly characterized by psychiatric comorbidity with PD. This confirms previous research findings and could have a relevant clinical implication, as this comorbidity should be considered in therapy [42]. However, more research should be carried out; in particular, what seems to be most needed is a fully prospective outcome evaluation that differentiates between individual personality disorders and co-occurring substance use (e.g. cocaine, marijuana) that proved to be frequent in our pilot patients even in a stable HAT, while making use of a greater number of instruments.

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Contributors

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Conflict of interest

All authors declare no conflict of interest.

Ethics

Authors confirm that the submitted study was conducted according to the WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects. This study has ethics committee approval. All patients gave their informed consent to the anonymous use of their clinical data for this study.

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